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The risk of developing alcohol addiction – what coping strategies do Ukrainian military personnel use after participating in intense hostilities?

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ABSTRACT

Introduction and aim. Since February 24, 2022, military personnel of the Ukrainian Defense Forces have been resisting the military aggression of the Russian Federation. After participating in combat operations, military personnel accumulated combat stress. Drinking alcohol was one of the ways to overcome it. The purpose of the article is to identify the types of coping strategies for the risk of developing alcohol addiction among Ukrainian military personnel who participated in intense hostilities.

Material and methods. Ukrainian Defense Forces military personnel (n=162 males, between 20 and 60 years of age) took part in this study. To determine coping strategies and the risk of developing alcohol addiction the AUDIT and the COPE Inventory were used.

Results. Cluster analysis made it possible to identify 4 types of coping strategies with different prevalence and levels of risk of developing alcohol addiction among participants.

Conclusion. Productive coping has been associated with a reduced risk of alcohol use in military personnel, but the ability to be situational flexible in the use of coping is important. Compulsive alcohol use was preceded by a period of intensive use of social support coping by military personnel. This period is sensitive to the risk of developing alcohol addiction.

Keywords. alcohol addiction, coping strategies, military personnel

Introduction

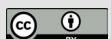
Since February 24, 2022, military personnel of the Ukrainian Defense Forces have been resisting the military aggression of the Russian Federation. Hundreds of thousands of military personnel from both sides participate in large-scale combat operations, where the combat contact zone is more than 1,100 kilometers.¹ Almost all military personnel who participated in combat experience

combat stress, which manifests itself in the form of acute stress reactions, affective and anxiety disorders, adaptation disorders, addictive and delinquent behavior, and suicidal manifestations.²⁻⁵ Especially for military personnel called up for mobilization, participation in hostilities became a significant stressful event.⁶ On the one hand, this forced them to look for ways and reserves to adapt to a situation in which they had to not only be

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but also actively act, carrying out assigned combat missions.⁷ On the other hand, after participating in intense combat operations, military personnel accumulated combat stress, manifested by negative mental reactions.⁵ Drinking alcohol was one of the ways to overcome it.⁸ It was used as a “folk” remedy in the absence of high-quality psychological assistance and knowledge about methods of self-help and self-regulation.⁹ Although the effectiveness of this method of overcoming negative experiences is relative, military personnel used this coping even if before the war they were not prone to drinking alcohol.

Traditionally alcohol has been used by the military to cope with the intense stress of battle but also as a way of mediating the transition from the heightened experience of combat to routine safety.^{8,10} The use of alcohol has divided researchers. Some viewed it as wholly harmful to both social and occupational function and to health, while others argued that alcohol had a specific role in lifting morale, aiding unit cohesion, and protecting soldiers from adjustment disorders.^{11,12} Although alcoholism has always been identified as incompatible with military service, the effects of habitual heavy drinking among military personnel are less well understood. Recent studies have suggested that young single males, who have less education, are of lower military rank and those who have undergone particularly stressful experiences are at the greatest risk of misusing alcohol.¹³

Overcoming difficult life situations, including combat stress, is often associated with mechanisms and strategies for coping with stress.^{14,15} The most common are problem-focused coping, which is aimed at getting out of a problem situation, and emotion-focused coping, aimed at experiencing difficult emotional events without the possibility of influencing them.^{16,17} In our opinion, the most used psychodiagnostic technique for determining strategies for coping with stress is the COPE Inventory.¹⁷

It was previously found that drugs, substance abuse, and alcohol were often used by military personnel in various military conflicts as a means of relieving stress both in the combat zone and after its completion.^{8,18-21} It has also been shown that alcohol may be a coping mechanism for traumatic events.²² However, excessive alcohol consumption can negatively affect the mental and physical health of military personnel and the combat effectiveness and combat readiness of troops as a whole.^{23,24}

The study on the impact of military service on military personnel's alcohol use found that changes in troop deployments, the dangerous nature of deployments, and combat stress were associated with alcohol abuse among military personnel.²⁵ The main factors influencing alcohol consumption among military personnel were: mental health, family status, age, type of army, active participation in hostilities, and family problems. Another study

found that alcohol use was considered highest among those who performed combat missions or participated in more intense combat.²² It was found that military personnel who had a higher risk of death or injury were more likely to abuse alcohol.²⁶ However, the prevalence of alcohol abuse among military personnel of different branches was not the same: among Special Operations Forces soldiers, alcohol use was the same or less than in the US military.²⁷ Although combat experience was positively correlated with alcohol abuse, killing experience significantly reduced alcohol use following deployments.²⁸ This was explained by the awareness of one's mortality and the inclusion of self-preservation mechanisms, manifested in a decrease in alcohol consumption.

Studies have revealed a relationship between the amount and frequency of alcohol consumption and the diagnosis of post-traumatic stress disorder (PTSD) in military personnel.²⁹⁻³¹ However, the results of studying the relationship between alcohol consumption and the consequences of stress on the body of military personnel were ambiguous. For example, stress was equally likely to predict increases, decreases, and no association with alcohol use, although overall stress showed a positive association with craving for alcohol.³² As a coping strategy with stress, alcohol consumption and its ability to reduce mental stress has been indicated in some studies.³³⁻³⁶ The results suggested a moderating effect of alcohol on stress levels and reactivity. However, these studies showed that as the intensity of acute stress increased or stress became chronic, alcohol abuse became more compulsive, moving from a method of stress reduction to a dominant or sole means of maintaining homeostasis.³⁷ Thus, long-term alcohol use may have increased baseline stress levels, causing persistent cravings to drink.

Coping strategies as moderators of the relationship between stress and alcohol use have also been examined in studies, but their effects have been mixed.³² Specifically, in the study with an all-female sample, it was determined that participants with low levels of problem-solving focus drank more alcohol during a low-stress week.³⁸ At the same time, other researchers using a different sample found the opposite result among college students.³⁹ They found that the effects of alcohol coping strategies differed significantly among college students by race/ethnicity: emotional rumination reduced alcohol use among African American students, had no effect among Hispanic students, and increased alcohol use among White students.³⁹

It should be noted that the nature of alcoholism is such that it does not matter for what reasons alcohol addiction was formed.⁸ Over time, these motives are lost, and alcohol abuse continues, destroying a person's physical and mental health, social connections, and personality.⁴⁰ This makes it urgent to search for preventive measures in situations that can provoke long-term alco-

hol consumption. It is also important to identify groups of military personnel who are prone to using coping to overcome negative experiences such as alcohol abuse and to study the tendency to use a certain type of coping associated with alcohol abuse.

Aim

The purpose of the article is to identify the types of coping strategies for the risk of developing alcohol addiction among Ukrainian military personnel who participated in intense hostilities.

Material and methods

Study design and participants

All participants gave their informed consent for inclusion before participating in the study. The ethics committee's approval was obtained before the initiation of the study (meeting date; 17/07/2023, decision number; 2023/19). All procedures performed in this study involving human participants were by the ethical standards specified by the institutional and national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards.

This study is a cross-sectional, descriptive study. Ukrainian Defense Forces military personnel ($n=162$ males, between 20 and 60 years of age, 41.84 ± 6.49 years) participated in this study. All participants (71% were privates, and 29% were non-commissioned officers) took part in the Russian-Ukrainian war and had combat experience 6–10 months (8.75 ± 2.58 months). Before the war, 62% of participants had urban origin, 38% had rural origin; 24% had secondary education, 57% had secondary specialized education, and 19% had higher education. The military personnel were sent to the rehabilitation center from combat positions to participate in the psychological recovery program ("Invincibility Program") lasting 14 days.⁴¹

The "Invincibility Program" goal was to reduce combat stress's impact on combatants, strengthen mental health and mobilize their psychological resources, improve adaptation and resilience, and promptly return to combat activities. The main criteria and indications for the selection of military personnel were: 1) acute stress reactions in the form of motor and mental disorders, requiring psychological first aid and subsequent outpatient or inpatient treatment; 2) prolonged states of psycho-emotional stress; various sleep disorders that worsen well-being, and performance and require psychotherapy; 3) an increase in irritability, unmotivated aggression, conflict, and decrease in behavioral, and cognitive functions, leading to a violation of combat activity, in which a critical attitude towards the mental state is not maintained; 4) vegetative disorders after minor psycho-emotional stress; 5) an anxious, pessimistic, depressive, or other negative mental reactions and

conditions detected during psychodiagnostics; 6) stable preservation of asthenic symptoms; 7) progressive isolation, the desire for loneliness, limiting the circle of communication with colleagues, a decrease in interest in life; 8) unmotivated and unusual for a serviceman increased activity during the performance of combat missions or after their completion, combined with an unstable mood; 9) signs of increasing distress, manifested in a decrease in the quality and volume of tasks performed, including daily duties, with a general desire to fulfill the assigned tasks; 10) long-term pain syndromes after traumas, wounds without signs of development of organic changes in the places of injuries. The participants were identified: with various manifestations of acute stress reactions; significant negative experiences, including signs of depression and suicidal ideation; presence of PTSD symptoms; sleep problems (more than 50%); somatic complaints (more than 80%), wounds and contusions (more than 75%); difficulties in returning to combat missions due to the consequences of illness, injury and wounds. According to military specialties, there were infantrymen, attack aircraft, scouts, snipers, tankers, artillerymen, and other military specialists.

The "Invincibility Program" began in June 2022 and continues to this day based on the sanatorium in the Kharkiv region of Ukraine. All participants were divided into 9–10 groups for group psychotherapy and psycho-correction (15–20 people in a group with 1–2 military psychologists). The total number of military personnel involved since the beginning of the psychological recovery program has amounted to more than 6,000 people. Female military personnel were excluded in this study because less than 0.5% of female combatants participated over the entire program period. Officers were also not included in the study because there were a small number of them in the psychological recovery program (less than 1%). Participants were randomly selected for the study.

Instruments

To determine the risk of developing alcohol addiction among study participants, the Alcohol Use Disorders Identification Test (AUDIT) was used, and the COPE Inventory was used to determine coping strategies.

The AUDIT (Cronbach's $\alpha=0.864$) is a 10-item screening tool developed by the World Health Organization to assess alcohol consumption, drinking behaviors, and alcohol-related problems.⁴² The test allows you to determine the risk levels of alcohol addiction: 0–7 points – a low level; 8–15 points – an average level; 16–19 points – a high level; 20 or more points – a probabilistic alcohol addiction level. According to researchers, the AUDIT and AUDIT-C are the most common tests for studies related to alcohol use problems in military personnel.²⁶

The COPE Inventory assesses a variety of functional and dysfunctional coping strategies utilized by individuals in their response to stress, adapted into Ukrainian.^{17,43} The Ukrainian-language version of COPE (Cronbach's $\alpha=0.732$) also consisted of 60 statements that must be answered on the Likert scale from "1" to "4". All items in the questionnaire are grouped into 15 scales, with 4 statements per scale, following the original version. The scores on the scales were determined simply by adding all the values of the answers to the statement (numbered from 1 to 60) included in a certain scale.

The COPE can determine someone's primary coping styles with scores on the following three subscales: "Problem-focused coping", "Emotion-focused coping" and "Avoidant coping". "Problem-focused coping" is characterized by the facets of active coping, the use of informational support, planning, and positive reframing. A high score indicates coping strategies that are aimed at changing the stressful situation, are indicative of psychological strength, grit, and a practical approach to problem-solving, and are predictive of positive outcomes. "Emotion-focused coping" is characterized by the facets of venting, the use of emotional support, humor, acceptance, self-blame, and religion. A high score indicates coping strategies that aim to regulate emotions associated with the stressful situation. High or low scores are not uniformly associated with psychological problems or ill health but can be used to inform a wider formulation of the respondent's coping styles. "Avoidant coping" is characterized by the facets of self-distraction, denial, substance use, and behavioral disengagement. A high score indicates physical or cognitive efforts to disengage from the stressor. Low scores are typically indicative of adaptive coping.

For the data presented basic descriptive statistics were used (arithmetical mean M , standard deviation SD). The reliability of differences in the results of the mean values in four interrelated groups was determined using the Student's t -test. For the assessment of the statistical significance of differences, we used the level of significance from $p<0.1$ to $p<0.001$. To determine the relationship between the risk of alcohol consumption by military personnel (dependent variable) and coping strategies (independent variables), multiple regression analysis (linear regression) was used. To identify groups of military personnel with different coping strategies, a hierarchical cluster analysis procedure was used. The statistical analysis of the study results was carried out using the program SPSS 20.0 (IBM, Armonk, NY, USA).

Results

Table 1 shows the prevalence of risk levels for developing alcohol addiction among participants in the psychological recovery program.

Table 1. The prevalence of risk levels for developing alcohol addiction among participants in the psychological recovery program

Risk levels for developing alcohol addiction	Low	Average	High	Probabilistic alcohol addiction
Prevalence (%)	69.14	29.01	1.23	0.62

High levels and probable alcohol addiction were identified in less than 2% of participants. However, almost 30% of participants were diagnosed with an average risk of developing alcohol addiction, which is the threshold at which a service member may lose the ability to control alcohol consumption.

The main indicators of alcohol consumption by study participants, identified using the AUDIT, were presented in Table 2.

Table 2. Indicators of alcohol consumption by study participants

	Indicators	%
Period of military service	Up to 6 months	7.37
	From 6 months to 1 year	17.89
	From 1 year to 3 years	45.26
	From 3 years to 5 years	17.89
	From 5 years to 10 years	8.42
	More than 10 years	3.16
Frequency of alcohol consumption	Never	11.92
	Once a month or less	28.5
	2–4 times a month	37.31
	2–3 times a week	16.58
	4 times a week or more	5.7
The number of servings of alcohol consumed in one typical day of alcohol consumption (a serving of 0.5 liters of beer; or 200 grams of wine; or 50 grams of vodka (or cognac)	Not a single portion	14.51
	1–2 servings	38.34
	3–4 servings	29.02
	5–6 servings	10.36
	7–9 servings	4.15
	10 servings or more	3.63

Using the multiple regression analysis procedure allowed us to create a regression equation:

$$RIAA =$$

$$3.867 - 0.330MD + 0.439SSSI + 0.654ADD - 0.321P + 0.79,$$

where RIAA is the risk indicator for alcohol addiction using AUDIT, 3.867 is a constant, MD is coping "Mental disengagement", UISS is coping "Use of instrumental social support", SU is coping "Substance use", P is coping "Planning", 0.79 is error.

However, despite the satisfactory indicators of the significance of the model ($F=10.99$; $p<0.001$) and the significance of the regression coefficients ($p\leq 0.05$), the calculations showed that for this model $R\text{-square}=0.213$. Therefore, it is inappropriate to use it to predict the risk of developing alcohol addiction.

The use of cluster analysis made it possible to identify four groups of participants according to indicators of coping strategies, taking into account the risk of developing alcohol addiction, two of which were less than 5% (Table 3).

Table 3. Indicators of coping strategies in participants groups identified using cluster analysis taking into account the risk indicator for alcohol addiction (points)

Scale name	Groups of participants			
	Group 1	Group 2	Group 3	Group 4
AUDIT				
Risk of developing alcohol addiction	6.09±4.24	4.77±3.5	8.60±1.67	16±11.4
COPE Inventory				
Positive reinterpretation and growth	12.91±1.80	8.86±2.38	8.60±2.07	12.5±3.11
Mental disengagement	9.50±2.43	7.75±2.23	11.80±4.09	14±1.41
Focus on and venting of emotions	10.08±2.29	8.16±2.8	12.60±1.14	13±4.76
Use of instrumental social support	11.66±2.15	7.98±2.1	13.40±1.14	15
Active coping	12.97±1.64	9.43±2.32	11.6±2.41	15.00±1.41
Denial	9.03±2.34	7.64±2.72	11.6±3.05	14.25±2.87
Religious coping	10.48±3.52	8.52±2.49	12.6±1.82	13±6
Humor	10.81±2.78	7.61±2.61	7.20±3.27	10.75±4.65
Behavioral disengagement	8.6±2.1	7.50±2.35	10.80±1.79	14.25±0.5
Restraint coping	11.19±1.7	8.25±2.23	11.6±1.14	14.25±1.5
Use of emotional social support	10.91±2.49	7.32±2.26	14.8±0.84	15.50±0.58
Substance use	7.21±3.11	6.61±2.4	13.8±1.92	11.25±4.99
Acceptance	11.45±2.43	8.41±2.48	9.40±3.85	13.75±1.71
Suppression of competing activities	12.37±1.87	8.91±2.38	10±1.87	14.75±2.22
Planning	13.43±1.66	9.34±2.47	13.2±1.79	12.75±3.77

Table 4. Differences in coping indicators between groups of participants (Student's t-test)^a

Scale name	Differences between groups					
	t ₁₋₂	t ₁₋₃	t ₁₋₄	t ₂₋₃	t ₂₋₄	t ₃₋₄
Risk of developing alcohol addiction	1.98*	3.15**	1.73 ⁰	4.43***	1.96 ⁰	1.29
Positive reinterpretation and growth	10.16***	4.99***	0.26	0.29	2.28*	2.20*
Mental disengagement	4.27***	1.37	6.04***	2.38*	7.98***	1.21
Focus on and venting of emotions	4.04***	4.89***	1.22	7.06***	2*	0.16
Use of instrumental social support	9.75***	3.42***	16.19***	9.64***	22.22***	3.44*
Active coping	9.24***	1.38	2.80**	2.08*	7.06***	2.81*
Denial	2.97**	2.03*	3.59***	3.02**	4.43***	1.39
Religious coping	3.87***	2.6*	0.83	4.90***	1.48	0.13
Humor	6.74***	2.65**	0.03	0.3	1.33	1.32
Behavioral disengagement	2.70**	2.90**	17.56***	4.07***	15.58***	4.47**
Restraint coping	7.84***	0.84	3.99***	5.83***	7.30***	3*
Use of emotional social support	8.62***	9.33***	12.24***	15.51***	18.32***	1.57
Substance use	1.27	7.84***	1.61	8.31***	1.84 ⁰	0.97
Acceptance	6.90***	1.29	2.59*	0.61	5.73***	2.43*
Suppression of competing activities	8.62***	3.02**	2.12*	1.29	5.01***	3.53**
Planning	10.09***	0.3	0.36	4.71***	1.77 ⁰	0.22

^a ⁰p<0.1, * p<0.05, ** p<0.01, *** p<0.001

The vast majority of coping indicators in the identified groups differed from each other at a statistically significant level (Table 4).

Participants in the four groups did not differ from each other in such demographic characteristics as military rank, the presence of wounds and concussions, and sleep problems. However, minor age differences were found.

When interpreting the data obtained, it turned out to be appropriate to present them graphically. The chosen form corresponded to the idea of the presence of coping strategies profiles and made it possible to form a visual representation of the general propensity (height of indicators) and the hierarchy of coping strategies used in each group (Fig. 1).

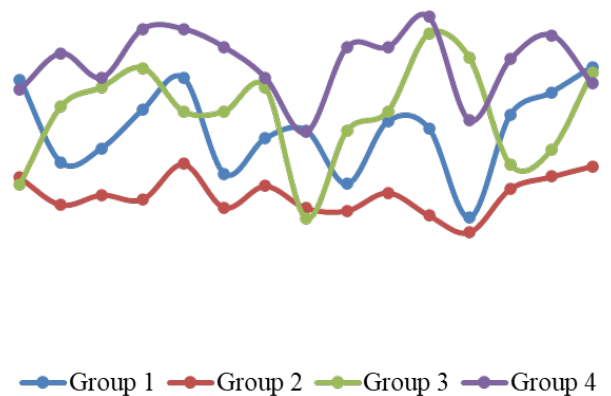


Fig. 1. Typical profiles of coping strategies used by study participants (points): 1) "Positive reinterpretation and growth"; 2) "Mental disengagement"; 3) "Focus on and venting of emotions"; 4) "Use of instrumental social support"; 5) "Active coping"; 6) "Denial"; 7) "Religious coping"; 8) "Humor"; 9) "Behavioral disengagement"; 10) "Restraint coping"; 11) "Use of emotional social support"; 12) "Substance use"; 13) "Acceptance"; 14) "Suppression of competing activities"; 15) "Planning"

As seen in Figure 1, each group occupies its niche, except for peaks, which may invade the niche of another group.

Discussion

The cluster analysis showed that the sample of participants was heterogeneous in using different coping strategies. The distribution of participants by group is presented in Table 5.

Participants in group 1 (66.67% of the total study sample) were the oldest: the average age of the participants was 43.6 years. This group was characterized by an average placement of the profile of coping strategies, and its hierarchy, which was achieved due to pronounced positive peaks ("Planning", "Active coping", "Positive reinterpretation and growth" and "Suppression of competing activities") and negative peaks ("Be-

havioral disengagement” and “Substance use”). These peaks formed a pronounced opposition between productive and unproductive coping. This profile was combined with AUDIT indicators, which indicates a low and average risk of developing alcohol addiction in participants in this group.

Table 5. Indicators in participants groups identified using cluster analysis taking into account the risk indicator for alcohol addiction

Indicators	Groups of participants			
	Group 1 (66.67%)	Group 2 (27.16%)	Group 3 (3.70%)	Group 4 (2.47%)
Age (years)	43.6	37.8	37.7	30.2
Positive peaks of coping strategies	“Planning”, “Active coping”, “Positive reinterpretation and growth” and “Suppression of competing activities”	“Planning” and “Active coping”	“Use of emotional social support”, “Substance use” and “Use of instrumental social support”	“Use of emotional social support”, “Use of instrumental social support” and “Active coping”
Negative peaks of coping strategies	“Behavioral disengagement” and “Substance use”	“Substance use”	“Humor”	“Humor”, “Substance use” and “Positive reinterpretation and growth”

Participants in group 2 (27.16%) were somewhat younger than group 1: the average age was 37.8 years. This group is characterized by a low and fairly smooth profile. However, weakly expressed peaks partly correspond to the tendency of participants to give preference to productive coping compared to unproductive ones. The positive peaks in this group were “Planning”, and “Active coping”, and the negative peak was “Substance use”. All other coping strategies are placed in a fairly narrow range of 7-9 points, which indicates a situational (flexible) attitude towards the use of coping strategies. In this group, the lowest risk of developing alcohol addiction and maintaining psychological safety of personality was determined among all groups.⁴⁴

Participants in group 3 (3.7%) had an average age of 37.7 years, which was almost identical to group 2. As in group 1, their profile of coping strategies was located in the average range of indicators and was characterized by a pronounced hierarchy. However, its peaks were, if not mirrored to the peaks of group 1, and then at least shifted towards socially oriented coping, occupying an intermediate position between productive and unproductive coping, as in these studies.^{15,16} The highest peaks in this group included copings: “Use of emotional social support”, “Substance use”, and “Use of instrumental social support”. The lowest point of the profile was “Humor”, which can indicate both emotional problems (inability to maintain a positive mood) and certain cognitive problems (inability to anticipate inconsistencies, the pressure of negative experiences over cognitive abil-

ities). This group of participants was characterized by an average risk of developing alcohol addiction.

Group 4 (2.47%) was the youngest, with a mean age of 30.2 years. Group 4 had the highest profile of coping strategies, located mainly in the range of 13–16 points, which comprised pronounced negative peaks “Humor”, “Substance use” and “Positive reinterpretation and growth”. If a high profile could indicate reactivity and tension of all resources, then negative peaks indicated an inability to maintain a positive mood, which was characteristic of compulsive behavior. It was in this group that the highest risk of developing alcohol addiction was diagnosed.

The results obtained allowed us to conclude that coping skills such as “Planning” and “Mental disengagement”, which allow the ability to manage one’s behavior while maintaining the ability, predicted a decrease in alcohol consumption, which kept military personnel from drinking it. It was expected that the risk of alcohol use increased with coping “Substance use”, given its ability to reduce stress previously described in research.^{8,25} It was interesting that the risk of drinking alcohol and coping “Use of emotional social support” increased, which could be associated with the existing tradition of “feast”, traditionally used in Ukrainian culture to overcome communication barriers and, if necessary, ask for help or the need to speak out.

Although military personnel undergoing the psychological recovery program had significant negative experiences, the prevalence of alcohol abuse among them was predominantly low. But, as experience in working with such servicemen shows, after leaving the combat zone, the number of servicemen who drank alcohol increased significantly. In our opinion, this was a consequence of the formation of PTSD symptoms, for which it is important to be able to influence reflection after leaving a traumatic situation, shifting the focus of attention from external events to their experiences, forming an attitude towards them, the possibility of processing them and “fitting them in” into one’s own experience. We also confirmed and identified the following factors of alcohol consumption among military personnel: physical and social availability of alcohol, which increases alcohol consumption among military personnel⁴⁴; less expectation of negative consequences from drinking alcohol (being in a zone of intense combat operations, military personnel sought to protect each other, commanders and colleagues reduced the possibility of drinking alcohol).

The results obtained in the regression equation about the positive relationship between coping “Use of instrumental social support” and the risk of developing alcohol addiction were consistent with the data that military personnel used alcohol to support social connections and sociability.⁸ The identified negative relationship be-

tween the risk of drinking alcohol and the coping “Mental disengagement” and “Planning” reflected the military personnel’s awareness of the negative consequences of alcohol abuse, and disapproval of this by comrades and commanders; these data were quite similar to the study.⁴⁶ Interestingly, the relationship between “awareness of the potential social benefits of alcohol use and awareness of the negative consequences of alcohol abuse” has also been pointed out by other researchers.²⁵

We found benefits from interpreting the types of coping profiles. The results obtained using cluster analysis confirmed previously established findings that adaptive coping was inversely associated with alcohol consumption.^{47,48} Consistent with other studies, these data also predicted that the use of coping “Planning” and “Suppression of competing activities” will be associated with less alcohol consumption.⁴⁸⁻⁵⁰

But the use of coping profiles seems to us more productive than the assessment of individual coping or their total assessment (combined scores on the scales “Active coping”, “Planning”, “Suppression of competing activities”, “Positive reinterpretation and growth”, “Religious coping”, “Acceptance”, “Use of instrumental social support” and “Use of emotional social support”) used in the study.³⁹ The use of profiles made it possible to identify such aspects as hierarchy (providing a pronounced advantage to certain copings), flexibility (situational use of copings), compulsivity (demand for almost all copings and the inability to maintain a positive mood in other ways (without alcohol)). The graphical representation made it possible to identify profiles of productive coping and counterproductive types of coping or focused on social support.

The results also suggested that compulsive alcohol use is preceded by an intense search for social support against the background of a decrease in one’s cognitive abilities due to stress, which was characterized by an average risk of developing alcohol addiction. Perhaps this is the most favorable period for preventing alcohol use in military personnel experiencing significant long-term stressful events. Our results supported those of researchers who have found that post-deployment cognitive decline in younger military personnel is associated with the risk of alcohol abuse.⁵¹

Study limitations

This study certainly had limitations. First, female military personnel were not included in this study because, over the entire period of the “Invincibility Program”, less than 0.5% of female combatants participated. Secondly, the sample of participants included only ordinary military personnel and sergeants; officers did not take part in the study. Thirdly, the study was limited by the short period of the psychological recovery program and the inappropriateness to overload participants with additional

activities that did not correspond to the purpose of the program, which reduced the possibility of using research methods, repeatability of the survey, etc. Finally, the current study was limited by not having an active comparison condition and by not having a longitudinal follow-up.

Conclusion

The use of profiles to interpret coping strategies provides new opportunities for assessing the risk of developing alcohol addiction among military personnel participating in intense combat operations. The study showed that productive coping is associated with a reduced risk of alcohol use in military personnel, but equally important is the ability to be situationally flexible in the use of coping. Compulsive drinking of alcohol, which occurs against the backdrop of strain on all coping resources and the inability to maintain a positive background of mood independently, is preceded by a period of intensive recourse to coping with social support due to the stress experienced. Perhaps this particular period is sensitive to the risk of developing alcohol dependence.

Before the mass rotation of military personnel from the combat zone, when alcohol abuse is not widespread, it is necessary to develop alcoholism prevention programs and evaluate their effectiveness. These activities should be aimed at those military personnel who have an average (threshold) level of risk of developing alcohol dependence. Such military personnel also need social support (the type of coping strategy characteristic of group 3 participants identified in the study).

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Author contributions

Conceptualization, I.P. and Y.M.; Methodology, I.P.; Software, M.B. and H.S.; Validation, Y.M., I.P. and M.B.; Formal Analysis, V.K.; Investigation, I.L.; Resources, O.Z.; Data Curation, Y.M. and I.P.; Writing – Original Draft Preparation, Y.M.; Writing – Review & Editing, I.P.; Visualization, K.M.; Supervision, Y.R.; Project Administration, I.P.; Funding Acquisition, H.S.

Conflicts of interest

The authors declare no competing interests.

Data availability

All data generated or analyzed during this study are included in this published article.

Ethical approval

The approval of the ethics committee was obtained before the initiation of the study (meeting date; 17/07/2023, decision number; 2023/19).

Reference

1. Prykhodko I, Kolesnichenko O, Matsehora Y, et al. Effects of posttraumatic stress and combat losses on the combatants' resilience. *Cesk Psychol.* 2022;66(2):157-169. doi: 10.51561/cspych.66.2.157
2. Adler AB, Gutierrez IA. Preparing Soldiers to Manage Acute Stress in Combat: Acceptability, Knowledge and Attitudes. *Psychiatry.* 2022;85(1):30-37. doi: 10.1080/00332747.2021.2021598
3. Kokun O, Pischko I, Lozinska N. Military personnel's stress reactivity during pre-deployment in a war zone. *Psychol Health Med.* 2022;1-12. doi: 10.1080/13548506.2022.2104882
4. Prykhodko I, Matsehora Y, Kolesnichenko O, et al. Psychological Markers of Suicides in Military Service During Wartime: A Contemporary Example. *Int J Psychol Psychol Ther.* 2021;21(1):45-57.
5. Prykhodko I, Matsehora Y, Kryvokon N, et al. Manifestations of post-traumatic stress in military personnel after participating in hostilities in the Russian-Ukrainian war. *Eur J Clin Exp Med.* 2023;21(4):776-784. doi: 10.15584/ejcem.2023.4.19
6. Shvets AV, Kalnysh VV, Marushchenko KY. Peculiarities of disadaptation characteristics in military personnel after being in a zone of armed conflict of different intensity. *Ukr J Mil Med.* 2023;4(3):38-48. doi: 10.46847/ujmm.2023.3(4)-038
7. Prykhodko II, Bielai SV, Hrynzovskiy AM, et al. Medical and psychological aspects of safety and adaptation of military personnel to extreme conditions. *Wiad Lek.* 2020;73(4):679-683.
8. Jones E, Fear NT. Alcohol use and misuse within the military: a review. *Int Rev Psychiatry.* 2011;23(2):166-172. doi: 10.3109/09540261.2010.550868
9. Prykhodko I, Matsehora Y, Kolesnichenko O, et al. Psychological First Aid for Military Personnel in Combat Operations: The Ukrainian Model. *Mil Behav Heal.* 2021;9(3):289-296. doi: 10.1080/21635781.2020.1864530
10. Larson MJ, Wooten NR, Adams RS, Merrick EL. Military Combat Deployments and Substance Use: Review and Future Directions. *J Soc Work Pract Addict.* 2012;12(1):6-27. doi: 10.1080/1533256X.2012.647586
11. Teeters JB, Lancaster CL, Brown DG, Back SE. Substance use disorders in military veterans: prevalence and treatment challenges. *Subst Abuse Rehabil.* 2017;8:69-77. doi: 10.2147/SAR.S116720
12. Witkiewitz K, Estrada AX. Substance Abuse and Mental Health Treatment in the Military: Lessons Learned and a Way Forward. *Mil Psychol.* 2011;23(1):112-123. doi: 10.1080/08995605.2011.548651
13. Brady LL, Credé M, Harms PD, Bachrach DG, Lester PB. Meta-analysis of risk factors for substance abuse in the US military. *Mil Psychol.* 2019;31(6):450-461. doi: 10.1080/08995605.2019.1657754
14. Merrill JE, Thomas SE. Interactions between adaptive coping and drinking to cope in predicting naturalistic drinking and drinking following a lab-based psychosocial stressor. *Addict Behav.* 2013;38(3):1672-1278. doi: 10.1016/j.addbeh.2012.10.003
15. Prykhodko I, Matsehora Y, Bielai S, et al. Classification of coping strategies influencing mental health of military personnel having different combat experience. *Georgian Med News.* 2019;(297):130-135.
16. Frydenberg E, Lewis R. Teaching Coping to adolescents: when and to whom? *Am Educ Res J.* 2000;37:727-745.
17. Carver CS, Scheier MF, Weintraub JK. Assessing coping strategies: a theoretically based approach. *J Pers Soc Psychol.* 1989;56(2):267-283.
18. Bergen-Cico DK. *War and Drugs: The Role of Military Conflict in the Development of Substance Abuse* (1st ed.). Routledge; 2012. doi: 10.4324/9781315631226
19. Kamienski L. *Shooting Up. A Short History of Drugs and War.* Oxford University Press; 2016.
20. Kan PR. *Drugs and Contemporary Warfare.* Dulles, VA: Potomac Books; 2009.
21. Korsmeyer P, Kranzler HR. *Encyclopedia of Drugs Alcohol & Addictive Behavior.* 3rd ed. Macmillan Reference USA; 2009.
22. Besse K, Hunt S, Lenk KM. How soldiers perceive the drinking environment in communities near military installations. *J Alcohol Drug Educ.* 2018;62:71-90.
23. Fear NT, Jones M, Murphy D, et al. What are the consequences of deployment to Iraq and Afghanistan on the mental health of the UK armed forces? A cohort study. *Lancet.* 2010;375(9728):1783-1797. doi: 10.1016/S0140-6736(10)60672-1
24. Vest BM, Homish DL, Fillo J, et al. Military status and alcohol problems: Former soldiers may be at greater risk. *Addict Behav.* 2018;84:139-143. doi: 10.1016/j.addbeh.2018.04.011
25. Osborne AK, Wilson-Menzfeld G, McGill G, et al. Military service and alcohol use: a systematic narrative review. *Occup Med (Lond).* 2022;72(5):313-323. doi: 10.1093/occmed/kqac045
26. Wilk JE, Bliese PD, Kim PY, et al. Relationship of combat experiences to alcohol misuse among U.S. soldiers returning from the Iraq war. *Drug Alcohol Depend.* 2010;108(1-2):115-121. doi: 10.1016/j.drugalcdep.2009.12.003
27. Dretsch MN, Neff D, Caserta R, et al. Rates of Behavioral Health Conditions and Health Risk Behaviors in Operators and Support Personnel in U.S. Special Operations Forces. *Psychiatry.* 2020;83(4):358-374. doi: 10.1080/00332747.2020.1768787
28. Russell DW, Russell CA, Riviere LA, et al. Changes in alcohol use after traumatic experiences: the impact of combat on Army National Guardsmen. *Drug Alcohol Depend.* 2014;139:47-52.
29. Norman SB, Schmied E, Larson GE. Predictors of continued problem drinking and substance use following military discharge. *J Stud Alcohol Drugs.* 2014;75(4):557-566. doi: 10.15288/jsad.2014.75.557

30. Jakupcak M, Tull MT, McDermott MJ, et al. PTSD symptom clusters in relationship to alcohol misuse among Iraq and Afghanistan war veterans seeking post-deployment VA health care. *Addict Behav.* 2010;35(9):840-843. doi: 10.1016/j.addbeh.2010.03.023
31. Capone C, McGrath AC, Reddy MK, et al. Trauma-related correlates of alcohol use in recently deployed OEF/OIF veterans. *J Trauma Stress.* 2013;26(3):354-360. doi: 10.1002/jts.21817
32. Wolkowicz NR, Peltier MR, Wemm S, et al. Subjective stress and alcohol use among young adult and adult drinkers: Systematic review of studies using Intensive Longitudinal Designs. *Drug Alcohol Depend Rep.* 2022;3:100039. doi: 10.1016/j.dadr.2022.100039
33. Baker TB, Piper ME, McCarthy DE, et al. Addiction motivation reformulated: an affective processing model of negative reinforcement. *Psychol Rev.* 2004;111(1):33-51. doi: 10.1037/0033-295X.111.1.33
34. Cooper M, Kuntsche E, Levitt A, et al. Motivational models of substance use: A review of theory and research on motives for using alcohol, marijuana, and tobacco. In: Sher K., ed. *The Oxford Handbook of Substance Use and Substance Use Disorders.* Oxford University Press (OUP); 2016:375-421.
35. Koob GF. Drug Addiction: Hyperkatifeia/Negative Reinforcement as a Framework for Medications Development. *Pharmacol Rev.* 2021;73(1):163-201. doi: 10.1124/pharmrev.120.000083
36. Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry.* 2016;8:760-773. doi: 10.1016/S2215-0366(16)00104-8
37. Verheul R, van den Brink W, Geerlings P. A three-pathway psychobiological model of craving for alcohol. *Alcohol Alcohol.* 1999;34(2):197-222. doi: 10.1093/alcalc/34.2.197
38. Breslin F, Keeffe MO, Burrell L, et al. A comparison of 2 report formats for alcohol and caffeine use. *Psychol Health.* 1995;10(5):439-448.
39. Aldridge-Gerry AA, Roesch SC, Villodas F, et al. Daily stress and alcohol consumption: modeling between-person and within-person ethnic variation in coping behavior. *J Stud Alcohol Drugs.* 2011;72(1):125-134. doi: 10.15288/jsad.2011.72.125
40. Prykhodko I, Matsehora J, Lipatov I, et al. Servicemen's Motivation in the National Guard of Ukraine: Transformation After the 'Revolution of Dignity'. *J Slav Mil Stud.* 2019;32(3):347-366. doi: 10.1080/13518046.2019.1645930
41. Prykhodko I, Matsehora Y, Kolesnichenko O, et al. The psychological recovery program of Ukrainian military personnel after completing combat missions in the Russian-Ukrainian war. *Cesk Psychol.* 2023;67(6):455-473. doi: 10.51561/cpsych.67.6.455
42. Saunders JB, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addiction.* 1993;88(6):791-804. doi: 10.1111/j.1360-0443.1993.tb02093.x
43. Kovalenko YV. Adaptation and validation of the Ukrainian dispositional 'cope' questionnaire. *Bull Alfred Nobel Univ Ser "Pedagogy Psychol."* 2019;2(18):75-84. doi: 10.32342/2522-4115-2019-2-18-9
44. Prykhodko I. The model of psychological safety of a soldier's personality. *Curr Issues Personal Psychol.* 2021;10(2):112-122. doi: 10.5114/cipp.2021.108684
45. Gruenewald PJ. Regulating availability: how access to alcohol affects drinking and problems in youth and adults. *Alcohol Res Health.* 2011;34(2):248-256.
46. Irizar P, Leightley D, Stevelink S, et al. Drinking motivations in UK serving and ex-serving military personnel. *Occup Med (Lond).* 2020;70(4):259-267. doi: 10.1093/ocmed/kqaa003
47. Cooper ML, Russell M, George WH. Coping, expectancies, and alcohol abuse: a test of social learning formulations. *J Abnorm Psychol.* 1988;97(2):218-230. doi: 10.1037//0021-843x.97.2.218
48. Willis A, Wallston K, Johnson K. Tobacco and alcohol use among young adults: Exploring religious faith, locus of health control, and coping strategies as predictors. In: Plante T, Sherman A, eds. *Faith and Health: Psychological Perspectives.* Guilford Press; 2001:213-239.
49. Britton PC. The relation of coping strategies to alcohol consumption and alcohol-related consequences in a college sample. *Addict Res Theory.* 2004;12(2):103-114. doi: 10.1080/16066350310001613062
50. McKee SA, Hinson RE, Wall AM, et al. Alcohol outcome expectancies and coping styles as predictors of alcohol use in young adults. *Addict Behav.* 1998;23(1):17-22. doi: 10.1016/s0306-4603(97)00008-7
51. Trautmann S, Schönfeld S, Behrendt S, et al. Predictors of changes in daily alcohol consumption in the aftermath of military deployment. *Drug Alcohol Depend.* 2015;147:175-182. doi: 10.1016/j.drugalcdep.2014.11.019



Alcohol and nicotine use among Polish undergraduate students – the preliminary results

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ABSTRACT

Introduction and aim. “DiSCO” (Dietary Supplements Consumption of Undergraduate Students) study aimed to characterize the chosen elements of lifestyle among university students, including alcohol consumption and nicotine use.

Material and methods. The cross-sectional study was realized in cooperation with Italian Universities. The anonymous online survey was conducted from 01.02.2022 to 30.06.2023 among 294 Polish students (age range: 19-37): 202 women (mean age: 21.77; median: 21; SD: 2.46) and 92 men (mean age: 22.73; median: 22; SD: 2.89). The statistical analysis was performed with the use of Excel (Fisher’s exact test; Chi² test; a significance level $p < 0.05$)

Results. 89.8% of students consumed alcohol in the last six months. 36.7% of students used tobacco products in the last year. The analysis of the frequency and type of nicotine products used and the frequency and circumstances of alcohol consumption by students did not reveal any significant differences among the sexes and age groups ($p > 0.05$). Most of the students declared to occasionally use nicotine products (up to 3 times a week), most often traditional cigarettes or shredded tobacco. Most students consume alcohol 2–4 times a month, most often regardless of the meals.

Conclusion. Alcohol consumption and nicotine use among Polish students are similar in both sexes.

Keywords. alcohol, nicotine, students

Introduction

The lifestyle can change in different stages of life. Recent studies pay attention to the fact that students often follow unhealthy lifestyles.¹⁻⁴ It can impact not only their physical health but also their psychological well-being.² Bad habits include alcohol and nicotine use.¹⁻³ The student’s behavioral changes in everyday functioning were revealed during the SARS-CoV-2 pandemic.⁵ The results showed that additional support would be beneficial in these groups.⁵ It seems that the knowledge about the consequences of unhealthy choices is insufficient to change the behavior.⁶

The concern about alcohol and nicotine among young adults is a key topic and a worrisome phenomenon.

Although alcohol consumption has long been considered a part of human culture, nowadays more is known about its adverse effects. The researchers confirm the relationship between chronic heavy alcohol consumption and physical and mental diseases. Among them are various types of cancer, liver disease, pancreatitis, and dementia.^{7,8} It is also worth underlining the fact alcohol’s contribution to injury-related premature loss of life, disability and ill-health are pervasive, touching individuals, families, and societies throughout the world remains significant.⁹

According to Lasota et al., 22% of all deaths from suicide can be attributed to the use of alcohol.¹⁰ Alcohol not only increases the risk of suicide but also other au-

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to-aggressive behaviors.^{11,12} The devastating influence of chronic alcohol consumption on human health is well established. Even authors who document the association of moderate wine consumption in a Mediterranean diet model with health benefits, underline the necessity to promote behavioral education to prevent abuse among young people.¹³

Greń et al. underline that the harm associated with psychoactive substances can be different in different people due to the fact, that the influence of psychoactive substances results from the interaction of many factors.¹⁴ According to the Drug, Set & Setting model, these factors include for example individual susceptibility and expectations of the substance's effects.¹⁴ A recent meta-analysis of 33 databases from alcohol use studies indicates that the amount and frequency of alcohol drinking alone explained only about 23% of the variance in related harms among college students.¹⁵

Wysokińska et al. showed that the knowledge of alcohol consumers about the negative effects of alcohol consumption on health is insufficient.¹⁶ The consumers were not aware of the term “standard drink” for ethyl alcohol and underestimated the energy value of alcoholic beverages and the health consequences of excessive consumption.¹⁶ There was a lack of knowledge on the impact of ethyl alcohol on pregnancies, and lactation.¹⁶

In Italy a cross-sectional Study on Dietary Supplements Consumption – DiSCO was carried out involving undergraduate students from public universities located in northern, central, and southern Italy to investigate the elements of young adults' lifestyle.¹⁷

Aim

To characterize the use of nicotine and alcohol among Polish university students.

Material and methods

The cross-sectional study “DiSCO” (Dietary Supplements Consumption of Undergraduate Students) is realized among Polish students in co-operation with Italian Universities.

The questionnaire designed by the Italian team (questions about lifestyle, use of alcohol and nicotine, etc.) was translated from Italian into Polish. The Italian team adapted to the Italian language and the guidelines of the Italian Ministry of Health the questionnaires used in the studies of Malinauskas et al. and Barnes et al. and structured in a Google module.¹⁷⁻²⁰ The questionnaire included questions about the sociodemographic information, behavioral features of participants, alcohol use, amount of weekly time spent in moderate-vigorous activities, and practice of sport, and specifically investigated the undergraduates' habits of dietary supplement consumption.¹⁷ The study was performed by the principles of the Declaration of Helsinki after the ethical ap-

proval was obtained from the research committee of the University of Rome “Foro Italico” (approval no. University Research Committee (CAR) 104/2021).¹⁷

To make sure that there was no misunderstanding in the questions the translation of the questionnaire from Italian to Polish also took place in the other direction – from Polish to Italian.

The anonymous online survey was created with the use of a Google module and distributed via the Internet to the Polish students. The distribution took place directly by the teachers who gave the students a link to the online questionnaire, also the QR code was generated and distributed via posters on the university campus and advertisements on social media.

A total of 294 students participated in the study. Among 294 participants of the study, there were 202 women (mean age: 21.77; median: 21; SD: 2.46) and 92 men (mean age: 22.73; median: 22; SD: 2.89). The students studied medicine (170), psychology (68), food technology and human nutrition (15), human biology (13), quality management and food analysis (6), pharmacology (4), medical analytics (3), dentistry (12), nursing (1), and biotechnology (1), robotics (1). The data were collected from 01.02.2022 to 30.06.2023.

The database was created in Excel. The statistical analysis was performed with the use of Excel (Fisher's exact test; Chi² test; a significance level $p < 0.05$).

To perform the Italian part of the study ethical approval was obtained from the research committee of the University of Rome “Foro Italico” (approval no. University Research Committee (CAR) 104/2021). However, to perform the study in Poland also the Bioethics Committee of the Medical University in Poland gave a positive opinion about the study (KB 240/2022).

Results

The participants were asked a question about the use of alcohol in the last six months. In 89.8% the answers were positive. 182 female and 82 male students drank alcohol during the last 6 months. Among the students who did not drink alcohol were 20 women and 10 men ($p > 0.05$).

Table 1. The use of alcohol and nicotine products by students according to sex

Question	Answer	Women		Men		Chi ² test p
		n	%	n	%	
Have you used tobacco products (cigarettes, roll-your-own tobacco, pipe tobacco, cigars, cigarillos, e-cigarettes, smokeless tobacco products in the last 1 year)?	no	132	65.35	54	58.7	0.273
	yes	70	34.65	38	41.3	
Have you consumed alcohol in the last 6 months?	no	20	9.9	10	10.87	0.799
	yes	182	90.1	82	89.13	

The students were also asked if they used tobacco products (cigarettes, roll-your-own tobacco, pipe to-

bacco, cigars, cigarillos, e-cigarettes, smokeless tobacco products) in the last 1 year. In 36.7% the answers were positive (70 women and 38 men). Among students who did not use tobacco products last year were 132 women and 54 men ($p>0.05$) (Table 1). No differences were seen among students in different age groups (Table 2).

Table 2. The use of alcohol and nicotine products by students in different age groups

Question	Answer	19–23 years old		≥24 years old		Chi ² test	p
		n	%	n	%		
Have you used tobacco products (cigarettes, roll-your-own tobacco, pipe tobacco, cigars, cigarillos, e-cigarettes, smokeless tobacco products in the last 1 year)?	no	130	61.32	56	68.29	0.266	
	yes	82	38.68	26	31.71		
Have you consumed alcohol in the last 6 months?	no	18	8.49	12	14.63	0.119	
	yes	194	91.51	70	85.37		

The analysis of the frequency and type of nicotine products used by students did not reveal any significant differences among the sexes and age groups (Tables 3 and 4). Most of the students declared to occasionally use nicotine products (up to 3 times a week), most often traditional cigarettes or shredded tobacco.

Table 3. Frequency and types of used nicotine products by female and male students

Frequency of use	Total		Women		Men		p
	n	%	n	%	n	%	
Yes, but I quit within a year	6	5.56	3	4.29	3	7.89	0.549
Yes, at least once a day	40	37.04	24	34.29	16	42.11	
Yes, 4 to 6 times a week	6	5.56	5	7.14	1	2.63	
Yes, occasionally/ up to 3 times a week	56	51.85	38	54.29	18	47.37	
Type of nicotine products							
electronic cigarettes (e-cigarettes)	30	27.78	22	31.43	8	21.05	0.450
tobacco heating products (e.g. IQOS, GLO, JUUL, etc.)	11	10.19	6	8.57	5	13.16	
traditional cigarettes or shredded tobacco	67	62.04	42	60.00	25	65.79	

Table 4. Frequency and types of used nicotine products in different age groups

Frequency of use	Total		19–23 years old		≥24 years old		p
	n	%	n	%	n	%	
Yes, but I quit within a year	6	5.56	5	2.36	1	1.22	0.719
Yes, at least once a day	40	37.04	32	15.09	8	9.76	
Yes, 4 to 6 times a week	6	5.56	5	2.36	1	1.22	
Yes, occasionally/ up to 3 times a week	56	51.85	40	18.87	16	19.51	
Type of nicotine products							
electronic cigarettes (e-cigarettes)	30	27.78	26	12.26	4	4.88	0.269
tobacco heating products (e.g. IQOS, GLO, JUUL, etc.)	11	10.19	8	3.77	3	3.66	
traditional cigarettes or shredded tobacco	67	62.04	48	22.64	19	23.17	

Most students consume alcohol 2-4 times a month, most often regardless of the meals. The analysis of the frequency and circumstances of alcohol consumption

did not reveal any significant differences among the sexes and different age groups (Tables 5 and 6).

Table 5. Frequency and circumstances of alcohol consumption by female and male students

Frequency	Total		Women		Men		p
	n	%	n	%	n	%	
2-3 times a week	44	16.67	31	17.03	13	15.85	0.353
2-4 times a month	123	46.59	81	44.51	42	51.22	
4 times a week or more	3	1.14	0	0	3	3.66	
once a month or less	94	35.61	70	38.46	24	29.27	
Circumstances							
most often regardless of meals	206	78.03	144	79.12	62	75.61	0.524
usually with a meal	58	21.97	38	20.88	20	24.39	

Table 6. Frequency and circumstances of alcohol consumption in different age groups

Frequency	Total		19–23 years old		≥24 years old		p
	n	%	n	%	n	%	
2-3 times a week	44	16.67	32	15.09	12	14.63	0.947
2-4 times a month	123	46.59	89	41.98	34	41.46	
4 times a week or more	3	1.14	2	0.94	1	1.22	
once a month or less	94	35.61	71	33.49	23	28.05	
Circumstances							
most often regardless of meals	206	78.03	156	73.58	50	60.98	0.119
usually with a meal	58	21.97	38	17.92	20	24.39	

Evaluation of the concomitant consumption habits evaluated that 104 (35.37%) students admitted to consuming alcohol and using nicotine products.

Discussion

The main advantage of the study is the fact that it uses the same questionnaire to study undergraduate students' lifestyles in different countries. Because the cross-sectional study "DiSCO" (Dietary Supplements Consumption of Undergraduate Students) is realized in other countries it facilitates the comparison between Polish and Italian students. Similarly to Polish students, most students do not smoke and no differences were found in smoking habits between the sexes.¹⁷ However, the results indicate that smoking is more popular among Polish male students because in Italy 63% of them do not smoke (in Poland 58.3%).¹⁷ However, among female students, more non-smokers were in Poland than in Italy (65.5% vs. 63.3%).¹⁷ In the study realized among students in Southern Thailand 93.3% of participants did not smoke.²¹ No differences were found among the nicotine products chosen by Polish students. The study realized among the students of medical colleges in Saudi Arabia men were more prone to e-cigarette use than women.²²

It is worth noticing that medical students represent significant percentage of the participants of the study. It can be explained that the study is realized by researchers from medical universities. Moreover, it can be assumed

that medical students are more interested in the topic of health than other students.

Prijić et al. noticed that even medical students use cigarettes during studies despite their knowledge about the health effects of smoking.⁶ They underline the role of the proper local environment in increasing the motivation for smoking cessation, for example, all the hospitals and university campuses should be smoke-free.⁶ In their opinion, the government is responsible for mobilizing the public media, school educators, youth organizations, and universities to keep schools and universities smoke-free.⁶

It is important to underline that in this study, the number of “light smokers” (62) was much higher than the number of most probably “heavy smokers” (addicted to nicotine) (40). These findings indicate that the questions probably were confusing for the responders and the answers could not reflect the situation. In the next study, with a higher number of participants, it would be worth considering the modification of the Italian questionnaire. For example, in the section “Frequency of use” should also be the answer “Yes, but I quit.” Moreover, it would be also useful to add the following questions: “If you are a smoker, when do you light your first cigarette in the morning after you get up from the bed - within 30, 45, 60 minutes, or later?”, “How many cigarettes a day do you usually smoke?”, “If you smoke occasionally, not every day, how many cigarettes a week do you smoke?”. In this way, the obtained data on smoking tobacco or other tobacco/nicotine products would be more adequate. In addition, it would be interesting to know how many students ‘light smokers’ would be candidates for easier weaning from smoking because they only have a psychological addiction. On the other hand, for “heavy smokers” it is very difficult to quit because they have both a physical and psychological addiction.

The use of e-cigarettes is a relatively new and important aspect of nicotine addiction. According to Mroczek et. al., who conducted a questionnaire survey in 2022–2023 in a group of 79 medical students (47 women and 32 men) aged 19–37 at the Medical University of Silesia in Katowice, the vast majority of respondents were exposed to passive smoking of e-cigarettes.²³ Moreover, many students did not know the harmful substances contained in e-cigarette smoke and e-cigarettes were often considered to be a healthier nicotine delivery system than cigarettes and supposed to help quit smoking.²³ Thus, the knowledge concerning the harmful effects of e-cigarette usage (such as increasing the risk of cancer or cardiac ischemia) should be disseminated, especially about the toxic compounds contained in e-cigarette smoke.²³ On the other hand, Mroczek et al. suggest that the awareness of the harmfulness of the e-cigarette aerosol is not bringing about any change in social be-

havior, even among young people studying medicine.²³ Mroczek suggests that the solution could be the introduction of regulations banning e-cigarette smoking in public spaces in the future.²³ It could be a promising option. Opoczyńska-Świeżewska et al. indicate that the respondents who participated in the study aimed to gather the opinions of smokers, non-smokers, and those who had quit smoking regarding the smoking ban (concerning traditional tobacco products) in public places, expressed satisfaction with the smoking ban in public places.²⁴

Similarly to Italian students, most Polish students used alcohol two to four times in 1 month.¹⁷ In Italian students, alcohol consumption differed among sexes.¹⁷ Women significantly more often did not consume alcohol than men (16.7% vs. 11.4%, $p=0.008$).¹⁷ In Polish students alcohol consumption was similar among sexes and fewer students declared not to consume alcohol (9.9% of women and 10.87% of men). The study realized among the Swedish students also did not detect significant differences between the proportions of male and female students concerning engagement in alcohol use.²⁵ However, significant differences between sexes were found in hazardous alcohol use by Spanish university students.²⁶ In general, alcohol consumption was less frequent among university students in Southern Thailand.²¹ Only 36% of them reported consuming alcohol in the last 6 months.²¹ However, the fact that 71.8% of participants declared the Islamic religion can play a role in this situation.²¹ The authors noticed that Muslim students were less likely to consume alcohol.²¹ There were also significant differences between the sexes.²¹ Males reported drinking more than females.²¹ The cultural differences in alcohol consumption were confirmed by Chu et al. who compared the alcohol consumption among Chinese and German university students and demonstrated a much lower consumption of alcohol in Chinese students.²⁷

Gambles et al. suggest that the consumption of alcohol among students is related to the perception of a heavy-drinking student culture.²⁸ Moreover, it is also determined by the knowledge about how drinking alcohol helps successful integration with peers.²⁸ Singh noticed that male students use alcohol as a source of courage to enact hegemonic heterosexual masculinities.²⁹ Moreover, the author concluded that when alcohol is seen as a tool to enhance men’s capacity to control women, it is also used to explain men’s loss of control over their behavior.²⁸

Gajda et al. aimed to characterize the determinants of alcohol consumption among medical students and analyzed data from the POLLEK cohort study on alcohol consumption and possible influencing factors. They revealed that 30.9% of students were hazardous drinkers according to the AUDIT test.³⁰ The risk factors of haz-

ardous/harmful drinking according to the results of this study were male gender and smoking cigarettes.³⁰ The worrisome discovery was the fact that in own study the evaluation of the concomitant consumption habits in the study group indicated that 35,37% of students consume alcohol and use nicotine products.

Alcohol consumption in Polish society is a known, and widely discussed problem. The results of Wilczyński et al. show that 95.5% of Polish students use it with a significant tendency towards overusing it.³¹ They revealed that their study group 3.32% of students may be in the group of a high alcoholism risk.³¹

The researchers confirm the negative impact of alcohol consumption on female health, especially the increasing risk of breast cancer.⁸ Also, the link between alcohol consumption during pregnancy and adverse birth outcomes is well documented.²²⁻³² The expected differences in alcohol consumption between women and men were not confirmed in the results of the own study.

Moreover, the fact that the differences between genders in the amount of alcohol consumed are blurred was noticed by other Polish authors. Brodziak-Dopierała et al. performed a study in a group of 196 students from two Silesian universities.³⁴ The authors also noticed that the popularity of alcohol use by students is associated with the fact that some of them already used alcohol during adolescence.³⁴

The realized study has some limitations. The presented data are preliminary results. Thus, more participants should be recruited to obtain more representative data for the whole population of Polish undergraduates. Moreover, the questionnaire was self-reported, which is related to the possibility of under- or overestimation of some habits. The fact that the questionnaire was designed to characterize different aspects of the student's lifestyle (mainly dietary supplement consumption) and translated from Italian to Polish, restricted the number of additional questions asked about nicotine and alcohol use due to length limitation.

The results of the study indicate the need for prevention. Wysokińska et al. proposed to conduct educational activities, taking into account the participation of health professionals and educational institutions, aimed at increasing consumer awareness of the impact of ethanol on health.¹⁶

The study of Bujalski aimed to investigate the prevalence of alcohol cancer awareness and examine the impact of drinking and sociodemographic variables on alcohol-attributable cancer awareness among the adult population in Poland.³⁵ Bujalski's results confirmed existence of the considerable differences in cancer awareness regarding different types of alcohol-attributable cancer and indicated that over 50% of the Polish adult population is aware that alcohol may affect the aerodi-

gestive tract.³⁵ However, the awareness of alcohol's impact on breast cancer is much lower.³⁵ The author underlines the importance of paying particular attention to increased breast cancer risk in public awareness campaigns on cancer and alcohol.³⁵

However, it seems that increasing knowledge about the negative impact of smoking and alcohol consumption on health seems to be insufficient to change human behavior. Surprisingly, according to the study of Bryl et al. realized on 268 Polish medical students drinking alcohol was a way of coping with stress in students of medical faculties.³⁶ These people were aware of the negative consequences related to alcohol use. It seems essential to create an environment for medical students that would enhance healthy stress-coping strategies and promote early prevention of alcohol abuse.³⁶ It would be necessary to change young people's perspectives about alcohol and nicotine use. Case et al. noticed the phenomenon of the social stigma evolved as a perceived disadvantage to e-cigarette use.³⁷ Nowadays, a socio-ecological approach that pays attention to the individual, social, and psychological influences seems to be the most effective way of reducing the hazardous use of alcohol and other substances.³⁸

The advantage of the study is the fact that it uses the same questionnaire to study undergraduate students' lifestyles in different countries. However, at the same time, this fact can be a disadvantage, because the questionnaire could not be adapted to the Polish population. Moreover, the length of the questions due to the questions about many elements of lifestyle included in the questionnaire sections did not afford the extension. However, in the future when performing the study on a larger population it would be useful to extend the questionnaire and include the questions such as the CAGE questionnaire or the Fagerstrom Test of Nicotine Dependence. In this way, the obtained results would have a greater value.³⁹⁻⁴¹

Conclusion

Alcohol consumption among Polish students is high (almost 89.8% of students consume alcohol) and does not differ among the sexes. 63.3% of students do not use tobacco products.

Traditional cigarettes or shredded tobacco are the most often chosen type of nicotine products.

The need for the implementation of preventive strategies, including the promotion of a healthy lifestyle, and education about the negative impact of alcohol and nicotine (including e-cigarettes) on human health is crucial.

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Declarations

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Author contributions

Conceptualization, A.K.; Methodology, A.K.; Software, A.K.; Validation, A.K.; Formal Analysis, A.K.; Investigation, A.K.; Resources, A.K.; Data Curation, A.K.; Writing – Original Draft Preparation, A.K.; Writing – Review & Editing, A.K.; Visualization, A.K.; Supervision, A.K.; Project Administration, A.K.

Conflicts of interest

The author declare no competing interests.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Wrocław Medical University (KB 240/2022).

References

- Griban GP, Lyakhova NA, Harlinska AM, et al. Students' health level as a result of their lifestyle. *Wiad Lek.* 2021;74(4):874-879.
- Velten J, Bieda A, Scholten S, et al. Lifestyle choices and mental health: a longitudinal survey with German and Chinese students. *BMC Public Health.* 2018;16:18(1):632. doi: 10.1186/s12889-018-5526-2
- Mak YW, Kao AHF, Tam LWY, et al. Health-promoting lifestyle and quality of life among Chinese nursing students. *Prim Health Care Res Dev.* 2018;19(6):629-636. doi: 10.1017/S1463423618000208
- Al-Awwad NJ, Al-Sayyed HF, Zeinah ZA, et al. Dietary and lifestyle habits among university students at different academic years. *Clin Nutr ESPEN.* 2021;44:236-242. doi: 10.1016/j.clnesp.2021.06.010
- Fila-Witecka K, Senczyszyn A, Kołodziejczyk A, et al. Lifestyle Changes among Polish University Students during the COVID-19 Pandemic. *Int J Environ Res Public Health.* 2021;18(18):9571. doi: 10.3390/ijerph18189571
- Prijic Ž, Igić R. Cigarette smoking and medical students. *J BUON.* 2021;26(5):1709-1718.
- Hendriks HFJ. Alcohol and Human Health: What Is the Evidence? *Annu Rev Food Sci Technol.* 2020;11:1-21. doi: 10.1146/annurev-food-032519-051827
- Starek-Świechowicz B, Budziszewska B, Starek A. Alcohol and breast cancer. *Pharmacol Rep.* 2023;75(1):69-84. doi: 10.1007/s43440-022-00426-4
- Chikritzhs T, Livingston M. Alcohol and the Risk of Injury. *Nutrients.* 2021;13(8):2777. doi: 10.3390/nu13082777
- Lasota D, Al-Wathinani A, Krajewski P, et al. Alcohol and the Risk of Railway Suicide. *Int J Environ Res Public Health.* 2020;17(19):7003. doi: 10.3390/ijerph17197003
- Lasota D, Pawłowski W, Krajewski P, et al. Alcohol Intoxication and Suicide by Hanging in Poland. *Alcohol Alcohol.* 2020;55(3):278-283. doi: 10.1093/alcal/agaa013
- Lasota D, Pawłowski W, Mirowska-Guzel D, et al. Ethanol as a stimulus to risky and auto-aggressive behaviour. *Ann Agric Environ Med.* 2021;28(2):220-223. doi: 10.26444/aem/118861
- Hrelia S, Di Renzo L, Bavaresco L, et al. Moderate Wine Consumption and Health: A Narrative Review. *Nutrients.* 2022;15(1):175. doi: 10.3390/nu15010175
- Greń J, Ostaszewski K. Protective behavioral strategies associated with psychoactive substance use in different contexts and populations. A literature review. *Alcoholism and Drug Addiction.* 2023;36(2):81-112. doi:10.5114/ain.2023.131110
- Prince MA, Pearson MR, Bravo AJ, et al. A quantification of the alcohol use-consequences association in college student and clinical populations: a large, multi-sample study. *Am J Addict.* 2018;27(2):116-123. doi: 10.1111/AJAD.12686
- Wysokińska M, Kołota A. The level of consumers' knowledge on the influence of ethyl alcohol on health – a review of literature. *Alcoholism and Drug Addiction.* 2022;35(4):307-324. doi: 10.5114/ain.2022.126947
- Gallè F, Valeriani F, De Giorgi A, et al. Assessment of dietary supplement consumption among Italian university students: The multicenter DiSCo study. *Nutrition.* 2023;107:111902. doi: 10.1016/j.nut.2022.111902
- Malinauskas BM, Aeby VG, Overton RF, Carpenter-Aeby T, Barber-Heidal K. A survey of energy drink consumption patterns among college students. *Nutr J.* 2007;6:35.
- Barnes K, Ball L, Desbrow B, Alsharairi N, Ahmed F. Consumption and reasons for use of dietary supplements in an Australian university population. *Nutrition.* 2016;32:524-530.
- Italian Ministry of Health. Integratori alimentari e Linee guida ministeriali. Dietary supplements and Ministry guidelines. Available at: https://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=1267&area=Alimenti%20particolari%20e%20integratori&menu=integratori. Accessed July 27, 2022.
- Buakate P, Thirarattanasunthon P, Wongrith P. Factors influencing alcohol consumption among university students in Southern Thailand. *Rocz Panstw Zakl Hig.* 2022;73(4):435-443. doi: 10.32394/rpzh.2022.0239
- Bin Abdulrahman KA, Khalaf AM, Bin Abbas FB, et al. The Lifestyle of Saudi Medical Students. *Int J Environ Res Public Health.* 2021;25;18(15):7869. doi: 10.3390/ijerph18157869

23. Mroczek PJ, Tyrpień-Golder KM, Janoszka BM, Szumska M. Świadomość studentów uczelni medycznych na temat nałogu używania e-papierosów. *Med Srod.* 2023;26(3-4):60-66. doi: 10.26444/ms/174281
24. Opoczyńska-Świeżewska D, Raciborski F. The support of young adults for the smoking ban in public places in Poland – a qualitative study. *Alcohol Drug Addict.* 2021;34(4):257-266. doi: 10.5114/ain.2021.112795
25. Sfindla A, Bador K, Paganelli M, et al. Swedish High School Students' Drug and Alcohol Use Habits throughout 2020. *Int J Environ Res Public Health.* 2022;19(24):16928. doi: 10.3390/ijerph192416928
26. Romero-Rodríguez E, Amezcua-Prieto C, Morales Suárez-Varela M, et al. Patterns of Alcohol Consumption and Use of Health Services in Spanish University Students: UniHcos Project. *Int J Environ Res Public Health.* 2022;19(10):6158. doi: 10.3390/ijerph19106158
27. Chu JJ, Jahn HJ, Khan MH, et al. Alcohol consumption among university students: a Sino-German comparison demonstrates a much lower consumption of alcohol in Chinese students. *J Health Popul Nutr.* 2016;35(1):25. doi: 10.1186/s41043-016-0062-0
28. Gambles N, Porcellato L, Fleming KM, et al. "If You Don't Drink at University, You're Going to Struggle to Make Friends" Prospective Students' Perceptions around Alcohol Use at Universities in the United Kingdom. *Subst Use Misuse.* 2022;57(2):249-255. doi: 10.1080/10826084.2021.2002902
29. Singh S. South African male university students' perspectives on gender norms concerning alcohol and related harmful behaviours towards female drinkers. *Cult Health Sex.* 2023;25(5):554-566. doi: 10.1080/13691058.2022.2070671
30. Gajda M, Sedlaczek K, Szemik S, Kowalska M. Determinants of Alcohol Consumption among Medical Students: Results from POLLEK Cohort Study. *Int J Environ Res Public Health.* 2021;18(11):5872. doi: 10.3390/ijerph18115872
31. Wilczyński K, Witowski Ł, Pawlik A, Krysta K, Krupka-Matuszczyk I. Consumption of alcohol and risk of alcohol addiction among students in Poland. *Psychiatr Danub.* 2013;25(2):78-82.
32. Okulicz-Kozaryn K. Is Public Health Response to the Phenomenon of Alcohol Use during Pregnancy Adequate to the Polish Women's Needs? *Int J Environ Res Public Health.* 2022;19(8):4552. doi: 10.3390/ijerph19084552
33. Hamułka J, Zielińska MA, Chądzyńska K. The combined effects of alcohol and tobacco use during pregnancy on birth outcomes. *Rocz Panstw Zakl Hig.* 2018;69(1):45-54.
34. Brodziak-Dopierała B, Fischer A, Ahnert B, et al. Alcohol consumption among students of Silesian universities. *Med Srod.* 2020;23(1-4):26-32. doi: 10.26444/ms/140064
35. Bujalski M. Public awareness of alcohol-attributable cancer in Poland. *Alcohol Drug Addict* 2021;34(4):247-256. doi: 10.5114/ain.2021.112307
36. Bryl N, Czarnecka-Iwańczuk M, Romanowska M, et al. Drinking alcohol as a way of coping with stress in students of medical faculties. *Psychiatr Pol.* 2020;54(2):265-277. doi: 10.12740/PP/99029
37. Case K, Crook B, Lazard A, et al. Formative research to identify perceptions of e-cigarettes in college students: Implications for future health communication campaigns. *J Am Coll Health.* 2016;64(5):380-389. doi: 10.1080/07448481.2016.1158180
38. Rømer Thomsen K, Vallentin-Holbech L, Xylander S, et al. Prevention of hazardous use of alcohol among high school students: a study protocol for the randomized controlled trial 'Our choice'. *BMC Public Health.* 2023;23(1):2079. doi:10.1186/s12889-023-16976-y
39. Sharma MK, Suman LN, Srivastava K, et al. Psychometric properties of Fagerstrom Test of Nicotine Dependence: A systematic review. *Ind Psychiatry J.* 2021;30(2):207-216. doi: 10.4103/ipj.ipj_51_21
40. Williams N. The CAGE questionnaire. *Occup Med (Lond).* 2014;64(6):473-474. doi: 10.1093/occmed/kqu058
41. Dhalla S, Kopec JA. The CAGE questionnaire for alcohol misuse: a review of reliability and validity studies. *Clin Invest Med.* 2007;30(1):33-41. doi: 10.25011/cim.v30i1.447



A cross-sectional study on knowledge, attitude, and practice among type 2 diabetes mellitus patients attending a primary health care center in the rural region of Tamil Nadu

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ABSTRACT

Introduction and aim. Diabetes mellitus (DM) is a basic metabolic disease of inadequate control of blood glucose levels. Hyperglycemia is exacerbated, and type 2 diabetes mellitus (T2DM) progresses both insulin resistance and β -cell dysfunction. Management of T2DM involves both lifestyle modification and pharmacological therapy. To achieve optimized health outcomes, the patient requires adequate knowledge, attitude, and practice, so educating the patients on these diseases is an effective strategy to reduce complications of T2DM.

Material and methods. This is a cross-sectional study which was conducted from August 2022 to January 2023. A total of 200 participants were enrolled with inclusion criteria to determine the knowledge, attitude, and practice of type 2 diabetes mellitus patients.

Results. The mean knowledge, attitude and practice (KAP) was 71.5%, 87.5%, and 40% respectively. There is a significant association between knowledge, attitude, practice questions, and socio-demographic characteristics. Education was strongly associated with having higher knowledge scores ($p=0.001$).

Conclusion. The study's conclusions made clear the necessity of well-planned interventions to raise T2DM awareness among patients with low levels of education. Patients with T2DM may benefit from well-designed educational programs that encourage healthy behavior and these interventions can improve the quality of life of patients in rural region of Tamil Nadu.

Keywords. attitude, cross-sectional study, knowledge, practice, type 2 diabetes mellitus

Introduction

Diabetes mellitus (DM) is a basic metabolic disease of inadequate control of blood glucose levels. The main subtypes of DM are type 1 DM and type 2 DM which classically result from defective insulin secretion (T1DM) and action (T2DM).¹ Type 2 diabetes mellitus is thought to affect middle-aged and older individuals who have chronic hyperglycemia as a result of poor lifestyles and nutritional choices. Whereas, T1DM is thought to manifest in chil-

dren or teenagers. Since the pathophysiology of T1DM and T2DM are very diverse from one another, each type has a separate etiology, presentation, and course of treatment. In India, 77 million people were estimated to have diabetes in 2019, and by 2045, that number is projected to reach over 134 million.^{2,3} Rising incidence in India is linked to changes in lifestyle as well as urbanization and fast industrialization. Diabetes and its mostly preventable consequences are progressing at an accelerated rate due to several fac-

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tors, including poor awareness and habits among diabetic individuals. Diabetes prevalence ranged from 5.4% in north-eastern states to as high as 15.5% in the southern Indian state of Tamil Nadu, according to epidemiological research carried out across the nation.⁵ Due to their lower socioeconomic status and lack of education, the majority of individuals are still susceptible to lifestyle disorders like diabetes and hypertension. Diabetes patients have a higher incidence of stroke and coronary heart disease than the general population. Complications such as diabetic kidney disease, diabetic retinopathy, and diabetic neuropathy, which are common in patients with inadequate glycemic control, worsen their quality of life. Approximately, 57% of these individuals remain undiagnosed.⁶⁻⁸ Type 2 diabetes mellitus, which accounts for the majority of the cases, can have multi-organ complications, broadly divided into microvascular and macrovascular complications. Blood glucose levels become usually high when the feedback loops between insulin action and insulin production are not working properly. As a result of decreased insulin secretion caused by cell malfunction, the body's ability to maintain physiological glucose levels is constrained. On the other side, insulin resistance helps to reduce glucose uptake in adipose tissues, muscles, and the liver while increasing glucose synthesis in the liver. Even while all these processes occur early in the pathophysiology and help to cause the disease to manifest, β -cell dysfunction is typically more severe than insulin resistance. However, hyperglycemia is exacerbated, and T2DM progresses if both insulin resistance and β -cell dysfunction are present.^{7,8} Management of T2DM involves both lifestyle modification and pharmacological therapy.⁹

Several studies that were conducted to assess the knowledge, attitude, and practice of patients with T2DM emphasized the need for patients to have a greater understanding of the disease's prevention, diagnosis, mitigation of risk factors, and reduction of consequences. It has been suggested that educating patients on their condition is an effective approach for lowering T2DM complications and achieving better blood glucose control.¹⁰ Increased understanding most likely could enhance patients' attitudes and practices regarding their conditions.¹¹ Prior research has demonstrated that patients with better knowledge of their type 2 diabetes and its complications reported better treatment adherence when compared to those with inadequate understanding of the condition. It's been suggested that T2DM patients might have better blood glucose management if they were aware of their condition.¹² The patient's health and quality of life may be enhanced by this. Furthermore, negative attitudes were linked to poor blood glucose control and a higher likelihood of complications. Prior research has demonstrated differences in the knowledge, attitude, and practices of T2DM patients in primary and tertiary healthcare settings in India, Saudi Arabia, Sri Lanka, and Ethiopia.^{14,16} Evaluating diabetes

knowledge has always been a critical component of assessing diabetes patients overall. A study by Al-Qazaz et al. found that patients are more likely to adhere to their treatment regimen and have fewer issues linked to their illness if they are better informed about their condition and its implications.¹⁷ Despite the large number of studies that has been done worldwide, people in rural regions still don't know enough about diabetes. Hence, to achieve optimized health outcomes, the patient requires adequate knowledge, attitude, and practice, it has been argued that educating patients on these diseases was an effective strategy to reduce complications of T2DM and achieve improved control over blood glucose.²⁰ Therefore, this study assesses the knowledge, attitude, and practice among type 2 diabetes mellitus patients in a rural region in Tamil Nadu about their disease.

Aim

The current study is to determine the knowledge, attitude, and practice of type 2 diabetes mellitus patients and the secondary objective is to find out the association between socio-demographic characteristics and KAP questions by categorizing the questions by good score and poor score.

Material and method

Study design, study period, and study population

We adopted a cross-sectional study design to evaluate the knowledge, attitudes, and practices of type 2 diabetes mellitus patients for a period of 6 months (From August 2022 to January 2023) in a primary health care hospital in a rural region, Chennai, Tamil Nadu, India. The study population was type 2 diabetic mellitus patients who visited the outpatient department during the study period and fulfilled the inclusion criteria.

Study variables

The dependent variables were knowledge, attitude, and practice, and the independent variables were age, gender, marital status, employed status, and educational status.

Sample size

The required sample size was calculated by using a single population proportion formula. Therefore, the proportion was taken at 50%, and the sample size calculation was made as the following proportion of the study with 95% confidence intervals (CI) and 5% margin error. $n = z^2 p(1-p)/w^2$, where n =sample size, p =proportion (50%), w =margin error (5%), $z=1.96$ confidence level, and $n = 1.96^2(0.5(1-0.5))/(0.05)(0.05) = 194.6$. Considering the 5% nonresponse rate, the sample size was 200. Totally, 200 participants were enrolled meeting the criteria.

Inclusion and exclusion criteria

Type 2 diabetes mellitus patients who are taking oral hypoglycemic drugs and willing to take part in the

study, and giving consent were included in the study. The type 1 diabetes mellitus patients, patients with serious co-morbidity conditions such as heart disease, and chronic kidney disease, patients taking insulin, patients with hearing impairment, mental health problems, and those unable to supply the necessary information were excluded from the study.

Data collection

Sociodemographic variables

The first section of the survey included questions about the participant's demographics, such as their age, gender, marital status, employed status and educational status, monthly income, duration of diabetes, fasting blood glucose, postprandial blood glucose, HbA1c, and body mass index.

Knowledge, attitude, and practice (KAP) questionnaire

The second section consisted of the knowledge, attitude, and practice (KAP) questionnaire. The KAP questionnaire comprised 18 questions (knowledge: 7; attitude: 5; and practice: 6). KAP scores were calculated such that correct answers were assigned a score of 1 (one), whereas wrong answers were assigned a score of 0 (zero). Participants who correctly responded to more than 50% of knowledge, attitude and practice assessing questions were considered as having good knowledge, attitude and practice towards type 2 diabetes mellitus whereas those who scored $\leq 50\%$ were considered as having poor knowledge, attitude, and practice towards type 2 diabetes mellitus.

Translation validity

In Tamil Nadu, Tamil is the primary language spoken. Thus, utilizing a standardized forward-backward translation process, the English survey questionnaire was first translated forward into Tamil and then backward into English. The English version was translated into Tamil by two separate bilingual translators working independently. To produce a translation that more closely mimics the original instrument, one translator was aware of the topics the questionnaire aimed to measure. The other translator was unable to identify any discrepancies between the two translations because she was unaware of the subject matter. The two translators discussed and resolved any discrepancies that had been raised.

Face validity, pilot testing, internal consistency, and reliability

Three experts with prior experience with T2DM examined the study tool. Using a Likert scale of 1 to 5, the researchers – physicians (n=1) and pharmacists (n=2) – rated each item's relevance (1 being completely irrelevant, and 5 being highly relevant). Excluded were items that received ratings of either not relevant at all or not relevant from all researchers. All researchers assessed the items as highly relevant or relevant, so they were kept. Discussion and agreement were used to settle ambiguous issues.

Twenty patients participated in pilot research to examine the study tool's readability and comprehension of the questions. The test-retest approach was employed to evaluate the stability of the scores across a brief time frame. Each questions were asked to the 20 patients twice. There was a brief break of thirty minutes to an hour between each round. Pearson's correlation was used to establish a link between the scores from the two rounds. A Pearson's correlation coefficient of 95% (95%CI=91.2 to 98.7%) with a p-value of less than 0.001 suggested excellent score stability. $>80\%$ was the predetermined threshold for acceptable coefficients, as it was in earlier research. The study tool's items were evaluated for internal consistency using Cronbach's alpha statistics. A Cronbach's alpha of 74.2% suggests that the test items had strong internal consistency. Between 70 and 95% were the acceptable coefficients that were predetermined.

Data collection procedure

The data were collected by the structured questionnaire, which contains different items like sociodemographic and KAP. Participants signed a written informed consent form after receiving a thorough explanation of the study's aims and objectives before the data collection. A face-to-face interview was undertaken to collect the data.

Statistical analysis

This study was analyzed using the student t-test with a 95% level of significance and a p-value of <0.05 is considered significant. The obtained data will be statistically analyzed with the help of SPSS software (IBM< Armonk, NY, USA) to find out the association between socio-demographic characteristics and KAP questions. A continuous and categorical analysis was conducted on the following variables: age, duration of diabetes, BMI, fasting plasma glucose, postprandial plasma glucose, and HbA1c. The Mann-Whitney U test and the Kruskal-Wallis test were used to compare categorical data. The correlation between variables was evaluated using Spearman's rank correlation. We used multivariate linear regression to compensate for confounding variables. The model kept every variable that was used in the Kruskal-Wallis and Mann-Whitney U tests. The following were included as continuous variables: age, time from diagnosis, BMI, plasma glucose levels during fasting and postprandial periods, and HbA1c. The coefficients were expressed as changes per unit of change.

Ethical considerations

The study was ethically approved by the institutional ethics committee (approval number 2148/2022). Every procedure used in this investigation that involved human participants complied with the 1964 Helsinki Declaration and its later revisions or similar ethical standards, as well as the ethical norms of the institutional and/or national research committee.

Results

Sociodemographic and clinical characteristics

Among 200 participants, table 1 shows that most of the participants were from the age group - >55 years (65.5%); Gender – male (50%); Marital status – married (91.5%); Employment status – employed (60%); Educational status – educated (87%). 105 (52.5%) had their usual fasting plasma glucose level of more than 140 mg/dL, 102 (51%) had their usual postprandial plasma glucose level of more than 200 mg/dL, 101 (50.5%) had their HbA1c level more than 7%, and 108 (54%) had a BMI of more than 25 kg/m².

Table 1. Sociodemographic and clinical characteristics

Socio-demographic and clinical characteristics	n	Percentage (%)
Age (years)		
<55	69	34.5
≥55	131	65.5
Gender		
Male	110	50
Female	90	45
Marital status		
Single	12	6
Married	183	91.5
Divorced/widowed	5	3
Employment status		
Unemployed	80	40
Employed	120	60
Educational status		
Educated	174	87
Uneducated	26	13
Monthly income (in rupees)		
≤20,000	158	79
Up to 50,000	42	21
>50,000	2	1
Duration of diabetes (years)		
≤7	103	52
>7	97	49
Fasting plasma glucose (mg/dL)		
<140	95	47.5
≥140	105	52.5
Postprandial plasma glucose (mg/dL)		
<200	98	49
≥200	102	51
HbA1c (%)		
<7	99	49.5
≥7	101	50.5
Body mass index (kg/m²)		
<25	92	46
≥25	108	54

Knowledge, attitudes, and practices concerning type – 2 diabetes mellitus

Table 2 shows the knowledge of the participants where the mean score is 143 (71.5%) of the participants gave the correct answer. Among these 7 knowledge questions majority of the participants, n=143 (71.5%) answered

correctly for question 5 (What are the various symptoms of diabetes?).

Table 2. Knowledge of the participants

	No. of participants with correct answer (n)	Percentage (%)
Whether I am aware that diabetes is a disease	192	96
What type of diabetes do you have	56	28
What is the level of blood sugar to diagnose diabetes	143	71.5
Is there positive family history necessary for development of diabetes	189	94.5
What are the various symptoms of diabetes	196	98
What occur if diabetes is not treated	127	63.5
What are the complications of diabetes	99	49.5
Mean score	143	71.5

Table 3. Attitude of the participants

	No. of participants with correct answer(n)	Percentage (%)
Should the patient follow a controlled and planned diet to prevent diabetes	198	99
Should we visit to physician regularly	190	95
Do you think regular oral hypoglycemic medication is important in diabetes	172	86
Do you think an estimation of blood sugar level is important	191	95.5
Should we exercise regularly for healthy life	124	62
Mean score	175	87.5

Table 4. Practice of the participants

	No. of participants with correct answer(n)	Percentage (%)
When was your blood pressure measured last	53	26.5
When was your last consultation with your physician	94	47
When was your last urine examination done	67	33.5
When did you have your last lipid profile checked	50	25
When was your blood sugar level checked last	186	93
When did you have gone for exercise last	30	15
Mean score	80	40

Table 3 shows the attitude of the participants where the mean score is 175 (87.5%) of the participants gave the correct answer. Among these 5 attitude questions majority of the participants, n=198 (99%) answered correctly for question 4 (Do you think an estimation of blood sugar level is important?).

Table 4 shows the practice of the participants where the mean score is 80 (87.5%) of the participants gave the correct answer. Among these 6 practice questions majority of the participants, n=186 (93%) answered correctly for question 5 (when was your blood sugar level checked last?).

Table 5 shows the knowledge, attitude, and practice scores showed a moderately positive connection (p-value < 0.001) when the continuous variables were correlated. The results showed that knowledge scores had a positive correlation with monthly income (Spearman's rho=0.16, p=0.001) and a negative correlation with age

Table 5. Correlation between knowledge, attitude, and practice scores with socioeconomic and clinical variables of the patients

Variable	Knowledge score	Attitude score	Practice score	Age	Monthly income	Duration of diabetes	HbA1c	FBS	PPBS	BMI
Knowledge score	Rho -	0.26	0.45	-0.22	0.16	-0.17	-0.13	-0.17	-0.08	-0.01
	p	<0.001	<0.001	<0.001	0.001	0.006	0.001	0.05	0.019	0.05
Attitude Score	Rho	0.29	0.35	0.001	0.05	0.005	-0.2	-0.19	-0.13	-0.18
	p	<0.001	<0.001	0.741	0.145	0.354	0.001	<0.37	0.001	0.002
Practice score	Rho	0.37	0.48	-0.10	0.12	-0.02	-0.20	-0.16	-0.21	-0.21
	p	<0.001	<0.001	0.001	0.11	<0.001	<0.001	<0.14	0.001	0.001

Table 6. The association between the sociodemographic and clinical characteristics and KAP questions

Sociodemographic and clinical characteristics	Knowledge (n)		Attitude (n)		Practice (n)	
	Good	Poor	Good	Poor	Good	Poor
Age (years)						
<55	87	46	67	47	23	45
≥55	44	23	36	68	112	20
p	0.002	0.016	0.003	0.012	0.008	0.005
Gender						
Male	45	77	62	42	40	69
Female	56	22	66	30	78	13
p	0.005	0.007	0.004	0.001	0.009	0.018
Marital status						
Single	5	2	4	3	3	3
Married	89	78	116	52	122	46
Divorced/widowed	19	7	15	10	12	14
p	<0.0001	<0.0001	0.0002	<0.0001	<0.0001	<0.0001
Employment status						
Unemployed	76	21	45	65	18	12
Employed	97	6	79	11	126	44
p	0.0041	0.0034	0.0078	0.0013	0.0065	0.0032
Educational status						
Educated	100	3	112	10	119	23
Uneducated	29	68	45	33	19	39
p	0.009	<0.0001	0.0052	0.003	0.001	0.003
Monthly income (in rupees)						
≤20,000	90	27	50	75	35	101
Up to 50,000	45	36	21	53	24	39
>50,000	1	1	1	0	1	0
Duration of diabetes (years)						
≤7	64	43	32	76	29	45
>7	23	70	45	47	44	82
Fasting plasma glucose (mg/dL)						
<140	98	8	25	106	20	125
≥140	22	72	32	37	17	38
p	<0.0001	0.04	0.001	<0.0001	0.02	<0.0001
Postprandial plasma glucose (mg/dL)						
<200	106	24	12	99	36	87
≥200	63	7	22	67	18	59
p	<0.0001	0.03	0.002	0.001	0.009	0.006
HbA1c (%)						
<7	80	41	34	67	16	58
≥7	42	37	29	70	52	74
p	<0.0001	0.005	0.004	<0.0001	0.001	0.001
Body mass index (kg/m²)						
<25	78	22	27	77	20	80
≥25	51	49	23	73	39	61
p	<0.0001	0.009	0.002	0.005	0.001	<0.0001

(Spearman’s rho=-0.22, p<0.001), duration of diabetes (Spearman’s rho=-0.17, p=0.006), fasting plasma glucose (Spearman’s rho=-0.17, p=0.05), postprandial glucose (Spearman’s rho=-0.08, p=0.019), and HbA1c (Spearman’s rho=-0.13, p<0.001). Positive attitude scores were inversely linked with plasma glucose levels during fasting (Spearman’s rho=-0.19, p<0.37), after meals (Spearman’s rho=-0.13, p=0.001), HbA1c (Spearman’s rho=-0.2, p=0.001), and body mass index (Spearman’s rho=-0.18, p=0.002). Practice scores correlated negatively with age (Spearman’s rho=-0.10, p<0.001), duration of diabetes (Spearman’s rho=-0.02, p<0.001), fasting plasma glucose (Spearman’s rho=-0.16, p=0.14), postprandial plasma glucose (Spearman’s rho=-0.21, p=0.001), HbA1c (Spearman’s rho=-0.20, p<0.001), and BMI (Spearman’s rho=-0.21, p=0.001).

Table 6 shows that the overall KAP questions assessment where shows age group <55, gender – female, marital status – married, employed status – employed, educational status – educated, fasting blood sugar <140 mg/dL, postprandial plasma glucose <200 mg/dL, HbA1c <7%, body mass index <25 kg/m² have the good significant score comparing to another batch of socio-demographic and clinical characteristics and was analyzed using the student t-test with a 95% level of significance and a p<0.05 is considered significant.

Table 7 shows the excluded confounding variables and finds predictors of greater knowledge, attitude, and practice scores, a multiple linear regression model was applied. The model’s R² was 0.22, with a p-value less than 0.001. According to the model, education was highly correlated with greater knowledge scores (p<0.001).

Discussion

Diabetes is a chronic metabolic condition marked by high blood glucose (also known as blood sugar), which over time can seriously harm the heart, blood vessels, eyes, kidneys, and nerves. Type 2 diabetes is the most prevalent type and typically affects adults. It develops when the body stops producing enough insulin or grows resistant to it. Type 2 diabetes prevalence has massively increased during the last three decades in countries of all income levels.¹⁹ Our goal was to find out the Knowledge, attitude, and practice among type 2 diabetes mellitus patients find the association between socio-demographic characteristics, and identify the obstacles to poor compliance.

Table 7. Multiple linear regression between sociodemographic and clinical variables of the patients with knowledge, attitude, and practice scores

Variable	Unadjusted coefficients	SE	Adjusted coefficients	t	p
Knowledge score					
Age	-0.02	0.30	-0.03	-0.09	0.589
Gender	-0.06	0.22	0.0001	-0.2	0.457
Marital status	0.17	0.32	0.01	0.20	0.396
Employment status	-0.10	0.26	-0.06	-0.72	0.264
Educational status	1.24	0.14	0.32	1.89	0.133
Monthly income	0.39	0.21	0.12	0.56	0.436
Duration of diabetes	-0.50	0.33	-0.07	-1.04	0.734
Fasting plasma glucose	0.23	0.44	0.02	0.16	0.378
Postprandial plasma glucose	-0.02	0.03	-0.18	-1.76	0.053
HbA1c	0.04	0.02	0.09	0.92	0.346
BMI	0.01	0.01	0.001	0.001	0.285
Attitude score					
Age	-0.16	0.25	-0.07	-0.92	0.624
Gender	0.12	0.43	0.03	0.50	0.165
Marital status	0.09	0.51	0.001	0.02	0.851
Employment status	-0.07	0.25	-0.05	-0.51	0.954
Educational status	0.36	0.66	0.09	0.08	0.856
Monthly income	0.0001	0.14	0.001	-0.01	0.943
Duration of diabetes	-0.04	0.19	-0.03	-0.40	0.385
Fasting plasma glucose	0.06	0.74	0.02	0.90	0.541
Postprandial plasma glucose	0.001	0.01	0.001	-0.02	0.854
HbA1c	0.02	0.01	0.09	0.70	0.388
BMI	-0.01	0.01	-0.04	-1.20	0.841
Practice score					
Age	-0.11	0.28	-0.02	-0.45	0.414
Gender	-0.03	0.12	-0.01	-0.23	0.985
Marital status	-0.78	0.98	-0.07	-0.95	0.855
Employment status	0.02	0.23	0.03	0.12	0.252
Educational status	0.26	0.84	0.08	0.25	0.849
Monthly income	-0.01	0.95	-0.06	-0.18	0.741
Duration of diabetes	-0.12	0.84	-0.02	-0.57	0.282
Fasting plasma glucose	0.63	0.37	0.19	2.03	0.056
Postprandial plasma glucose	-0.04	0.02	-0.04	-0.63	0.036
HbA1c	-0.05	0.01	-0.03	-0.79	0.066
BMI	-0.02	0.01	-0.12	-1.12	0.556

The study conducted by Muhammed Alqahtani et.al, estimated about 70.9% of the participants had good knowledge scores approximately. In this study, approximately 71.5 % of the participants scored well on knowledge questions, demonstrating similar outcomes.²² Ravi Kant et.al estimated that 75% of the participants had a good attitude score which is nearly the same as the present study. While the practice questions are considerably lower, the study conducted by Saadiaz et.al also reported lower practice and attitude among type-2 diabetes mellitus patients.^{11,13} Overall the results of knowledge, attitude, and practice scores were found to be higher than those reported by Upadhyay et al.⁶ A significant association between knowledge, attitude, and practice overall scores with sociodemographic and clinical characteristics similar to that of a study conducted

by Ng SH et al. also showed that there is a significant association between sociodemographic and clinical characteristics and KAP questions ($p < 0.05$).⁹

The findings of the research brought into focus patients' problems in T2DM knowledge, attitudes, and practices. In this study, relationships and correlations between the patient's clinical and sociodemographic characteristics and knowledge, attitude, and practice were found. Furthermore, indicators of increased knowledge, decreased attitude, and practice were found. The results of this study may help those in the authority of making decisions, medical professionals, and patient advocate organizations who may need to create treatments to enhance the health of T2DM patients. Remarkably, scores for knowledge, attitude, and practice showed a moderately favorable association. This could, at least in part, corroborate the idea that individuals with type 2 diabetes may be more likely to adopt a positive mindset and appropriate behavior if they have an education. However, our results showed that 71.5% of patients practiced T2DM with a lower attitude and good knowledge. Patients who met certain criteria performed better on the knowledge test: they were under 55 years old, married, educated, employed, and had a higher income. They also had normal fasting plasma glucose levels of less than 140 mg/mL, an HbA1c of less than 7%, and a BMI of less than 25 kg/m². According to Hearth et al.'s pilot study carried out in Sri Lanka, 77% of T2DM patients have moderate to above-average awareness of their condition. Studies conducted in various contexts have revealed that T2DM patients in Mongolia, Sri Lanka, Bangladesh, India, Jordan, and Lebanon had varying levels of understanding.³¹⁻³⁵ Higher knowledge scores were substantially correlated with education when potential confounding variables were taken into account. The results of this study may suggest that patients with higher levels of education are more likely to understand their condition and strategies for controlling their blood sugar. Hearth et al.'s study demonstrated a positive correlation between education and patients increased T2DM knowledge in Sri Lanka. In a similar study, Karaoui et al. demonstrated that among patients in Lebanon, a higher degree of education was positively connected with a greater understanding of type 2 diabetes.³⁶ Fatema et al.'s research in Bangladesh revealed that male T2DM patients knew a great deal more about their condition than their female counterparts.³⁷

The study demonstrated that 87.5% of the patients had negative opinions regarding their illness. The ability to maintain a typical fasting plasma glucose level below 140 mg/dL, postprandial plasma glucose level below 200 mg/dL, HbA1c below 7%, and BMI below 25 kg/m² were all positively correlated with attitude ratings. Attitude scores had no correlation with potential confounding variables when we accounted for them. The results of this study conflicted with those published by Belsti et

al. in Ethiopia, where the patients' attitudes were linked to their income and educational attainment.³⁸ Prior research indicated that compared to patients with lower incomes, those with greater incomes may have better access to healthcare services, be able to attend routine checks and engage in physical activity.

Based on practice, our research revealed that forty percent of T2DM patients had less aggressive approaches to managing their condition. Lower practice scores were recorded by patients who were younger than 55 years old, educated, and had normal fasting glucose levels of less than 140 mg/dL, postprandial plasma glucose of less than 200 mg/dL, HbA1c greater than or equal to 7%, and BMI of less than or equal to 25 kg/m². Our findings aligned with those published in various contexts in Ethiopia, Bangladesh, Mongolia, Sri Lanka, and Lebanon.³¹⁻³⁷ According to these studies, which adjusted for potential confounding variables, attending a diabetic education program was somewhat linked to better practice scores. Our results may corroborate earlier research on the benefits of educational initiatives for enhancing health outcomes and patient self-management among T2DM patients living in rural region of Tamil Nadu.

Study limitations

First, this study was a cross-sectional study. An interventional design could have permitted enhancing knowledge, improved positive attitude, and promoted good practice among patients with T2DM about their disease. Second, the sample size used in this study was relatively small and it might not apply to the entire population because it was carried out at a single primary healthcare center located in a rural region in Chennai, Tamil Nadu, India. However, the sample size used in this study was comparable to those used in other studies. Third, since the study was only done for six months, it may be difficult to extrapolate the results to a larger population because there are fewer data. The results of this cross-sectional study cannot be applied to a larger population over an extended period. Fourth, a convenience sampling method was followed to recruit the sample needed for this study. It is noteworthy to mention that the sample recruited in this study was diversified by the inclusion of patients from both genders, different educational levels, and income levels. Finally, the number of items relevant to knowledge, attitude, and practice was relatively small. Despite the small number of items, we were able to expose the level of knowledge, attitude, and practice of patients with T2DM concerning their disease.

Conclusion

The current study provides insight into the knowledge attitudes, and practices of Tamil Nadu's rural T2DM population. The research found an association and correlation between the knowledge, attitude, and practice scores and the clinical and sociodemographic character-

istics of T2DM patients at a primary healthcare facility in a rural area of Tamil Nadu. The study's conclusions made clear the necessity of well-planned interventions to raise patient's low educational attainment's understanding of type 2 diabetes. Patients with T2DM may benefit from well-designed educational programs that encourage healthy behavior. Future research is still required to determine whether these therapies could help T2DM patients in Tamil Nadu's rural areas achieve better health outcomes and a higher quality of life.

Declarations

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Author contributions

Conceptualization, H.W. and S.R.; Methodology, H.W.; Software, H.W.; Validation, H.W. and S.R.; Formal Analysis, H.W.; Investigation, H.W.; Resources, H.W.; Data Curation, H.W.; Writing – Original Draft Preparation, H.W.; Writing – Review & Editing, H.W.; Visualization, H.W.; Supervision, H.W. and S.R.; Project Administration, H.W.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical approval

The Bhaarath Medical College and Hospital research institution review board gave its approval for this study. The study period was August 2022 to January 2023 (approval number 2148/2022)

Reference

1. Palaniswamy LD. Knowledge, attitude and practice of exercise among patients with type 2 diabetes mellitus. *J Med Sci Res.* 2020;8(4):145-149. doi: 10.17727/JMSR.2020/8-19
2. Al-Maskari F, El-Sadig M, Al-Kaabi JM, Afandi B, Nagelkerke N, Yeatts KB. Knowledge, attitude and practices of diabetic patients in the United Arab Emirates. *PLoS One.* 2013;8(1):e52857. doi: 10.1371/journal.pone.0052857
3. El Arifeen S, Christou A, Reichenbach L, et al. Community-based approaches and partnerships: innovations in health-service delivery in Bangladesh. *Lancet.* 2013; 382(9909):2012-2026. doi: 10.1016/S0140-6736(13)62149-2
4. Steyn NP, Mann J, Bennett P, et al. Diet, nutrition and the prevention of type 2 diabetes. *Public Health Nutr.* 2004;7(1a):147-165. doi: 10.1079/PHN2003586

5. Okonta HI, Ikombele JB, Ogunbanjo GA. Knowledge, attitude and practice regarding lifestyle modification in type 2 diabetic patients. *African J Primary Health Care Family Med.* 2014;6(1):6. doi: 10.4102/phcfm.v6i1.655
6. Upadhyay DK, Palaian S, Shankar PR, Mishra P, Pokhara N. Knowledge, attitude and practice about diabetes among diabetes patients in western Nepal. *Rawal Med J.* 2008;33(1):8-11. doi: 10.5812/RMJ.114088
7. Shah VN, Kamdar P, Shah N. Assessing the knowledge, attitudes and practice of type 2 diabetes among patients of Saurashtra region, Gujarat. *Int J Diab Developing Countries.* 2009;29(3):118. doi: 10.4103/0973-3930.54288
8. Ambigapathy R, Ambigapathy S, Ling H. A knowledge, attitude and practice (KAP) study of diabetes mellitus among patients attending Klinik Kesihatan Seri Manjung. *NCD Malaysia.* 2003;2(2):6-16. doi: 10.18203/2394-6040.ijcmph20183824
9. Ng SH, Chan KH, Lian ZY, Chuah YH, Noora A. Reality vs illusion: knowledge, attitude and practice among diabetic patients. *Int J Collab Res Internal Med.* 2012;4(5):723. doi: 10.14503/3745-7649.34109
10. Mohammadi S, Karim NA, Talib RA, Amani R. Knowledge, attitude and practices on diabetes among type 2 diabetic patients in Iran: A cross-sectional study. *Sci J Public Health.* 2015;3:520-524. doi: 10.11648/j.sjph.20150304.20
11. Rahaman KS, Majdzadeh R, Holakouie Naieni K, Raza O. Knowledge, attitude and practices (KAP) regarding chronic complications of diabetes among patients with type 2 diabetes in Dhaka. *Int J Endocrinol Metab.* 2017;15:e12555. doi: 10.5812/ijem.12555
12. Magbanua E, Lim-Alba R. Knowledge and practice of diabetic foot care in patients with diabetes at Chinese general hospital and medical center. *J ASEAN Federat Endocrine Soc.* 2017;32:1-19. doi: 10.15605/jafes.032.02.05
13. Karaoui LR, Deeb ME, Nasser L, Hallit S. Knowledge and practice of patients with diabetes mellitus in Lebanon: A cross-sectional study. *BMC Public Health.* 2018;18:525. doi: 10.1186/s12889-018-5416-7
14. Phuong CM, Hue DT, Thuy NH. Communication on health education to prevent pre-diabetes-diabetes. *J Pract Med.* 2011;11:6-9. doi: 10.11080/JPM.2011.02.555594
15. Nhung NT, Dao MA. Knowledge and practice of diabetes prevention among elderly people in two communes of Vu Ban, Nam Dinh province in 2001. *J Pract Med.* 2013;5:72-75. doi: 10.13073/JPM.2013.03.54862
16. Saadia Z, Rushdi S, Alsheha M, Saeed H, Rajab M. A study of knowledge attitude and practices of Saudi women towards diabetes mellitus. A (KAP) study in Al-Qassim Region. *Internet J Health.* 2009;11:1-7. doi: 10.5580/1d29
17. Singh R, Maharjan PL, Gupta N. Knowledge of diabetes among diabetic patients attending diabetes clinic in Kathmandu Nepal. *Int J Health Sci Res.* 2013;3(10):37-40. doi: 10.864-65/76540
18. Wong N, Wang SS, Lamoureux E, et al. Blood pressure control and awareness among patients with diabetes and hypertension attending a tertiary ophthalmic clinic. *Diabet Med.* 2009;26(1):34-39. doi: 10.1111/j.1464-5491.2008.02614.x
19. Zaheera S, Salah A, Muneera S, et al. A study of knowledge attitude and practices of Saudi women towards diabetes mellitus. A (KAP) study in Al-Qassim region. *Int J Health.* 2010;11(2):29. doi: 10.5580/1d29
20. Tan MY, Magarey J. Self-care practices of Malaysian adults with diabetes and sub-optimal glycaemic control. *Patient Education Counsel.* 2008;72(2):252-267. doi: 10.1016/j.pec.2008.03.017
21. Blasco-Blasco M, Puig-García M, Piay N, Lumbreras B, Hernández-Aguado I, Parker LA. Barriers and facilitators to successful management of type 2 diabetes mellitus in Latin America and the Caribbean: A systematic review. *PloS One.* 2020;15(9):e0237542. doi: 10.1371/journal.pone.0237542
22. Srinivasan NK, John D, Rebekah G, Kujur ES, Paul P, John SS. Diabetes and diabetic retinopathy: knowledge, attitude, practice (KAP) among diabetic patients in a tertiary eye care Centre. *J Clin Diagn Res.* 2017;11(7):NC01. doi: 10.7860/JCDR/2017/27027.10174
23. Rahaman KS, Majdzadeh R, Holakouie Naieni K, Raza O. Knowledge, attitude and practices (KAP) regarding chronic complications of diabetes among patients with type 2 diabetes in Dhaka. *Int J Endocrinol Metabol.* 2017;15(3):e12555. doi: 10.5812/ijem.12555
24. Belsti Y, Akalu Y, Animut Y. Attitude, practice and its associated factors towards diabetes complications among type 2 diabetic patients at Addis Zemen District hospital, Northwest Ethiopia. *BMC Public Health.* 2020;20(1):785. doi: 10.1186/s12889-020-08953-6
25. Butler R, McClinchy J, Morreale-Parker C, Marsh W, Rennie KL. BMI calculation in older people: the effect of using direct and surrogate measures of height in a community-based setting. *Clin Nutr.* 2017;22:112-115. doi: 10.1016/j.clnesp.2017.07.078
26. Shawahna R, Fahed B, Qadri D, Sharawi L, Soroghli M, Dweik M. Awareness and knowledge of autism Spectrum disorders among pharmacists: a cross sectional study in Palestinian pharmacy practice. *J Autism Dev Disord.* 2017;47(6):1618-1627. doi: 10.1007/s10803-017-3085-5
27. Shawahna R, Atrash A, Jebriil A, Khalaf A, Shaheen E, Tahboosh H. Evaluation of pharmacists' knowledge of women's issues in epilepsy: a cross-sectional study in Palestinian pharmacy practice. *Seizure.* 2017;46:1-6. doi: 10.1016/j.seizure.2017.01.002
28. Shawahna R, Atrash A, Jebriil A, Khalaf A, Shaheen E, Tahboosh H. Pharmacists' knowledge of issues in pharmacotherapy of epilepsy using antiepileptic drugs: a cross-sectional study in Palestinian pharmacy practice. *Epilepsy Behav.* 2017;67:39-44. doi: 10.1016/j.yebeh.2016.11.027
29. Shawahna R, Al-Rjoub M. Risk of error estimated from Palestine pharmacists' knowledge and certainty on the adverse effects and contraindications of active pharmaceu-

- tical ingredients and excipients. *J Educ Eval Health Prof.* 2016;13:1. doi: 10.3352/jeehp.2016.13.1
30. Shawahna R, Haddad A, Khawaja B, Raie R, Zaneen S, Edais T. Medication dispensing errors in Palestinian community pharmacy practice: a formal consensus using the Delphi technique. *Int J Clin Pharm.* 2016;38(5):1112-1123. doi: 10.1186/s12913-019-4485-3
31. Shawahna R, Zyoud A, Jallad D, Hadwan L, Ihssan N, Hlail H. Blood zinc levels in nursing women from different regions of the West Bank of Palestine. *Women Health.* 2018;58(7):822-833. doi: 10.1080/03630242.2017.1342743
32. Demaio AR, Otgontuya D, de Courten M, et al. Exploring knowledge, attitudes and practices related to diabetes in Mongolia: a national population-based survey. *BMC Public Health.* 2013;13:236. doi: 10.1186/1471-2458-13-236
33. Fatema K, Hossain S, Natasha K, et al. Knowledge attitude and practice regarding diabetes mellitus among nondiabetic and diabetic study participants in Bangladesh. *BMC Public Health.* 2017;17(1):364. doi: 10.1186/s12889-017-4285-9
34. Karaoui LR, Deeb ME, Nasser L, Hallit S. Knowledge and practice of patients with diabetes mellitus in Lebanon: a cross-sectional study. *BMC Public Health.* 2018;18(1):525. doi: 10.1186/s12889-018-5416-7
35. Alsous M, Abdel Jalil M, Odeh M, Al Kurdi R, Alnan M. Public knowledge, attitudes and practices toward diabetes mellitus: a cross-sectional study from Jordan. *PLoS One.* 2019;14(3):e0214479. doi: 10.1371/journal.pone.0214479
36. Saleh F, Mumu SJ, Ara F, Begum HA, Ali L. Knowledge and self-care practices regarding diabetes among newly diagnosed type 2 diabetics in Bangladesh: a cross-sectional study. *BMC Public Health.* 2012;12:1112. doi: 10.1186/1471-2458-12-1112
37. Deepa M, Bhansali A, Anjana RM, et al. Knowledge and awareness of diabetes in urban and rural India: the Indian Council of Medical Research India diabetes study (phase I): Indian Council of Medical Research India diabetes 4. *Indian J Endocrinol Metabol.* 2014;18(3):379-385. doi: 10.4103/2230-8210.131191
38. Chatterjee S, Davies MJ, Heller S, Speight J, Snoek FJ, Khunti K. Diabetes structured self-management education programmes: a narrative review and current innovations. *Lancet Diabet Endocrinol.* 2018;6(2):130-142. doi: 10.1016/S2213-8587(17)30239-5
39. Rashed OA, Sabbah HA, Younis MZ, Kisa A, Parkash J. Diabetes education program for people with type 2 diabetes: an international perspective. *Eval Program Plan.* 2016;56:64-68. doi: 10.1016/j.evalprogplan.2016.02.002.
40. Brassard D, Laramée C, Robitaille J, Lemieux S, Lamarche B. Differences in population-based dietary intake estimates obtained from an interviewer-administered and a self-administered web-based 24-h recall. *Front Nutr.* 2020;7:137. doi: 10.3389/fnut.2020.00137
41. Bakare P, Sethi S, Mushtaq I, et al. A study of knowledge attitude practices and identification of perceived barriers towards screening for diabetic retinopathy amongst diabetics in an industrial area in western Maharashtra. *Eur J Clin Exp Med.* 2023;21(3):539-545. doi: 10.1186/s12875-023-02068-8
42. Lalwani RK, Shah JD, Chatterjea T, Nadakuduru PR, Erande S. Prevalence of depression in Indian patients with type 2 diabetes mellitus and/or hypertension: DEPTH Study. *Eur J Clin Exp Med.* 2019;17(4):315-325. doi: 10.15584/ejcem.2019.4.5
43. Islam FMA, Chakrabarti R, Dirani M, Islam MT, Ormsby G, et al. Knowledge, Attitudes and Practice of Diabetes in Rural Bangladesh: The Bangladesh Population Based Diabetes and Eye Study (BPDES). *PLoS One.* 2014;9(10):e110368. doi: 10.1371/journal.pone.0110368
44. Thabit MF. Awareness regarding diabetes mellitus and its complication in Type 2 diabetic patients. *KMCJ.* 2013;9(2):25-28. doi: 10.12889/9876.8
45. Shrestha L, Nagra JS. Knowledge, attitude and practice (KAP) study on diabetes mellitus among Nepalese diabetic patients. *Nepal Med Coll J.* 2005;7(1):51-53. doi: 10.16539/NMC.2005.5.7
46. Smalls BL, Walker RJ, Hernandez-Tejada MA, et al. Associations between coping, diabetes knowledge, medication adherence and self-care behaviors in adults with type 2 diabetes. *Gen Hosp Psychiatry.* 2012;34(4):385-389. doi: 10.1016/j.genhosppsy.2012.03.018



Pectus excavatum treatment with the Nuss procedure: comparative results in pediatric and adult patients – experiences of a single physician

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ABSTRACT

Introduction and aim. Pectus excavatum (PE) is a chest wall deformity characterized by a collapse of the rib cage. The Nuss procedure, originally intended for pediatric patients, is now also used in adults. The main aim of this study is to investigate whether the Nuss procedure can also lead to successful results in adult patients, although it is a widely used treatment method in pediatric patients.

Material and methods. Data from 90 patients (October 2008-May 2020) included age, gender, preoperative findings, Haller index, operative details, and postoperative outcomes. The groups were divided into pediatric (<18 years) and adult (≥18 years) patients. Mann-Whitney U and chi-square tests were used to assess group differences.

Results. The adult group had a significantly higher bar length and preoperative complaints rate ($p < 0.05$). No significant differences were found for other parameters ($p > 0.05$).

Conclusion. The Nuss procedure is safe and effective in both pediatric and adult PE patients. Age and preoperative symptoms influence surgical planning and outcomes, emphasizing their importance for treatment strategies.

Keywords. adult, Nuss procedure, pectus excavatum, pediatric

Introduction

Pectus excavatum (PE) is a congenital deformity characterized by an inward collapse of the sternum due to abnormal growth of the cartilaginous parts of the ribs on the anterior chest wall. There are symmetrical and asymmetrical forms. This condition is four times more common in men than in women. Pectus excavatum can occur at any age, but is usually recognized in the first year after birth and is more common during or after puberty. This deformity is more common in Caucasians. Although the etiology of PE is not exactly known, it is assumed that genetic factors play a role. A familial predisposition is present in 15–45% of patients with PE. There is also an association with some genetic syndromes such

as Marfan syndrome, Ehlers-Danlos syndrome, Noonan syndrome and Turner syndrome; however, the exact interaction of these syndromes in the development of PE has not yet been clarified.¹

The adverse health effects of PE can be physical and psychological. Physically, the depression of the sternum can put pressure on the lungs and heart, impairing respiratory and cardiac function and causing symptoms such as chest pain, shortness of breath and cardiac arrhythmias. Psychologically, it can lead to problems such as lack of self-confidence, social isolation, depression and anxiety due to the shape of the ribcage.²

Pectus excavatum can be diagnosed based on the shape of the anterior chest wall. The severity and symp-

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toms of PE can vary with age. Imaging techniques and tests such as magnetic resonance imaging (MRI), thoracic computed tomography (CT), echocardiography and pulmonary function tests (PFT) can be used to measure the severity of PE and its impact on cardiopulmonary function. The Haller Index is a measure used to assess the severity of PE and to determine the need for surgery. The Haller index is calculated based on the ratio between the widest transverse diameter of the chest and the anteroposterior diameter in the plane of maximum PE. While this ratio is 2.56 ± 0.35 in normal individuals, it can be 3.25 or more in patients with PE. Surgical treatment is recommended for patients with a Haller index above 3.25.³

Surgical and non-surgical methods are used to treat PE. However, there is no scientific evidence that non-surgical methods lead to anatomical correction. One of these treatment methods is the vacuum bell, a device used to pull the sternum forward by applying negative pressure to the chest wall. However, it is not suitable for all patients and its success depends on the age of the patient, the flexibility of the chest wall and the type and severity of the PE. Surgical treatment methods include the modified Ravitch and Nuss procedures. In the modified Ravitch procedure, an incision is made in the anterior chest wall, the cartilaginous parts of the ribs are removed and the sternum is corrected. The Nuss procedure is a minimally invasive procedure and was described in 1998.⁴

The ideal age for the Nuss surgery is usually between 12 and 17 years. At this age, the procedure can be more effective because the rib cage is more flexible and the healing process is faster. With increasing age, the flexibility of the rib cage can decrease and the difficulty of the procedure can increase. The likelihood of recurrence after surgery can also increase with age. It is therefore recommended that Nuss surgery be performed before puberty if possible. Thanks to the Nuss procedure, successful results can now also be achieved in patients in their 30s and 40s.^{5,6}

The Nuss procedure is a surgical intervention performed under general anesthesia. To correct the depression in the chest, a metal bar is inserted through 2-centimeter incisions. This bar is rotated 180 degrees with a special tool to push the rib cage outwards and correct the depression. An aluminum model is also used to determine the height, and the bar is shaped according to this model and inserted into the chest. The operation is performed with a video thoracoscope (VATS) and the procedure is completed by suturing the incisions.⁶

Aim

The main aim of this study is to investigate whether the Nuss procedure can also lead to successful results in adult patients, although it is a widely used treatment method in pediatric patients.

Material and methods

This study comprises a retrospective review of the Nuss procedure performed on patients with PE. Data were collected at a single center between October 2008 and May 2020 (Fig. 1A, 1B, 1C). A total of 90 patients who had not previously undergone surgical PE treatment and had been diagnosed with PE took part in the study. Patients were divided into two groups: under 18 years of age (pediatric group, n=53) and 18 years and older (adult group, n=37). Data examined in the study included age, gender, preoperative findings, Haller index, duration of surgery, length and number of bars used, number of stabilizers, length of hospital stay, perioperative and postoperative complications, and mortality. Haller index above 3.3 were included in the study. These data were taken from hospital records and patient files. This study was conducted in accordance with the Declaration of Helsinki. The study was approved by Istanbul Training and Research Hospital; protocol number (2020/450). Informed consent was obtained from all patients participating in the study.

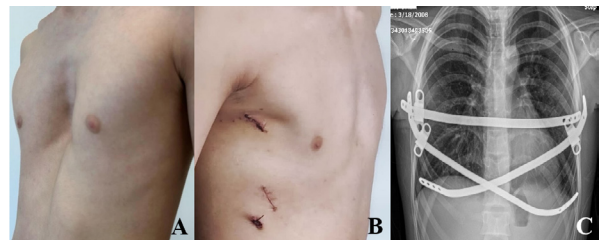


Fig. 1. A: PE, preoperative, B: postoperative image, C: postoperative x-ray

Statistical analysis

Descriptive statistics were used to analyze the data. Mean, standard deviation, median, minimum and maximum values were calculated for numerical data. The distribution of categorical data was examined and statistical significance was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for quantitative independent data and the chi-square test for categorical independent data. All analyzes were performed using SPSS 27.0 software (IBM, Armonk, NY, USA). The significance level was accepted as $p < 0.05$.

Results

The mean age of all patients in the study was 16.6 years (20 ± 7.8 , min. 12, max. 42), with 24.4% female (n=22) and 75.6% male (n=68), and the mean Haller index was 4.2 (4.3 ± 0.7 , min. 3.4 max. 6.1).

The patients' concomitant diseases included scoliosis, kyphoscoliosis, Marfan syndrome, Ehlers-Danlos syndrome, asthma, congenital heart defects, valvular heart disease and cardiac arrhythmias. Preoperative patient complaints included cosmetic and psychological problems, chest pain, palpitations, dyspnea on ex-

ertion and fatigue. Early postoperative complications in patients included pneumothorax, hemothorax, pleural effusion, skin infection, allergic reaction to the bar, early bar displacement, and need for reoperation. Late postoperative complications included chronic persistent pain, relapse after bar removal, and change in bar position (Table 1).

Table 1. Clinical and demographic characteristics of all patients

	Min–max	Median	Mean±SD/n (%)
Age	21–42	16.5	20±7.8
Gender	Woman		22 (24.4)
	Male		68 (75.6)
Haller index	3.4–6.1	4.2	4.3±0.7
Concomitant symptoms of diseases	(–)		22 (24.4)
	(+)		68 (75.6)
	Scoliosis		30 (33.3)
	Kyphoscoliosis		11 (12.2)
	Marfan syndorme		4 (4.4)
	Ehler-Danlos syndrome		1 (1.1)
	Asthma		13 (14.4)
	Congenital heart anomaly		1 (1.1)
	Heart valve disorder		7 (7.8)
	Cardiac arrhythmia		1 (1.1)
Duration of operation/minute	20–85	35	39.9±13.1
Bar length/mm	240–360	290	293.6±30
Number of bars	1–3	1	1.18±0.46
Number of stabilizers	1–3	1	1.17±0.46
Preoperative complaints	(–)		6 (6.7)
	(+)		84 (93.3)
	Cosmetic and psychological		28 (31.1)
	Pain in the chest		33 (36.7)
	Palpitations		41 (45.6)
	Shortness of the breath with increasing exertion, Rapid fatigue		38 (42.2)
Postoperative early complications (<3 months)	(–)		80 (88.9)
	(+)		10 (11.1)
	Pneumothorax		2 (2.2)
	Hemothorax		2 (2.2)
	Pleural effusion		2 (2.2)
	Skin infection		1 (1.1)
	Bar-related allergic reaction		2 (2.2)
	Early slippage of the bar and re-operation		
Postoperative complaints (>3 months)	(–)		75 (83.3)
	(+)		15 (16.7)
	Chronic persistent pain		9 (10)
	Relapse after bar extraction		4 (4.4)
	Change in bar position (late phase)		2 (2.2)
Duration of hospitalization	3–7	4	4.3±1
Time of bar extraction (year)	1.5–5	3	3.2±0.7
Pediatric group			53 (58.9)
Adult group			37 (41.1)

The study included 53 pediatric patients (age range: 12–17, mean age: 15, female: 13, male: 40) and 37 adult patients (age range: 18–42, mean age: 26, female: 9, male: 28). The mean Haller index was 4.2 (4.4±0.6) in the pediatric group and 4.1 (4.3±0.7) in the adult group.

The prevalence of concomitant diseases was 69.8% in the pediatric group and 83.8% in the adult group.

The most common concomitant disease in the pediatric group was scoliosis (34%), the second most common disease was bronchial asthma (15%). In the adult group, the most common concomitant disease (32.4%) was scoliosis, while the second most common diseases (13.5%) were kyphoscoliosis, asthma and valvular heart disease, in equal proportions.

The frequency of preoperative complaints was reported as 88.7 % in the pediatric group and 100 % in the adult group. The most common complaint in the pediatric group (45.3%) was palpitations, while the second most common complaint (37.7%) was shortness of breath and fatigue, which increased with exertion. In the adult group, the most common preoperative complaints (48.6%) were shortness of breath and fatigue, which increased with exertion, while the second most common (45.9%) were chest pain and palpitations in equal proportions.

The average bar length (mm) used in the surgery was 280 mm (279.1±24) in the pediatric group and 320 mm (314.3±25.2) in the adult group. The mean number of bars applied was calculated as 1 (1.1±0.38) in the pediatric group and 1 (1±0.105) in the adult group. The average number of stabilizers used was 1 (1.09±0.35) in the pediatric group and 1 (1.00±0.055) in the adult group. The average operation time was 35 minutes (39.0±12) in the pediatric group and 37 minutes (41.2±14.6) in the adult group. The average length of hospital stay (days) was 4 (4.2±0.9) in the pediatric group and 4 (4.4±1.1) in the adult group (Table 2).

Table 2. Comparison of complications between pediatric and adult groups

		Pediatric group		Adult group		p
		n	%	n	%	
Postoperative early complication	(–)	48	90.6	32	86.5	0.545 ^x
	(+)	5	9.4	5	13.5	
	Pneumothorax	1	1.9	1	2.7	
	Hemothorax	1	1.9	1	2.7	
	Pleural effusion	0	0	2	5.4	
	Skin infection	0	0	1	2.7	
	Bar associated allergic reaction	2	3.8	0	0	
	Early bar displacement and re-surgery	1	1.9	0	0	
Postoperative late complication	(–)	44	83	31	83.8	0.924 ^x
	(+)	9	17	6	16.2	
	Chronic persistent pain	8	15.1	1	2.7	
	Relapse after bar removal	0	0	4	10.8	
	Change in bar position (late phase, 3<month)	1	1.9	1	2.7	

X²-chi-square-test

The early postoperative complication rate was determined in the pediatric group (9.4%, n1: 5) and in the adult group (13.5%, n2: 5). The most common early postoperative complications in the pediatric group

included pneumothorax (1.9%, n1: 1), hemothorax (1.9%, n1: 1), early bar slippage and reoperation (1.9%, n1: 1). In the adult group, the most common early postoperative complication was pleural effusion (5.4%, n2: 2), followed by pneumothorax (2.7%, n2: 1), hemothorax (2.7%, n2: 1) and skin infections (2.7%, n2: 1), which were found in equal proportions. No mortality was observed in either group. The postoperative late complication rate was found to be 17% in the pediatric group (n1: 9) and 16.2 % in the adult group (n2: 6). While the most common late postoperative complication in the pediatric group was chronic persistent pain (15.1%, n1: 8), recurrence after bar removal (10.8%, n2: 4) was the second most common in the adult group. The duration of bar removal (years) was analyzed with an average of 3 years (3.2±0.7) in the pediatric group and an average of 3 years (3.0±0.354) in the adult group (Table 2).

Table 3. Comparative result between pediatric and adult group

	Pediatric group		Adult group		p
	Mean±SD/n (%)	Median	Mean±SD/n (%)	Median	
Gender	Woman	13 (24.5)	9 (24.3)		0.982 ^{x²}
	Male	40 (75.5)	28 (75.7)		
Haller index	4.4±0.6	4.2	4.3±0.7	4.1	0.450 ^m
Concomitant disease	(-)	16 (30.2)	6 (16.2)		0.129 ^{x²}
	(+)	37 (69.8)	31 (83.8)		
Operation duration/minute	39±12	35.0	41.2±14.6	37	0.626 ^m
Bar length (mm)	279.1±24	280.0	314.3±25.2	320	<0.001 ^m
Number of bars	1.11±0.38	1.00	1.27±0.56	1	0.105 ^m
Number of stabilizers	1.09±0.35	1.00	1.27±0.56	1	0.055 ^m
Preoperative complaints	(-)	6 (11.3)	0 (0)		0.034 ^{x²}
	(+)	47 (88.7)	37 (100)		
Postoperative early complication	(-)	48 (90.6)	32 (86.5)		0.545 ^{x²}
	(+)	5 (9.4)	5 (13.5)		
Postoperative late complication	(-)	44	31 (83.8)		0.924 ^{x²}
	(+)	9 (17)	6 (16.2)		
Length of hospital stay	4.2±0.9	4.0	4.4±1.1	4	0.377 ^m
Period of bar removal (years)	3.2±0.7	3.0	3.1±0.7	3	0.354 ^m

Mann-Whitney-U-test / X²-chi-square-test

In patients who developed significant pneumothorax in both groups, lung expansion was achieved by tube thoracotomy (2/day). As culture examination revealed no growth for the skin infection, non-specific antibiotic therapy (1000 mg cephalexin 2×1, 5 days) was administered. Epidural analgesics, opioids and non-steroidal analgesics were used for early postoperative pain control. Other complications resolved spontaneously. In the late phase, some patients were consulted by the algology clinic and placed on an analgesic treatment protocol for patients with chronic pain. Patients who were found to have bar displacement during postoperative follow-up were readmitted for revision.

Given these results, statistical analysis did not detect a significant difference between the adult and pediatric groups in terms of gender distribution, Haller index, comorbidity rate, operative time, number of bars, number of stabilizers, postoperative early and late complication rates, hospital stay, and bar removal time (p>0.05). However, it was found that the bar length and the preoperative discomfort rate were significantly higher in the adult group than in the pediatric group (p<0.05) (Table 3, Figures 2 and 3).

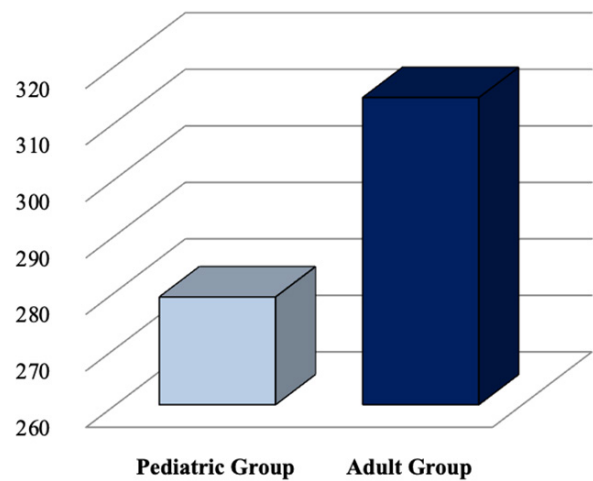


Fig. 2. Comparison between the groups of pediatric and adult in terms of bar length

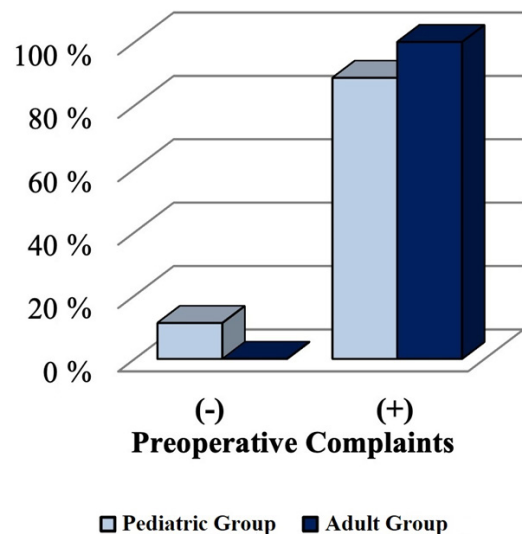


Fig. 3. Comparison between the groups of pediatric and adult in terms of preoperative complaints

Discussion

The Nuss procedure generally takes between 35 minutes and 2 hours, depending on the number of bars to be used. No intensive care is usually required after the operation. Patients usually stay in hospital for 3–5 days. Discomfort such as pain and shortness of breath may occur during the first week, but this can be reduced with

painkillers, physiotherapy and exercises. After the operation, patients lie on their back and avoid lying on their side for about a month.⁶

In our study, there was no significant difference between the pediatric and adult groups in terms of surgery time, suggesting similar success rates. The fact that there was no significant difference between the two groups in terms of hospitalization suggests that the postoperative recovery process does not depend on age. Positive surgical outcomes were achieved in the adult group, which are consistent with the results reported in the literature, but differences in postoperative morbidity were found between the two groups.

The Nuss procedure offers advantages such as a short operation time, minimal blood loss, minimal scarring and rapid recovery. Displacement of the bar may have potential disadvantages such as pneumothorax, infection and recurrence of the pectus and, in rare cases, complications may arise such as nickel allergy to the steel rod. For patients who develop a nickel allergy, the bar may need to be removed or replaced with a titanium bar. A skin test for nickel allergy can be carried out before the operation. Sports should be avoided for a period of time after surgery, but activities such as swimming or fitness can be resumed after 3 months. Sports that require contact can be practiced after 6 months. Removal of the metal bar usually performed after 2 to 4 years. This procedure is shorter and less painful, and patients are usually discharged after one day.^{4,6}

In the original procedure described by Nuss, a single bar was used in most cases. In cases where additional stabilization was required due to more severe deformities, two bars were used. This technique was later slightly modified in some cases by using shorter and more bars to reduce the possibility of bar displacement.⁷

The Nuss procedure has had a positive effect on cardiopulmonary function in adult patients, with studies showing a significant improvement in maximal oxygen uptake during exercise.⁵

One of the most common known failures of the Nuss procedure is the displacement of the bar. The reason for bar displacement may be due to inadequate stabilization of the bar or the patient's movements, e.g., heavy contact sports, etc., in the postoperative period. Complications such as chronic pain lasting longer than 3 months have been reported to be more common in adult patients than in pediatric patients.^{8,9}

In the selection of our patients, no distinction was made between symmetric and asymmetric PE, and asymmetric PE was present in both groups, but its number was low. Early and late displacement or shift of the bar was observed in 1.9% and 0.0% of pediatric patients and in 1.9% and 2.7% of adult patients, respectively.

The surgical technique and the number of stabilizers used were similar in both groups. In the pediatric

group, bar slippage was associated with the patient not following certain rules after surgery. For example, activities such as sports or sleeping on the side can cause increased bar slippage. In contrast, late displacement or slippage of the bar in the adult group was attributed to the stiffer chest wall. Inadequate fixation of the bar was possible in both groups.

Patients compliance with certain restrictions and consideration of anatomical differences in the postoperative period are important to prevent or reduce rod slippage.

In our study, multiple bars were used in both groups. In the pediatric group, more bars (2 or 3) were preferred due to the Grand Canyon Deep Type PE. In addition, the number of stabilizers used was similar in both groups. The reason for using 3 bars in the adult group was that more bars were required due to the hardness of the rib cage. Therefore, we assume that the displacement rates of the bars could decrease due to the altered force distribution.

Kim et al. reported that the risk of postoperative complications was higher in adult patients due to the more frequent asymmetric deformity. The most common complication of asymmetric deformity is bar displacement. They reported that the risk of complications and outcomes in adults with symmetric deformities were comparable to those of children and adolescents, and they emphasized the importance of appropriate patient selection for the Nuss procedure.¹⁰

Jaroszewski and colleagues reported that bar displacement was observed after the Nuss procedure in 1%, 4% and 2% of patients in different age groups, aged 7–14, 15–20 and 21 years, respectively.¹¹

In a study by Casamassina and colleagues, similar displacement rates of 2% and 7% in patients aged 18–29 years and 30–72 years, respectively, were reported. In patients with an average age of 31 years, a bar displacement rate of 4% was observed.¹²

The excessive stiffness of the sternum in adults is also likely the reason why they require more than one bar compared to pediatric patients; this could explain their higher observed average operative times and postoperative infection rates.^{13,14}

Durry al. added a subxiphoid incision to the Nuss procedure to allow better visualization of the anterior mediastinum and reduce the risk of cardiac or pericardial perforation. However, they pointed out that this additional incision increases the operating time and that this can lead to complications.^{15–17}

In our study, apart from the Nuss procedure, no additional surgical intervention was required in only one patient, apart from a 5 mm incision to place a sternal sling at the deepest point of the deformity due to scoliosis and asymmetric deep pectus. We can say that the Nuss procedure can prove its effectiveness in the surgical treatment of PE.

In the study conducted by Di Salvo et al, the most common complication in the early postoperative period in pediatric patients was pleural effusion that did not require chest drainage (8.3%), while the most common late complication was seroma that did not require drainage (55%).¹⁸

In our study, the most common complication in the early postoperative period among patients in the pediatric group was an allergic reaction related to the bar (3.8%), while the most common complication in the late postoperative period (15.1%) was chronic persistent pain. This difference is probably due to several factors, such as the patient population and differences in treatment during postoperative follow-up. Additionally, bar-related allergic reactions in pediatric patients may indicate a special situation that should be considered in the postoperative follow-up of this group.

Study limitations

The main limitations of this study include the fact that it was conducted in a single center, its retrospective design and associated bias, and the limited size of the study group. In future studies, larger participant groups and a prospective design can be used to ensure that the results obtained are more robust.

Conclusion

This study confirms that the Nuss procedure is a safe surgical treatment technique for PE in both young and adult patients. Although the risk of long-term pain after surgery is more common in the pediatric population, adult patients are not more prone to other complications compared to pediatric patients.

Declarations

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Author contributions

Conceptualization, T.D.; Methodology, T.D.; Software, T.D.; Validation, T.D.; Formal Analysis, T.D.; Investigation, T.D.; Resources, T.D.; Data Curation, T.D.; Writing – Original Draft Preparation, T.D.; Writing – Review & Editing, T.D.; Visualization, T.D.; Supervision, T.D.; Project Administration, T.D.; Funding Acquisition, T.D.

Conflicts of interest

No potential conflict of interest was reported.

Data availability

The data used in the study and the details of the method can be requested from the corresponding author.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by Istanbul Training and Research Hospital; protocol number (2020/450). Informed consent was obtained from all patients participating in the study.

References

1. Akhtar M, Razick D I, Saeed A, et al. Complications and Outcomes of the Nuss Procedure in Adult Patients: A Systematic Review. *Cureus*. 2023;20;15(2):e35204. doi: 10.7759/cureus.35204
2. Brungardt J G, Chizek PW, Schropp KP. Adult pectus excavatum repair: national outcomes of the Nuss and Ravitch procedures. *J Thorac Dis*. 2021;13(3):1396-1402. doi: 10.21037/jtd-20-2422
3. Li H, Wang F, Ji G, et al. Modified Nuss procedure for the treatment of pectus excavatum: Experience of 259 patients. *Asian J Surg*. 2023;46(2):692-697. doi: 10.1016/j.asjsur.2022.06.080
4. Torre M, Guerriero V, Wong MCY, Palo F, Lena F, Mattioli G. Complications and trends in minimally invasive repair of pectus excavatum: A large volume, single institution experience. *J Pediatr Surg*. 2021;56(10):1846-1851. doi: 10.1016/j.jpedsurg.2020.11.027
5. Loos ERD, Pennings AJ, Roozendaal LMV, et al. Nuss Procedure for Pectus Excavatum: A Comparison of Complications Between Young and Adult Patients. *Ann Thorac Surg*. 2021;112(3):905-911. doi: 10.1016/j.athoracsur.2020.10.017
6. Squillaro AI, Melhado C, Ozgediz D, Idowu O, Palmer B, Kim S. Minimally invasive repair of asymmetric pectus excavatum: An alternative technique to treating asymmetric morphology. *J Pediatr Surg*. 2022;57(6):1079-1082. doi: 10.1016/j.jpedsurg.2022.01.035
7. Zuidema WP, Steeg AFWVD, Heide SVD, et al. The Outcome of the Single Step Questionnaire in Pectus Excavatum Patients is Phase Dependent. *Eur J Pediatr Surg*. 2020;30(2):205-209. doi: 10.1055/s-0039-1681025.
8. Ye J, Lu G, Feng J, Zhong W. Effect on Chest Deformation of Simultaneous Correction of Pectus Excavatum with Scoliosis. *J Healthc Eng*. 2017;2017:8318694. doi: 10.1155/2017/8318694
9. Zuidema WP, van der Steeg AFW, Oosterhuis JWA, van Heurn E. Trends in the treatment of pectus excavatum in the Netherlands. *Eur J Pediatr Surg*. 2021;31(3):261–265. doi: 10.1055/s-0040-1712182
10. Kim DH, Hwang JJ, Lee MK, Lee DY, Paik HC. Analysis of the Nuss procedure for pectus excavatum in different age groups. *Ann Thorac Surg*. 2005;80:1073-1077. doi: 10.1016/j.athoracsur.2005.03.070
11. Jaroszewski DE, Ewais MM, Chao CJ, et al. Success of minimally invasive pectus excavatum procedures (modified Nuss) in adult patients (30 years). *Ann Thorac Surg*. 2016;102:993-1003. doi: 10.1016/j.athoracsur.2016.03.105

12. Sacco Casamassima MG, Gause C, Goldstein SD, et al. Patient satisfaction after minimally invasive repair of pectus excavatum in adults: long-term results of Nuss procedure in adults. *Ann Thorac Surg.* 2016;101:1338-1345. doi: 10.1016/j.athoracsur.2015.09.102.
13. Ewais MM, Chaparala S, Uhl R, Jaroszewski DE. Outcomes in adult pectus excavatum patients undergoing Nuss repair. *Patient Relat Outcome Meas.* 2018;9:65-90. doi: 10.2147/PROM.S117771
14. Haecker FM, Krebs T, Kocher GJ, Schmid RA, Sesia SB. Sternal elevation techniques during the minimally invasive repair of pectus excavatum. *Interact Cardiovasc Thorac Surg.* 2019;29:497-502. doi: 10.1093/icvts/ivz142
15. Durry A, Gomes Ferreira C, Tricard T, Gicquel P, Becmeur F. Minimally invasive repair of pectus excavatum in children: Results of a modified Nuss procedure. *Ann Chir Plast Esthet.* 2017;62(1):8-14. doi: 10.1016/j.anplas.2016.10.001
16. Johnson WR, Fedor D, Singhal S. A Novel Approach to Eliminate Cardiac Perforation in the Nuss Procedure. *Ann Thorac Surg.* 2013;95(3):1109-1111. doi: 10.1016/j.athoracsur.2012.10.016
17. Kabbaj R, Burnier M, Kohler R, Loucheur N, Dubois R, Jouve JL. Minimally invasive repair of pectus excavatum using the Nuss technique in children and adolescents: indications, outcomes, and limitations. *Orthop Traumatol Surg Res.* 2014;100(6):625-630. doi: 10.1016/j.otsr.2014.05.019
18. Di Salvo N, Ruggeri G, Thomas E, Parente G, Di Mitri M, Lima M. Long-term evaluation of patient satisfaction and quality of life in pectus excavatum repair. *Annals of Pediatric Surgery.* 2022;18:84. doi: 10.1186/s43159-022-00226-8



Prevalence and predictors of job stress among healthcare workers in secondary health centers in a Nigerian City

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ABSTRACT

Introduction and aim. Stress is prevalent in all aspects of our lives and it seems particularly overwhelming in the workplace. This study identified prevalence and factors associated with job stress among healthcare workers in public secondary health facilities in the Ibadan metropolis, Nigeria.

Material and methods. The study was a cross-sectional study. Two hundred and sixty-nine healthcare workers were recruited over three months. The respondents were recruited using the systematic sampling techniques.

Results. The age range of the participants was 20–59 years with a mean age of 39.28(SD 9.39). The prevalence of job stress among physicians was 42.1%, health management staff 31.3%, pharmacists 28.6%, nurses 23.5%, and laboratory personnel 23.1%. Most participants 162(61.1%) had functional families. Participants from polygamous families were about 70% less likely to report job stress compared with those from monogamous setting (OR=0.3, 95%CI 0.07–0.9). Participants from dysfunctional families were about 2 times more likely to report job stress compared to those with functional families. OR=2.0, 95%CI (1.09–3.56).

Conclusion. Compared with nurses, this study demonstrated a higher prevalence of job stress among physicians and other healthcare workers. Family type and family support were predictors of job stress among healthcare workers. The outcome of this study would be used as a source of information for practice and policy making for health facilities in Nigeria, and some places in Africa, with the aim of planning improved conditions for health workers through appropriate job stress management.

Keywords. healthcare, job stress, predictors, prevalence, workers

Introduction

Stress is a situation where the human's homeostasis is threatened or the individual perceives a situation as threatening either emotionally or physically. It is a subjective phenomenon and an anxiety-based syndrome, which manifests differently in different persons and hence, the lack of a stereotyped definition.¹ According to the stress framework system, there are three kinds of stress; sustress (inadequate stress), eustress (good

stress), and distress (bad stress). Eustress may have health benefits, but both sustress and distress may lead to the impairment of normal physiological functions and could result in pathological conditions.² A strong challenge on the homeostasis produces distress (stress) which triggers a stress response and the consequent damaging effects. Stress can therefore be described as the adverse psychological and physical reactions that occur in an individual as a result of his or her inability

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ity to cope with the demands being made on him or her.³ Stress is a universal and inevitable component of life, and hence, some degree of stress is not harmful. It is found in all aspects of our lives; it seems particularly overwhelming in the workplace.⁴ According to the World Health Organization (WHO), stress, especially that relating to work, is the second most frequent health problem, impacting one third of employed people in the European Union.⁵ Job stress has been defined by the Center for Disease Control (CDC) as the harmful physical and emotional responses that occur when the requirements of the job do not match the capabilities, resources or needs of the worker.⁶ It is a subjective experience and the predisposing factors include previous life experiences, gender, genetic endowment, personality traits and age.⁷ Job stressors may contribute to organizational inefficiency, high staff turnover, absenteeism due to sickness, decreased quality, and quantity of practice, increased costs of health care, and decreased job satisfaction.¹ Globally, the costs of job-related stress are estimated to be approximately \$5.4 billion each year, second only to the most frequent occupational health problem, low back pain.⁸ Inadequate staff to cover the different units is the most reported source of stress for healthcare workers in several studies, while emotional issues relating to patient death and dying is the second most reported. These findings are supported by studies in Malaysia and Jordan that revealed major sources of stress as work load and death and dying.⁹

Certain scientists showed that nurses are the backbone of the health industry.¹⁰ They develop closer relationship with the patients more than any other healthcare personnel and are crucial to the smooth running of any hospital. This enormity of work that nurses have to contend with results in stress which is a major cause of concern for many nurses at work.¹¹ Also, medical doctors often go through some stress related to their profession while carrying out their duties.¹² Several studies have shown that there is a higher level of stress among doctors as compared to the general population.¹³ Rates of stress are elevated in all doctors, regardless of the setting in which they work, but junior and female doctors are particularly at risk. The stress management program will help to reduce the job stress, create job effectiveness, and have a good work–life balance.¹⁴

In Nigeria, there is limited health related studies in this area, despite the level of the industrial disharmony in the health sector, increasing complaints in service delivery in health institutions and increasing evidence of impact of stress on health workers. The prevalence of psychosocial stress among health workers in a mission hospital in South-Western Nigeria, was reported to be 26.2%.¹⁵ The WHO has viewed stress as a global epidemic as stress has recently been observed to be associated with 90% of visits to physicians.¹⁶ The most

common negative consequences of job stress are physical injuries, headaches, back pain, inability to concentrate, poor judgment, irritability, use of drugs and cigarette, absenteeism, increased number of accidents and inability to organise.¹⁷ Recent studies have indicated that job stress has a major effect on individual physiology, psychology, and behavior, for example, job performance.¹⁸ What are the determinants of job stress among healthcare workers in public secondary health facilities? Job stress has been recognized as a major risk factor for the development of physiological and psychological problems among employees of modern work organizations including healthcare workers.¹⁹

Aim

This study aimed to identify the prevalence and predictors of job stress among healthcare workers in public secondary health facilities in Ibadan metropolis in order to suggest policies and guideline to manage job stress among healthcare workers. In addition, research on family dynamics is still inadequate and family support of healthcare workers were assessed in this study. The exploration of family dynamics of the participants in this study has made it different from the other studies on job stress.

Material and methods

Study setting

The study was conducted among Healthcare workers in Government-owned secondary health facilities in Ibadan, Oyo state, Nigeria. Ibadan is located about 125 kilometers inland from Lagos. The population of the city is approximately 3,800,000 according to 2006 census estimates. Ibadan is made up of 11 local government areas and has ten State public secondary health facilities within her metropolis. The total health workforce for the secondary health facilities in Ibadan metropolis is 1,395.

Scope of the study

The scope of the study covered hospital job stress and included all categories of workers involved in the delivery of health care.

Study population

The study population was healthcare workers in the State public secondary health facilities, within Ibadan metropolis.

Study design

The study was a hospital-based cross-sectional study and was conducted from July to September 2021.

Inclusion criteria: Healthcare workers at the designated public secondary health facilities within Ibadan metropolis who consented to participate in the study.

Exclusion criteria: These included pregnant health workers, because of their vulnerability and obvious confounder, and health workers with hemoglobinopathy, as their clinical state could ordinarily be stressful.

Sample size determination The Cochran formula below was used for sample size determination.²⁰ This is for populations that are large ($\geq 10,000$).

$$n_0 = \frac{Z^2 pq}{d^2}$$

where n_0 is the minimum sample size.

Z is the Standard normal deviate, usually set at 1.96, at 95% confidence interval.

p is the prevalence rate of job-related stress. A prevalence of 26% was reported in a study among healthcare workers at a mission hospital in South West Nigeria.¹⁵ q is $1 - p$, and the desired level of precision was 0.05.

Sample size

$$n_0 = \frac{1.96^2 \times 0.26 \times (1 - 0.26)}{(0.05 \times 0.05)}$$

$n_0 = 296$.

Allowing for a 10% non-response, the minimum sample size (n_0) required for this study was $(29.6 + 296) = 325.6$ (326) participants.

The finite population correction factor was then applied because the population to be studied was less than 10,000. The study population was 1,395. And for a finite population of less than 10,000, then the adjusted sample size was calculated below:

$$n = \frac{n_0 N}{n_0 + (N - 1)}$$

n is the minimum sample size

N is finite population size ($< 10,000$) = 1,395

n_0 is the sample size with no correctional factor

$$n = \frac{326 \times 1,395}{326 + (1,395 - 1)} = \frac{454,770}{1,720}$$

$n = 265$. This was the minimum sample size for this study.

Sampling techniques

The sampling technique involved five steps:

Step one: calculation of total population of health workers

The population of all health workers in the Secondary Health facilities in Ibadan metropolis was taken and the total workforce for each facility and the grand total were calculated. The grand total was 1,395 health workers.

Step two: stratification

For the purpose of this research, healthcare workers were divided into the modified six broad categories according to the WHO 2013 Global Atlas of the Health Workforce.²¹ The broad groups are Physicians and Den-

tists (Specialists and Generalists), Nursing and Midwifery personnel, Pharmaceutical personnel, Laboratory health workers, Health management and support workers, and other health workers (Dieticians and Nutritionists, Medical assistants, Physiotherapists, Medical trainees, Interns, Respiratory therapists, operators of medical and dental equipment).

Step three: proportional allocation of study participants to health centers

Each facility was allotted study participants using a stratified proportionate method, based on each facility's staff strength, using the sample size, as shown in Table 1. For Ring Road State Hospital, the study participants; $280/1395 \times 265 = 53$.

Step four: calculation of study participants for professional groups

The study participants for each professional group were also proportionately calculated for each facility, using their number in the facility, the staff strength, and the number of study participants already allotted to the facility. For example, at the Ring Road State Hospital, the total staff strength was 280, and 53 participants were allotted to the facility. Since there are 23 Doctors in the facility, the number of Physicians recruited at the facility was:

$$\frac{23 \times 53}{280} = 4$$

The number of doctors recruited at Jericho Specialist Hospital was

$$\frac{17 \times 33}{173} = 3$$

The total population of health workers at Jericho Specialist Hospital was 173. Thirty-three participants were allotted to the facility and the total number of doctors was 17 (Table 1).

Step five: systematic random sampling techniques

Their nominal rolls were accessed, and this served as a sampling frame for data collection. The sampling interval was calculated for each professional group in each facility. For Doctors at Ring Road State Hospital, the total number of doctors was 23 and 4 was recruited, then the sampling interval, $K = 23/4 = 5.7$. The first patient was selected by simple random technique by the use of Microsoft Excel 2016 and every 6th patient was selected until the required study participants were recruited. The same formula was applied to other professional groups in all the study facilities, having proportionately calculated the number of study participants for each professional group in the health facilities, the total number of study participants for each professional group, making up the required sample size was shown in Table 2.

Table 1. Study participants required per each public secondary health facility

Facility	Study population per facility	Calculation	Number of respondents
Ring Road State Hospital	280	$\frac{280 \times 265}{1395}$	53
Adeoyo Maternity Hospital	408	$\frac{408 \times 265}{1395}$	77
General Hospital, Moniya	90	$\frac{90 \times 265}{1395}$	17
Oni Memorial Children Hospital	121	$\frac{121 \times 265}{1395}$	23
Government Dental Centre	57	$\frac{57 \times 265}{1395}$	11
Jericho Specialist Hospital	173	$\frac{173 \times 265}{1395}$	33
Jericho Nursing Home	110	$\frac{110 \times 265}{1395}$	21
Maternal and Child health Hospital	77	$\frac{77 \times 265}{1395}$	15
St Peter's Maternity Hospital	61	$\frac{61 \times 265}{1395}$	12
Secretariat Clinic	18	$\frac{18 \times 265}{1395}$	3
Total			265

Table 2. Study participants required for each professional group per facility*

Professional group	RRSH	AMTH	JNH	AREMO	Dugbe	Apata	OMCH	Moniya	JSH	Sec Clin	Total
Doctors	4	5	1	1	1	1	2	1	3	-	19
Nurses/midwives	23	32	7	3	1	5	9	5	11	1	97
Pharmacy	1	1	1	-	-	1	1	1	1	-	7
Laboratory staff	5	7	3	1	-	1	3	1	3	1	25
Other health workers	8	18	2	2	5	2	3	4	8	-	52
Health Mgt support workers	12	14	7	5	4	5	5	5	7	1	65

* RRSH – Ring Road State Hospital, AMTH – Adeoyo Maternity Teaching Hospital, JNH – Jericho Nursing Home, Aremo – St Peter's Maternity Hospital Aremo, Dugbe – Government Dental Centre Dugbe, Apata – Maternal and Child Health Hospital Apata, OMCH – Oni Memorial Children Hospital, Moniya – General Hospital Moniya, JSH – Jericho Specialist Hospital, Sec Clin – Secretariat Clinic

Study instruments

A pretested study questionnaire

The questionnaire was pretested on 30 health workers chosen randomly among some of the public secondary health facilities namely Adeoyo Maternity Teaching Hospital, Ring Road State Hospital, and Jericho Specialist Hospital, Ibadan to ensure there is no ambiguity in its content. The structured questionnaire consists of:

1. Socio-demographic data and family characteristics

This section contains information on the socio-demographic characteristics of participants including age, sex, marital status, family size, family type, family stage,

religion, tribe, occupational group, and duration of employment in the civil service.

2. Medical history

This section assessed respondent's past and present clinical history, to rule out chronic disabilities like sickle cell disease and people with chronic pain outside work. A menstrual history was also obtained. The mandatory pre-employment medical records of respondents were checked, to retrieve their hemoglobin genotype.

Perceived job-related stress scale (Job-Demand control scale)

The job contents questionnaire embedded with the Job-Demand-Control-Model was used to assess psychological job demand, job control, and social support among respondents. The Cronbach alpha coefficients acceptable for decision latitude and psychological job demands are 0.70 and 0.72, respectively while it is 0.86 for social support.²² This portion of the instrument uses the occupational stress questionnaire, otherwise called 'job contents questionnaire'. It divides job strain into four modalities: high job strain, low job strain, passive job, and active job; based on psychological job demand and decisional latitude. The section contains three subsections which include psychological job demand with five questions, decisional latitude (job control) with six questions, and social support at work with four questions. The combination of the psychological job demand and the decisional latitude (job control) was used to determine stress levels among study participants. The median values were used to divide the study participants into four groups as documented in previous studies.²³

Assessment of job satisfaction (job satisfaction scale)

This section contains four parts measuring job satisfaction among respondents.²⁴ They responded with very dissatisfied, dissatisfied, satisfied, and very satisfied to each statement, with a scale of one to four. The score from the four items was summed up, and the median value was used to categorize respondents' view on their job satisfaction into low and high.

Assessment of family functioning and support

The family APGAR questionnaire is designed to measure family functioning. It was used to measure family support for respondents in a previous study.²⁵ It is a five-item questionnaire developed to assess family support using five parameters of family functioning. It allows three possible responses (2, 1, 0) to each of the five parameters of adaptation, partnership, growth, affection, and resolve. The total score ranging from zero to ten was used to range respondents' satisfaction as no, low or high satisfaction with family function, and their families were classified respectively as either severely dysfunctional (0–3), moderately dysfunctional (4–6) or functional family (7–10).

Data analysis

The data collection lasted over three months. Data collected were cleaned and data analysis was done using the Statistical Package for Social Sciences (SPSS) version 23 (IBM, Armonk, NY, USA). Findings were presented in tables and all were interpreted. The Chi-square test was used to assess the association between two categorical variables. The level of significance was put at $\leq 5\%$ ($p \leq 0.05$). Logistic regression was used to assess the predictors of job stress.

Ethical clearance

Ethical clearance was obtained from the Ethical Committee of the Ministry of Health, Oyo state, Nigeria and written informed consent was obtained from every subject, prior to participation. The reference number for ethical approval is AD 13/479, 2089^c.

Table 3. Socio-demographic characteristics of the studied health workers (n=265)

Characteristics		Number	Percentage (%)
Gender	Male	54	20.4
	Female	211	79.6
Age group, years	20 to 29 years old	45	17
	30 to 39 years old	89	33.6
	40 to 49 years old	86	32.5
	50 to 59 years old	45	17
Mean age (SD)	39.28 (9.39)		
Marital Status	Single	56	21.1
	Married	209	78.9
Educational Status	University graduate	172	64.9
	Post-secondary	68	25.7
	Secondary	22	8.3
	Primary School	3	1.1
Occupational Groups	Doctors	19	7.2
	Nurse/Midwives	102	38.5
	Pharmaceutical personnel	7	2.6
	Laboratory personnel	26	9.8
	Other health workers (physiotherapist, dietician, social workers, ward aids, laundry staff, cleaners)	63	23.8
	Health management and support workers (admin staff, account, medical records, security, ambulance drivers)	48	18.1
Family Type	Monogamous	222	83.8
	Polygamous	32	12.1
	Single parents	11	4.2
Family Size	Two members	15	5.7
	Three members	32	12.1
	Four members	110	41.5
	Five members and above	108	40.8

Results

Socio-demographic characteristics of the study participants

Table 3 shows the demographic characteristics of healthcare workers in public secondary health facilities in Ibadan metropolis. Out of the 265 subjects,

the mean age of the participants was 39.28 years, with a standard deviation (SD) of 9.39. Most participants, 33.6% were between 30 to 39 years of age, while the rest belonged to other age group categories. Most respondents, 83.8%, were from monogamous settings, 12.1% were from polygamous settings, 4.2% were single parents.

Pattern of job stress among the health workers in secondary health facilities in Ibadan

Table 4 shows the pattern of job stress among healthcare workers in public secondary health facilities in Ibadan, Nigeria. Majority of the participants, 183(69.1%) reported no job stress, while 82(30.9%) reported job stress and this is the prevalence of job stress among public secondary health care workers in Ibadan metropolis. Of the no job stress category, 14.3% reported their job as passive, 17.4% had low job strain, and 37.4% reported their job scheduled as active job.

Table 4. Pattern of job stress among the health workers (n=265)

Characteristics	Number	Percentage
Job stress groups		
Job stress	82	30.9
No job stress	183	69.1
Job stress levels		
Job stress (High job strain)	82	30.9
No job stress	0	0
Passive job	38	14.3
Low job strain	46	17.4
Active job	99	37.4
Job demand		
Low	84	31.7
High	181	68.3
Job control		
Low	120	45.3
High	145	54.7
Social support at work		
Low	125	47.2
High	140	52.8

Association between job stress and socio-demographic characteristics of the respondents

As shown in Table 5, job stress was commoner among age group 30 to 39 with 44.9% having job stress while 25.6% of age group 40 to 49 reported job stress. The prevalence of job stress among physicians was 42.1%, other health workers 42.9%, health management and support staff 31.3%, pharmaceutical personnel 28.6%, nurses and midwives 23.5%, and laboratory personnel 23.1%. Out of the 222 respondents that came from a monogamous setting, 34.7% reported job stress, while 9.4% of the 32 respondents from a polygamous setting had job stress, while 18.2% of the 11 single parents had job stress.

Table 5. Association between job stress and socio-demographic characteristics of the respondents

Characteristics	Stress		No stress		χ^2 (df)	P	
	Number	%	Number	%			
Gender	Male	15	27.8	39	72.2	0.318 (1)	0.573
	Female	67	31.8	144	68.2		
Age group, years	20 to 29 years old	9	20	36	80	12.733 (3)	0.005*
	30 to 39 years old	40	44.9	49	55.1		
	40 to 49 years old	22	25.6	64	74.4		
	50 to 59 years old	11	24.4	34	75.6		
How long have you been in service?	Less than 5 years	25	30.5	57	69.5	9.641 (3)	0.022*
	5 to 9 years	26	46.4	30	53.6		
	10 to 14 years	15	28.8	37	71.2		
	15 years and above	16	21.3	59	78.7		
Marital status	Single	12	21.4	44	78.6	3.008 (1)	0.083
	Married	70	33.5	139	66.5		
Educational status	University graduate	47	27.3	125	72.7	4.721 (2)	0.094
	Post-secondary school	23	33.8	45	66.2		
	Secondary or less	12	48	13	52		
Occupational groups	Doctors	8	42.1	11	57.9	8.690 (5)	0.122
	Nurse/Midwives	24	23.5	78	76.5		
	Pharmacists	2	28.6	5	71.4		
	Laboratory personnel	6	23.1	20	76.9		
	Physiotherapist, dietician	27	42.9	36	57.1		
	Admin staff and others	15	31.3	33	68.8		
Family type	Monogamous	77	34.7	145	65.3	9.259 (2)	0.010*
	Polygamous	3	9.4	29	90.6		
	Single parents	2	18.2	9	81.8		
Family size	Family size of 2 or 3 members	16	34.0	31	66	1.194 (2)	0.551
	Family size of 4 members	30	27.3	80	72.7		
	Family size of 5 members and above	36	33.3	72	66.7		

Table 6. Association between job stress, job satisfaction and family support among the respondents

Characteristics	Stress		No stress		χ^2 (df)	P	
	Number	%	Number	%			
Levels of family support	Functional family	37	22.8	125	77.2	13.459 (2)	0.001
	Highly dysfunctional family	5	55.6	4	44.4		
Characteristics	Stress		No stress		χ^2 (df)	P	
	n=82	%	n=183	%			
Levels of job Satisfaction	Low	21	29.2	51	70.8	0.146 (1)	0.702
	High	61	31.6	132	68.4		

Association between job stress and family support among study participants

Table 6 shows the association between job stress and family support among respondents. Overall, there was a statistically significant relationship between job stress and family support. Out of the 9 respondents with highly dysfunctional families, 5 (55.6%) reported job stress while 40

(42.6%) of the 94 respondents with dysfunctional families reported job stress whereas only 37 (22.8%) of the 165 respondents with functional families had job stress.

Logistic regression analysis of variables affecting level of job stress

Table 7 shows the binary logistic regression analysis of variables affecting level of job stress. Overall, participants from polygamous families and having functional families were protective against job stress. Participants from polygamous families were 70% less likely to report job stress compared to those from monogamous setting. OR=0.3, 95%CI (0.07- 0.9). Participants from dysfunctional families were about 2 times more likely to report job stress compared to those with functional families OR=2.0, 95%CI(1.09 - 3.56).

Table 7. Binary logistic regression analysis of variables affecting job stress among healthcare workers*

	Job stress	Odds ratio	(95%CI)	P
Age group, years	20 to 29 years old	Reference		
	30 to 39 years old	2	(0.72–5.65)	0.183
	40 to 49 years old	1.4	(0.41–4.88)	0.587
	50 to 59 years old	2.3	(0.47–11.54)	0.297
How long have you been in service? (In years)	Less than 5 years	Reference		
	5 to 9 years	1.4	(0.58–3.36)	0.455
	10 to 14 years	0.8	(0.27–2.14)	0.605
	15 years and above	0.5	(0.13–1.64)	0.235
Family type	Monogamous	Reference		
	Polygamous	0.3	(0.07–0.9)	0.033
	Single parents	0.5	(0.07–2.6)	0.374
Family support	Functional family	Reference		
	Highly dysfunctional family	4.1	(0.82–20.85)	0.085
	Dysfunctional family	2	(1.09–3.56)	0.024

* Dependent variable: job stress, predictors: family support, family type

Discussion

Summary of main findings

The age range 30 to 39 years had the largest subjects in the study with 33.6% of the study participants and was mostly affected by job stress with 44.9% reporting job stress. The prevalence of job stress in this study was 30.9%, higher in female (31.8%) participants than the males (27.8%) and high among physicians. Also, the prevalence of job stress was found to be higher among married respondents (33.5%) as against 21.4% reported among the unmarried, single respondents and respondents from monogamous family reported more job stress than other family types. The type of family was also a predictor of job stress. The prevalence of job stress was lower among those who had spent at least 15 years in service. The prevalence of musculoskeletal pain was 54.3%, and 38.9% of the respondents believe their work schedule caused their musculoskeletal pain. Respondents from highly dysfunctional families were more likely to report job stress compared

to those with functional families. The family support was also a predictor of job stress.

Interpretation of findings and comparison with existing literatures

From this study, the prevalence of job stress among physicians was high which was similar to the findings from a study among health workers in Korea where the prevalence of job stress was highest among the physicians.²⁶ This suggests that the prevalence of stress among physicians is high in our environment, as seen in many other studies. A United States of American study also reported that higher-status healthcare workers, physicians, and nurse practitioners are more likely than their colleagues to report work-life conflict, irregular work hours, and heavy work pressure.²⁷ These stressors explain an appreciable amount of the higher levels of burnout found among physicians and nurse practitioners. Collectively, the results lend support to “the stress of higher status” hypothesis and provide insights into the job demands and mental health issues confronted by today’s medical workforce.²⁸ Physicians have to cope with decision-making on administrative and emotional issues at work and at home. Respondents within the age group 30 to 39 years were mostly affected by job stress in this study. However, this is in contrast to the findings in a similar study among health workers in Oyo state, Nigeria where respondents aged less than 30 years were mostly affected but similar to that among medical workers in China where respondents aged 31 to 40 years were mostly affected.^{15,29} The higher stress level in the relatively younger age groups could be explained by the fact that those are the most productive ages when individuals have to cope with the demands of managing spouses, children, and aged parents along with the demands of the workplace. The prevalence of job stress in this study was higher in female participants than in their male counterparts. The finding was similar to a study conducted among health workers in Southeast Nigeria, where the prevalence of stress was higher in females than in male participants.³⁰ The female preponderance may have to do with family demands, emotional issues with patients, and other workplace demands.

In this study, the prevalence of job stress was found to be higher among married respondents than single respondents. This is contrary to some previous studies where job stress was found to be more common among single healthcare workers.³¹ However, the finding was similar to that of a study of healthcare workers when caring for COVID-19 patients in China, where married health workers were found to have higher levels of stress.³² It follows that marital status may have varying effects across studies and geographical locations on the ability to cope with work stress. Married health workers could be deriving emotional support from their spouses and thus able to douse the job tension after the days’

work while single health workers may be free from the pressure of coping with additional responsibilities at the home front. However, COVID-19 pandemic would add to the level of stress among the subjects.³³ Married health workers might however had a higher prevalence of job stress, as found in this study, due to the fact that they are confronted with other demanding responsibilities at the home front. In this study, respondents from monogamous families reported higher level of job stress than other family types. This finding was consistent with the findings in a study among hospital nurses in a tertiary health centre in Nigeria where depersonalization was associated with a monogamous family setting and smaller family size.³⁴ Higher levels of stress among health workers in a monogamous setting may be explained on the basis of inadequate social support as compared to those from a polygamous setting.

Job stress improves with the number of years in service according to this study. Respondents that had spent between five to nine years in service had the highest level of job stress which is least among those who had spent 15 years or more in service. Job stress is likely going to be commoner among younger workers due to inexperience, inadequate orientation, poor coping strategies for stressful workplace demands, and unmet needs after a few years in service. With longer years in service, they would have adjusted and have better coping mechanisms. The finding was similar to the reports of other studies on health workers in other places.³⁵ The prevalence of musculoskeletal pain was high in this study. This finding was similar to that of a systematic review of the evaluation of the prevalence of musculoskeletal disorders in nurses.³⁶ Repetitious movements, awkward postures, and high force levels were the three primary risk factors that have been associated with work-related musculoskeletal disorders. The nursing profession in particular, and healthcare work in general, is considered as physically and psychologically demanding, and a risk factor for musculoskeletal disorders.³⁷ Generally, studies have shown that musculoskeletal problems are particularly common in healthcare workers who are in direct contact with patients.³⁸ In this study, the prevalence of job stress was highest among the highly dysfunctional families and lowest among the functional families. Social support is an important protective factor for psychological resilience that alleviates mental stress and lifts psychological barriers.³⁹

Implications for education and training

Job stress awareness should be incorporated into the training curriculum of health care workers, right from their training days and the need to pro-actively take steps to prevent its damaging effects.

How this study might affect research, practice or policy

The outcome of this study would be used as a source of

information for practice and policy making for health facilities in Nigeria and some places in Africa, with the aim of planning improved conditions for health workers through appropriate job stress management. Family physicians should use available opportunities to explore family dynamics during routine visitations by health workers in view of their being predictors of job stress. The findings would serve as the basis for future research work involving healthcare workers in health facilities. This study has helped to determine job stress prevalence among healthcare workers in public secondary health facilities. It also broadened knowledge about gender and socio-demographic considerations, as well as differential response by different professional group to job stress. The knowledge obtained from this study would therefore be beneficial, both to the health workers and the practice population accessing health care in the facilities.

Study strengths and limitations

This study was a cross-sectional study by design, which means findings may not be a reflection of causal relationships of job stress among health workers. However, the findings would help in the care of both the health care workers and their practice population, by serving as a data base for further studies. It was a public secondary health facility-based study, so the findings are representative of health care workers in these facilities and may not completely be a true reflection of other categories of healthcare workers at other levels of healthcare delivery. Additionally, most of the subjects were females which showed that there are more female health workers, mostly nurses and other professionals in the employment of Oyo State in Nigeria. The study showed that the factors associated with job stress among healthcare workers cannot be limited to work characteristics such as work overload, shortage of manpower, poor incentives, poor social support, row conflict, career progression, lack of reward system etc., but also linked to certain socio-demographic characteristics of the workers.

Suggestions for further studies

There is need for further studies to understand the concept, predisposition, features, effect and possible coping strategies of job stress among other cadres of health care workers apart from the current emphasis on nurses. Future research on work-related stress should be bigger, multi-centered and involve health care workers at the different levels of health care delivery, that is, primary, secondary and tertiary, in order to discover which level of health care poses the greatest risk of job stress among health workers and help health administrators to channel resources appropriately

Conclusion

This study demonstrated the fact that job stress is

common among healthcare workers and that there is a need for prompt attention to prevent its debilitating effect on the health of the healthcare workers. Unlike several other studies that reported nurses as the most stressed group of healthcare workers, this study was able to demonstrate higher prevalence of job stress among physicians and other healthcare workers. The study showed that age, number of years in service, family type and family support were associated with job stress among healthcare workers. The study also showed that family type and family support were predictors of job stress.

Declarations

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Author contributions

Conceptualization, D.F.O, I.A.A, F.A.O and T.H.I; Methodology, D.F.O, I.A.A, F.A.O and T.H.I; Software, D.F.O, I.A.A, F.A.O and T.H.I; Validation, D.F.O, I.A.A, F.A.O and T.H.I; Formal Analysis, D.F.O, I.A.A, F.A.O and T.H.I; Investigation, D.F.O, I.A.A, F.A.O and T.H.I; Resources, D.F.O, I.A.A, F.A.O and T.H.I; Data Curation, D.F.O, I.A.A, F.A.O and T.H.I; Writing – Original Draft Preparation, D.F.O, I.A.A, F.A.O and T.H.I; Writing – Review & Editing, D.F.O, I.A.A, F.A.O and T.H.I; Visualization, D.F.O, I.A.A, F.A.O and T.H.I; Supervision, I.A.A, F.A.O and T.H.I; Project Administration, D.F.O, I.A.A, F.A.O and T.H.I; Funding Acquisition, D.F.O, I.A.A, F.A.O and T.H.I.

Conflicts of interest

The authors declare that there is no conflict of interest.

Data availability

The datasets generated during and/or analysed during the current study are not publicly available due to the caveat for ethical approval that the responses of the respondents would be kept confidential. However, they would be available from the corresponding author on reasonable request.

Ethics approval

Ethical clearance was obtained from the Ethical Committee of the Ministry of Health, Oyo state, and written, informed consent was obtained from every subject, prior to participation. The reference number for ethical approval is AD 13/479, 2089^c.

References

1. Babatope IS. Causes and effects of job-related stress among polytechnic librarians in Delta State, Nigeria. *Int J Libr Sci.*

- 2013;2(1):1-5.
2. Agyapong B, Chishimba C, Wei Y, et al. Improving Mental Health Literacy and Reducing Psychological Problems Among Teachers in Zambia: Protocol for Implementation and Evaluation of a Wellness for Teachers. Email Messaging Program. *JMIR Res Protoc.* 2023;12(1):e44370. doi: 10.2196/44370
 3. Ekienabor EE. Impact of job stress on employees' productivity and commitment. *Int J Res Bus Manag Account.* 2016;2(5):124-133.
 4. Aslam HD, Jamil R, Tariq A. Stress in medical practitioners in private healthcare industry. *Asian Soc Sci.* 2014;10:111-116.
 5. World Health Organization. Regional Office for Europe. Mental health: facing the challenges, building solutions: report from the WHO European Ministerial Conference. World Health Organization. Regional Office for Europe. <https://iris.who.int/handle/10665/326566>. Accessed January 2, 2024.
 6. The National Institute for Occupational Safety and Health. Stress at work. <https://www.cdc.gov/niosh/docs/99-101/default.html>. Accessed September 6, 2023.
 7. Sandi C. Stress and cognition. *Wiley Interdisciplinary Reviews: Cognit Sci.* 2013;4(3):245-261.
 8. Health and Safety Executive. Stress-related and psychological disorders. <http://www.hse.gov.uk/statistics/causdis/stress.pdf>. Accessed August 4, 2018.
 9. Brookes K, Limbert C, Deacy C, O'Reilly A, Scott S, Thirlaway K. Systematic review: Work-related stress and the HSE Management Standards. *Occup Med.* 2013;63(7):463-472, doi: 10.1093/occmed/kqt078
 10. Thian JHM, Kannusamy P, Klainin-Yobas P. Stress positive effectively and work engagement among nurses: An integrative literature review. *Singapore Nurs J.* 2013;40:24-33.
 11. Francis A, Josephine E, John M, et al. Assessing Nurses capacity for Health Research and Policy Engagement in Nigeria. *J Appl Med Sci.* 2013;2(4):35-51.
 12. Halpin Y, Terry LM, Curzio J. A longitudinal, mixed methods investigation of newly qualified nurses' workplace stressors and stress experiences during transition. *J Adv Nurs.* 2017;73(11):2577-2586. doi: 10.1111/jan.13344
 13. Issa BA, Yussuf AD, Olanrewaju GT, Abiodun OA. Mental health of doctors in a tertiary hospital in Nigeria. *Pan Afr Med J.* 2014;19:178. doi: 10.11604/pamj.2014.19.178.3642
 14. Ntaji MI, Okhakhu AI, Bamidele JO. Job satisfaction and stress among medical practitioners in Edo State, Nigeria. *Niger Res J Clin Sci.* 2011;1:27-33.
 15. Owolabi AO, Owolabi MO, Olaolorun AD, Olofin A. Work-related stress perception and hypertension amongst health workers of a mission hospital in Oyo State, south-western Nigeria. *Afr J Prim Health Care Fam Med.* 2012;4(1):307. doi: 10.4102/phcfm.v4i1.307
 16. Olayinka OA, Ogbebor SO, Ojo AA. Occupational stress management among nurses in selected hospitals in Benin City, Edo State, Nigeria. *Eur J Exp Biol.* 2013;3:473-481.
 17. Mwinga C, Mugula D. Prevalence and causes of stress among nurses at Ndola Hospital- A nurses perspective. *Int J Novel Res Health Care Nurs.* 2015;2(3):158-116.
 18. Deng J, Guo Y, Ma T, et al. How job stress influences job performance among Chinese healthcare workers: a cross-sectional study. *Environ. Health Prev Med.* 2019;24(1):2. doi: 10.1186/s12199-018-0758-4
 19. Schaufeli W, Salanova MA. Burnout, boredom and engagement at the workplace. In: Maria C. W. Peeters, Jan de Jonge and Toon W. Taris. *An Introduction to Contemporary Work Psychology.* John Wiley & Sons, Ltd. 2014:293-320.
 20. Israel GD. Determining Sample Size. <https://www.studocu.com/en-us/document/messiah-university/anatomy-and-physiology-2/2-glenn-d-determining-sample-size-for-research/55626030>. Accessed November 15, 2023.
 21. World Health Organization. Global Atlas of the Health Workforce: definitions of the HealthWorkforceData. <http://www.who.int/entity/hrh/en/>. Accessed November 20, 2023.
 22. Nehzat F, Huda BZ, Tajuddin SH. Reliability and validity of job content questionnaire for university research laboratory staff in Malaysia. *Southeast Asian J Trop Med Public Health.* 2014;45(2):481-489.
 23. Valente MD, Menezes PR, Pastor-Valero M, Lopes CDS. Depressive symptoms and psychosocial aspects of work in bank employees. *J Occup Med.* 2015;66(1):54-61.
 24. Kolo ES. Job satisfaction among healthcare workers in a tertiary center in kano, Northwestern Nigeria. *Niger J Basic Clin Sci.* 2018;15:87-91.
 25. Alabi A, Otoru O, Uvomata A, Adekanye A, Ojebode T. Family support and Blood pressure pattern in adult patients attending Baptist Medical centre, Saki, Oyo state. *Niger J Fam Pract.* 2015;6(2):27-34.
 26. Shin SY, Lee SG. Effects of Hospital Workers' Friendship Networks on Job Stress. *PLoS One.* 2016;22;11(2):e0149428. doi: 10.1371/journal.pone.0149428
 27. Hunsaker S, Chen HC, Maughan D, Heaston S. Factors influencing compassion fatigue, burnout, and compassion satisfaction in emergency department nurses. *J Nurs Scholarsh.* 2015;47(2):186-194.
 28. Grace MK, Van-Heuvelen JS. Occupational variation in burnout among medical staff: Evidence for the stress of higher status. *Soc Sci Med.* 2019;232:199-208.
 29. Zhang C, Yang L, Liu S, et al. Survey of insomnia and related social psychological factors among medical staff involved in the 2019 novel coronavirus disease outbreak. *Front Psychiatry.* 2020;11:306. doi: 10.3389/fpsy.2020.00306
 30. Aguwa EN, Nduka I, Arinze-Onyia SU. Assessment of burnout among health workers and bankers in Aba south local government area, Abia state, South East Nigeria. *Niger. J Clin Pract.* 2014;17(3):296-302.
 31. Wang H, Liu Y, Hu Ket, al. Healthcare workers' stress when caring for COVID-19 patients: An altruistic per-

- spective. *Nursing Ethics*. 2020;27(7):1490-500.
32. Theme FM, Costa MA, Guilam MC. Occupational stress and self-rated health among nurses. *Rev Lat Am Enferm*. 2013;21(2):475-483.
 33. Olatunji SO, Mokuolu BO. The influence of sex, marital status and tenure of service on job stress and job satisfaction of health workers in a Nigerian federal health institution. *Afr Res Rev Ethiopia*. 2014;8(1):126-133.
 34. Abayomi O, Emmanuel B, Gbolagade A, Peter O, Kofoworola O. Burnout Syndrome and Anxiety Disorders among Hospital Nurses in a Tertiary Health Center in Nigeria. *Int Neuropsychiatric Dis J*. 2018;11(2):1-11. doi: 10.9734/INDJ/2018/39640
 35. Akar N. The relationships among perceived job stressors, workplace bullying and job stress in the health care services in Turkey: A Structural Equation Modelling (SEM) approach. *Int J Humanit Soc Sci*. 2013;3(14):248-257.
 36. Soyler P, Ozer A. Evaluation of the prevalence of musculoskeletal disorders in nurses: a systematic review. *Med Sci*. 2018;7(3):479-485.
 37. Arsalani N, Fallahi-Khoshknab M, Josephson M, Lagerström M. Musculoskeletal disorders and working conditions among Iranian nursing personnel. *Int J Occup Safety Ergo*. 2014;20(4):671-680.
 38. Oyewole OO, Adeniyi EA, Ajayi BF, Olajitan AA, Oritogun KS. Work-related musculoskeletal disorders and ergonomic stressors among direct and non-direct contact health care workers from a Nigerian tertiary health facility. *Afr J Med Health Sci*. 2016;15(1):7-13. doi: 10.4103/2384-5589.183891
 39. Su Q, Guo L. Relationship between psychological elasticity, work stress and social support of clinical female nurses. *Chinese Occupational Medicine*. 2015;42(1):55-58.



Patterns of physical activity amidst COVID-19 among medical interns

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ABSTRACT

Introduction and aim. The COVID-19 pandemic restricted our daily lives significantly. This adversely affected the physical activity (PA) and productivity of students, including medical interns, who worked tirelessly during the pandemic. The study aimed to evaluate the changes in PA patterns and associated factors due to the imposed lockdown in medical interns compared to pre-pandemic levels.

Material and methods. A cross-sectional study was conducted among consenting medical interns of the 2020-21 batch in a medical college in Bhubaneswar, selected by convenience sampling. They were contacted by email and briefed about the study. Data on demography, exercise patterns (pre-, during, and post-COVID-19), and associated factors was collected by an electronic survey format (Google form). Data was analyzed using EPI info and interpreted in frequencies, percentages, and the chi-square test. A p-value < 0.05 was considered statistically significant.

Results. Of 104, 54.28% were females. The frequency of exercise reduced by 13.92% during COVID-19. Around 56.9% of interns exercised regularly pre-pandemic which dropped to 33.3% during the pandemic. The change in PA pattern was significantly associated with regularity of exercise (p < 0.001).

Conclusion. Evaluating the extent of physical inactivity will enable the administration to provide appropriate support to the interns to take equal care of their health as their patients.

Keywords. COVID-19, exercise, lockdown, medical interns, physical activity, well-being

Introduction

A novel coronavirus known as COVID-19, which originated in Wuhan, China, first appeared in India at the beginning of 2020. The World Health Organization declared it a pandemic and a global public health emergency on March 11, 2020.¹ Fever, cough, and sore throat were common symptoms of this acute respiratory illness. On the other hand, in moderate-to-severe cases, the illness worsens and leads to breathing problems,

problems with non-respiratory organs like the heart and kidneys, and even death.² Lockdowns were implemented everywhere to mitigate the risk of infection and stop its spread.³ Other preventive strategies included social distancing, self-isolation, working from home, home quarantines, social gathering bans, and the closure of local recreation centers, parks, and playgrounds. These unexpected drastic measures caused significant disruption of the daily routines and lifestyles of the general

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public. This had a significant impact on the daily physical activity (PA) (defined as any skeletal muscle-produced movement that causes an energy expenditure above the basal level) of millions of people in India and around the world.^{4,5} Worldwide, people reported difficulties in getting the recommended amount of physical activity during the pandemic, with some regions seeing a 50 percent drop in physical activity. The scarcity and unequal distribution of safe outdoor community resources (such as parks, trails, sports facilities, and sidewalks) that encourage physical activity is one factor contributing to this decline.⁶ These undesirable behaviors have been connected to a lower level of cardiopulmonary health as well as a higher chance of developing long-term illnesses like obesity, cardiometabolic disease, and early mortality.⁷⁻⁹ The World Health Organization (WHO) suggests engaging in at least 150 minutes of moderate exercise, 75 minutes of intense exercise, or a mix of the two each week.¹⁰ WHO aims to reduce the prevalence rate of physical inactivity by 15% worldwide by 2030.¹¹ Internship is a crucial phase in the life of medical students which comes with new responsibilities and added stress with tireless duty hours.¹² Due to erratic working hours, and lack of adequate sleep, the motivation to engage in physical activity fades away.¹³ The COVID-19 restrictions further created an imbalance in their physical activity patterns, motivational status, and mental well-being among the medical interns.¹⁴ A lot of research has been done comparing the disease status of people pre and post-pandemic.^{15,16} Studies have been done on the changes in physical activity patterns among the general population in China and Europe where there was a significant decline in physical activity engagement during the COVID-19 pandemic.¹⁷⁻²⁰

Aim

However, there is a paucity of literature about the PA patterns and mental well-being of medical students in India amidst the COVID-19 pandemic. Hence this study aimed to evaluate the changes in PA patterns, and associated factors due to the imposed lockdown in medical interns compared to pre-pandemic levels.

Material and methods

A cross-sectional study was conducted by the Department of Community Medicine, Kalinga Institute of Medical Sciences, Bhubaneswar between May 2021 and June 2021. The ethical approval was obtained from the Institutional Ethics Committee (reference number: KIIT/KIMS/IEC/684/2021) and the study was carried out following the Declaration of Helsinki. The target population was medical interns of the 2020-21 academic batch. Interns who consented to the study and completed the questionnaire were included as the final study sample. There were no exclusion criteria. A total of 150 medical interns

were selected through convenient sampling. The survey questionnaire used was pre-validated and pre-tested. It consisted of four sections: demographics, exercise patterns (pre-COVID-19, during COVID-19, and post-COVID-19 after reduction in restrictions and resumption of normal duty hours in the hospital), motivating factors for regular physical activity, and finally the barriers to regular physical activity. The exercising patterns were analyzed by including questions like if the participants exercised, the type of exercise they were involved in, duration of time spent exercising per week, place preferred for carrying out the physical activity, and regularity of the physical activity. The type of physical activity was classified into 'vigorous', 'moderate', and 'light' as per WHO guidelines.²¹ The regularity of physical activity was classified arbitrarily as 'irregular (< 2 days/week)', 'regular but skipped sometimes (2-3 days/week)', and 'very strict (5 days/week)'. The participants were contacted by email and briefed about the purpose of the study. The participants answered the online questionnaire via the link shared in their email. There was no time constraint, so the participants could answer the questions leisurely. The confidentiality of the participants was ensured. Data collected was compiled in Microsoft Excel and was analyzed using EPI info software. The descriptive data was interpreted in frequencies and percentages. The chi-square test was used for testing association. Linear trend analysis showed the changes in PA. A p-value < 0.05 was considered statistically significant.

Results

Out of 150 medical interns, a total of 104 participants completed the questionnaire. The study sample consisted of 57 (54.8%) females and 47 (45.2%) males. The mean (\pm SD) age of the study sample was 25.04 (\pm 1.29). The baseline characteristics showed that around 65 (62.7%) interns exercised pre-pandemic, 56 (53.8%) exercised during the pandemic, and 62 (59.6%) exercised after the imposed pandemic restrictions were reduced. Figure 1 depicts the linear trend diagram of the changes in the engagement of study participants in PA pre-, during, and post-COVID-19 pandemic.

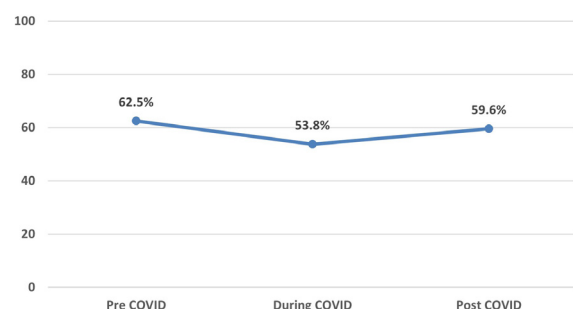


Fig. 1. Linear trend analysis of the changes in engagement in physical activity (%) pre-, during, and post-COVID-19

Pre-COVID-19, the study participants who exercised, were mostly involved in moderate exercise (28, 26.9%), for 2–4 hours/week (34, 32.7%), and exercise in the room (26, 25%). Around 37 (35.6%) of the interns were regular in their exercise schedule with the occasional skipping. Table 1 shows the characteristics of the patterns of PA before the COVID-19 pandemic.

Table 1. Characteristics of the patterns of PA before the COVID-19 pandemic

Variable	Frequency of respondents (n=104)	Percentage	
Did you exercise?	No	39	37.5
	Yes	65	62.5
If yes, how would you categorize it?	Light	27	26
	Moderate	28	26.9
	Vigorous	10	9.6
	No exercise	39	37.5
How much time did you spend weekly?	<2 hours	22	21.2
	2–4 hours	34	32.7
	>4 hours	9	8.8
	No exercise	39	37.5
Where did you exercise?	Gym	15	14.4
	Park	24	23.1
	Room	26	25
	No exercise	39	37.5
How regular were you?	Irregular	20	19.2
	Regular, though skipped sometimes	37	35.6
	Very Strict	8	7.7
	No exercise	39	37.5

Table 2. Characteristics of the patterns of PA during the COVID-19 pandemic

Variable	Frequency of respondents (n=104)	Percentage	
Did you exercise?	No	48	46.2
	Yes	56	53.8
If yes, how would you categorize it?	Light	22	21.2
	Moderate	23	22.1
	Vigorous	12	11.5
	No exercise	47	45.2
How much time did you spend weekly?	<2 hours	17	16.3
	2–4 hours	24	23.1
	>4 hours	16	15.4
	No exercise	47	45.2
Where did you exercise?	Gym	10	9.6
	Park	14	13.5
	Room	33	31.7
	No exercise	47	45.2
How regular were you?	Irregular	18	17.3
	Regular, though skipped sometimes	19	18.3
	Very Strict	20	19.2
	No exercise	47	45.2

During COVID-19, the study participants who exercised were mostly involved in moderate exercise (23, 22.1%), for 2–4 hours/week (24, 23.1%), and exercised

in the room (33, 31.7%). Around 20 (19.2%) of the interns were regular in their exercise schedule with the occasional skipping. Table 2 shows the characteristics of the patterns of PA during the COVID-19 pandemic.

Table 3. Characteristics of the patterns of PA after the COVID-19 pandemic

Variable	Frequency of respondents (n=104)	Percentage	
Did you exercise?	No	42	40.4
	Yes	62	59.6
If yes, how would you categorize it?	Light	15	14.4
	Moderate	38	36.5
	Vigorous	9	8.7
	No exercise	42	40.4
How much time did you spend weekly?	<2 hours	17	16.3
	2–4 hours	39	37.5
	>4 hours	6	5.8
	No exercise	42	40.4
Where did you exercise?	Gym	11	10.6
	Park	23	22.1
	Room	28	26.9
	No exercise	42	40.4
How regular were you?	Irregular	18	17.3
	Regular, though skipped sometimes	38	36.5
	Very Strict	6	5.8
	No exercise	42	40.4

Table 4. Association of different variables with the changing patterns of PA amidst COVID-19

Variable	Group	χ^2 (p-value) *			
		Pre COVID	During COVID	Post COVID	
Did you exercise?	No	n 39	48	42	1.665 (0.435)
	Yes	% 37.5%	46.2%	40.4%	
Categorization of exercise	Light	n 27	22	15	7.082 (0.132)
		% 41.5%	37.5%	24.2%	
	Moderate	n 28	23	38	
		% 43.1%	41.1%	61.3%	
	Vigorous	n 10	12	9	
		% 15.4%	21.4%	14.5%	
Time spent weekly	<2 hours	n 22	17	17	10.361 (0.11)
		% 32.3%	28.6%	27.4%	
	>4 hours	n 9	16	6	
		% 13.8%	28.6%	9.7%	
	2–4 hours	n 34	24	39	
		% 52.3%	42.9%	62.9%	
Regularity of exercise	Irregular	n 20	18	18	17.728 (<0.001)
		% 30.7%	31.6%	29.03%	
	Regular, though skipped sometimes	n 37	19	38	
		% 56.9%	33.3%	61.3%	
	Very strict	n 8	20	6	
		% 12.3%	35.1%	9.7%	

Post-COVID-19, the study participants who exercised, were mostly involved in moderate exercise (38, 36.5%), for 2–4 hours/week (39, 37.5%), and exercised in the room (28, 26.9%). Around 38 (36.5%) of the interns were regular in their exercise schedule with the occasional skipping. Table 3 shows the characteristics of the patterns of PA after the COVID-19 pandemic when the restriction measures were relaxed.

The association of different variables with the outcome was tested by the chi-square test. The regularity of the exercise schedule was significantly associated with the changes in PA patterns pre-, during, and post-COVID-19 ($p < 0.001$). Table 4 depicts the association of different variables with the changing patterns of PA amidst COVID-19.

Perceived physical benefits like losing weight that improved their appearance were the most common motivating factors for exercising. The different motivating factors are depicted in Figure 2.

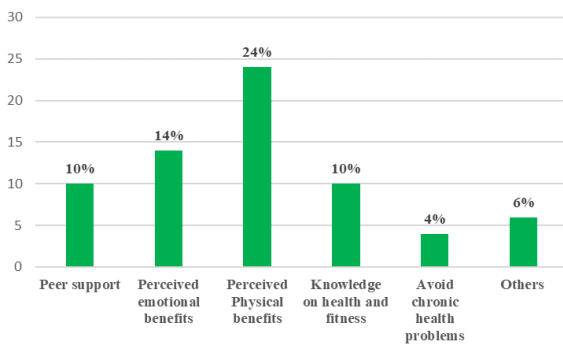


Fig. 2. Motivating factors facilitating PA among study participants (in %)

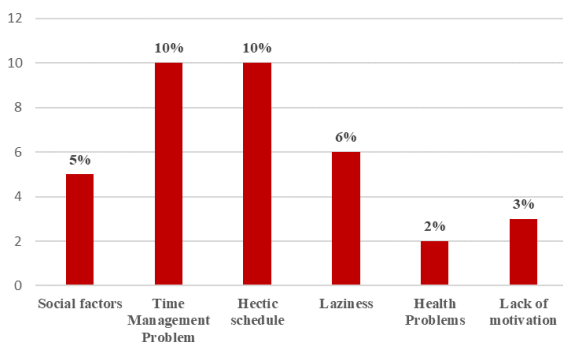


Fig. 3. Inhibiting factors affecting PA among study participants (in %)

The most common inhibiting factors affecting physical activity among the study participants were time management problems and hectic schedules due to erratic work timings. The other factors have been depicted in Figure 3.

Discussion

This study aimed to evaluate the changes in the physical activity patterns, and associated factors due to the

imposed lockdown in medical interns compared to pre-pandemic levels. Out of 120 medical interns, a total of 104 participants were included in the final analysis. The study sample consisted of 57 (54.8%) females and 47 (45.2%) males. The mean (\pm SD) age of the study sample was 25.04 (\pm 1.29). A study by Al-Hindawi et al. also reported female preponderance with 68 (62%) females and 42 (38%) males.²² The baseline characteristics showed that around 65 (62.7%) interns exercised pre-pandemic, 56 (53.8%) exercised during the pandemic, and 62 (59.6%) exercised after the imposed pandemic restrictions were reduced. There was a 14% decline in PA during the pandemic. Larrad-Rodriguez et al. also reported a 29.5% and 18.3% decline in vigorous and moderate PA among university students during lockdown.²³ A similar decrease in physical activity during the pandemic was also observed by Constandt et al. and Rosa D et al.^{24,25} This decrease may be due to the increase in sedentary behavior due to the imposed lockdown restrictions. Additional research has demonstrated that these patterns negatively impact people’s health, leading to immunological dysfunction and a decline in mental well-being.²⁶ Therefore, maintaining PA is crucial for people in good health or those with chronic illnesses to avoid or lessen the likelihood of developing new health issues and a deterioration in their quality of life down the road.^{27,28} In our study, the study participants preferred to exercise in the room, which increased by 26% during the lockdown. This was probably due to the closure of parks and gyms. Someway or the other, the medical interns remained physically active during the lockdown. A study by Wafi et al. also reported higher odds of maintaining physical activity among medical students who had exercise equipment in their homes during the pandemic.²⁹ The pattern of physical activity was significantly associated with the regularity of exercise among the participants ($\chi^2 = 17.728$, $p = 0.0013$). However, there was no significant association of physical activity patterns with the type of exercise and the time spent on exercise weekly. A study by Al-Mhanna et al. however found a significant association between the type of exercise and physical activity ($p < 0.001$).³⁰ The changes in the regularity of physical activity might be due to added household tasks like cooking, washing utensils, and cleaning rooms due to the non-availability of housekeeping staff during the lockdown, which made it difficult to devote time to exercise. The motivating factors for engaging in physical activity, as mentioned by the study participants, were the perceived physical and emotional benefits, the importance of being physically fit, avoiding chronic diseases, and support from peers. The barriers mentioned were time management, hectic work schedule, laziness, social embarrassment, current health problems, and lack of motivation. Nielsen et al. and Cornine A et al. also reported anxi-

ety, fear, and lack of motivation as factors responsible for decreased PA levels during the pandemic.^{31,32} Research also suggests that since exercise self-efficacy and motivation can be difficult to overcome early in the behavioral change process, social and institutional support may play a significant role in helping inactive people change their behavior.³³ Providing social, mental, and institutional opportunities for regular PA is crucial for sustaining a healthy lifestyle and lowering all-cause mortality.³⁴ To help medical interns understand the value of exercise and prepare them to suggest physical activity interventions in their future clinical practice, a concentrated education program on physical activity should be incorporated throughout the curriculum.³⁵

Study limitations

Although the current study emphasizes how the COVID-19 lockdown negatively affected medical interns' physical activity, it should be noted that there are a few limitations. The study is cross-sectional and was conducted in a single institute, using convenience sampling and self-selection. This makes the result less generalizable and subject to selection bias. We only received 104 responses out of the 120 participants in the intended sample. Even though we were able to identify significant correlations between the variables and changes in physical activity, more participants would have allowed for the possibility of additional insights, and a larger study is necessary to delve deeper into this topic. Participants' recollections of their physical activity levels before the COVID-19 lockdown were entirely dependent on them, which makes them potentially inaccurate or overestimated. The online questionnaire used for data collection is prone to recall bias.

Conclusion

The COVID-19 pandemic disrupted all regular human activities which forcefully restrained the students to a limited environment. These forced measures affected the PA patterns of the medical interns to a great extent. Future research using longitudinal study designs and objectively measuring PA before, during, and after additional health crisis-related restrictions is necessary to investigate the potential long-term impact of a health crisis on PA. All students should be encouraged to engage in alternate forms of exercise in case there is another pandemic. Furthermore, suitable assistance ought to be designed to cater to student's living circumstances.

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Declarations

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Author contributions

Conceptualization, B.S. and I.M.; Methodology, I.M. and I.D.; Software, S.P.; Validation, I.M., I.D. and A.S.; Formal Analysis, S.P.; Investigation, R.S.; Resources, I.D. and I.M.; Data Curation, S.P., I.M. and I.D.; Writing – Original Draft Preparation, I.D. and I.M.; Writing – Review & Editing, I.D. and I.M.; Visualization, I.M., and A.S.; Supervision, I.D. and I.M.; Project Administration, A.S., I.D., and I.M.; Funding Acquisition (not applicable).

Conflicts of interest

The authors declare no competing interests.

Data availability

Since it is sensitive data, it can be shared with the journal and reviewers upon request.

Ethics approval

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted under the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Kalinga Institute of Medical Sciences (KIIT/KIMS/IEC/684/2021).

References

1. Director-general's opening remarks at the media briefing on COVID-19 – 10 May 2021. World Health Organization. <https://www.who.int/director-general/speeches/detail/director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-10-may-2021>. Accessed December 23, 2023.
2. Guo YR, Cao QD, Hong ZS, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (Covid-19) outbreak – an update on the status. *Military Medical Research*. 2020;7(1):1-11. doi: 10.1186/s40779-020-00240-0
3. Coronavirus disease. World Health Organization. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed December 23, 2023.
4. Thivel D, Tremblay A, Genin PM, et al. Physical activity, inactivity, and sedentary behaviors: Definitions and implications in Occupational Health. *Front Public Health*. 2018;6:288. doi: 10.3389/fpubh.2018.00288
5. Stockwell S, Trott M, Tully M, et al. Changes in physical activity and sedentary behaviours from before to during the COVID-19 pandemic lockdown: a systematic review. *BMJ Open Sport Exerc Med*. 2021;7(1):e000960. doi:10.1136/bmjsem-2020-000960

6. Tison GH, Avram R, Kuhar P, et al. Worldwide Effect of COVID-19 on Physical Activity: A Descriptive Study. *Ann Intern Med.* 2020;173(9):767-770. doi: 10.7326/M20-2665
7. Mok A, Khaw KT, Luben R, Wareham N, Brage S. Physical activity trajectories and mortality: population based cohort study. *BMJ.* 2019;365:l2323. doi: 10.1136/bmj.l2323
8. Owen N, Sparling PB, Healy GN, Dunstan DW, Matthews CE. Sedentary behavior: emerging evidence for a new health risk. *Mayo Clin Proc.* 2010;85(12):1138-1141. doi: 10.4065/mcp.2010.0444
9. Healy GN, Matthews CE, Dunstan DW, et al. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. *Eur Heart J.* 2011;32(5):590-597. doi: 10.1093/eurheartj/ehq451
10. Global recommendations on physical activity for health. National Center for Biotechnology Information. <https://pubmed.ncbi.nlm.nih.gov/26180873/>. Accessed December 23, 2023.
11. Global action plan on physical activity 2018-2030. <https://iris.who.int/bitstream/handle/10665/272722/9789241514187-eng.pdf>. Accessed December 23, 2023.
12. Liu CH, Tang WR, Weng WH, et al. The process of coping with stress by Taiwanese medical interns: a qualitative study. *BMC Med Educ.* 2016;16:10. doi: 10.1186/s12909-016-0534-3
13. Kalmbach DA, Fang Y, Arnedt JT, et al. Effects of Sleep, Physical Activity, and Shift Work on Daily Mood: a Prospective Mobile Monitoring Study of Medical Interns. *J Gen Intern Med.* 2018;33(6):914-920. doi: 10.1007/s11606-018-4373-2
14. Faulkner J, O'Brien WJ, McGrane B, et al. Physical activity, mental health and well-being of adults during initial COVID-19 containment strategies: A multi-country cross-sectional analysis. *J Sci Med Sport.* 2021;24(4):320-326. doi: 10.1016/j.jsams.2020.11.016
15. Maugeri G, Castrogiovanni P, Battaglia G, et al. The impact of physical activity on psychological health during covid-19 pandemic in Italy. *Heliyon.* 2020;6(6):4315. doi: 10.1016/j.heliyon.2020.e04315
16. Lesser IA, Nienhuis CP. The Impact of COVID-19 on Physical Activity Behavior and Well-Being of Canadians. *Int J Environ Res Public Health.* 2020;17(11):3899. doi: 10.3390/ijerph17113899
17. Wang X, Lei SM, Le S, et al. Bidirectional Influence of the COVID-19 Pandemic Lockdowns on Health Behaviors and Quality of Life among Chinese Adults. *Int J Environ Res Public Health.* 2020;17(15):5575. doi: 10.3390/ijerph17155575
18. Qin F, Song Y, Nassis GP, et al. Physical Activity, Screen Time, and Emotional Well-Being during the 2019 Novel Coronavirus Outbreak in China. *Int J Environ Res Public Health.* 2020;17(14):5170. doi: 10.3390/ijerph17145170
19. Górnicka M, Drywień ME, Zielinska MA, Hamułka J. Dietary and Lifestyle Changes During COVID-19 and the Subsequent Lockdowns among Polish Adults: A Cross-Sectional Online Survey PLifeCOVID-19 Study. *Nutrients.* 2020;12(8):2324. doi: 10.3390/nu12082324
20. Castañeda-Babarro A, Arbillaga-Etxarri A, Gutiérrez-Santamaría B, Coca A. Physical Activity Change during COVID-19 Confinement. *Int J Environ Res Public Health.* 2020;17(18):6878. doi: 10.3390/ijerph17186878
21. WHO guidelines on physical activity and sedentary behaviour: At a glance. World Health Organization. January 1, 1970. <https://apps.who.int/iris/handle/10665/337001>. Accessed December 23, 2023.
22. Al-Hindawi A, Kumar N, Gaynor D. Exploring changes in levels and patterns of physical activity in undergraduate medical and nursing students during the COVID-19 pandemic. *Front Publ Health.* 2022;10:42071. doi:10.3389/fpubh.2022.1042071
23. Rodríguez-Larrad A, Mañas A, Labayen I, et al. Impact of COVID-19 Confinement on Physical Activity and Sedentary Behaviour in Spanish University Students: Role of Gender. *Int J Environ Res Public Health.* 2021;18(2):369. doi:10.3390/ijerph18020369
24. Constandt B, Thibaut E, De Bosscher V, Scheerder J, Ricour M, Willem A. Exercising in Times of Lockdown: An Analysis of the Impact of COVID-19 on Levels and Patterns of Exercise among Adults in Belgium. *Int J Environ Res Public Health.* 2020;17(11):4144. doi: 10.3390/ijerph17114144
25. De la Rosa A, Monterrosa Quintero A, Camacho-Villa MA, et al. Physical Activity Levels and Psychological Well-Being during COVID-19 Lockdown among University Students and Employees. *Int J Environ Res Public Health.* 2022;19(18):11234. doi: 10.3390/ijerph191811234
26. Dwyer MJ, Pasini M, De Dominicis S, Righi E. Physical activity: Benefits and challenges during the COVID-19 pandemic. *Scand J Med Sci Sports.* 2020;30(7):1291-1294. doi: 10.1111/sms.13710
27. Chen P, Mao L, Nassis GP, Harmer P, Ainsworth BE, Li F. Coronavirus disease (COVID-19): The need to maintain regular physical activity while taking precautions. *J Sport Health Sci.* 2020;9(2):103-104. doi: 10.1016/j.jshs.2020.02.001
28. Denay KL, Breslow RG, Turner MN, Nieman DC, Roberts WO, Best TM. ACSM Call to Action Statement: COVID-19 Considerations for Sports and Physical Activity. *Curr Sports Med Rep.* 2020;19(8):326-328. doi: 10.1249/JSR.0000000000000739
29. Wafi AM, Mosleh AA, Mutaen AA, et al. The Impact of COVID-19 on Maintaining Physical Activity and Its Associated Factors among Medical Students. *Int J Environ Res Public Health.* 2022;19(23):15752. doi: 10.3390/ijerph192315752
30. Al-Mhanna SB, Wan Ghazali WS, Mohamed M, et al. The Impact of COVID-19 on Physical Activity Patterns of Dental Students: A Multinational Survey. *Healthcare (Basel).* 2022;10(11):2140. doi: 10.3390/healthcare1011214

31. Background paper - Motivation and aging - National Institute. <https://www.nia.nih.gov/sites/default/files/d7/background.pdf>. Accessed December 23, 2023.
32. Cornine A. Reducing Nursing Student Anxiety in the Clinical Setting: An Integrative Review. *Nurs Educ Perspect.* 2020;41(4):229-234. doi: 10.1097/01.NEP.0000000000000633
33. Lachman ME, Lipsitz L, Lubben J, Castaneda-Sceppa C, Jette AM. When Adults Don't Exercise: Behavioral Strategies to Increase Physical Activity in Sedentary Middle-Aged and Older Adults. *Innov Aging.* 2018;2(1):1-12. doi: 10.1093/geroni/igy007
34. Lindsay Smith G, Banting L, Eime R, O'Sullivan G, van Uffelen JGZ. The association between social support and physical activity in older adults: a systematic review. *Int J Behav Nutr Phys Act.* 2017;14(1):56. doi: 10.1186/s12966-017-0509-8
35. Strong A, Stoutenberg M, Hobson-Powell A, Hargreaves M, Beeler H, Stamatakis E. An evaluation of physical activity training in Australian medical school curricula. *J Sci Med Sport.* 2017;20(6):534-538. doi: 10.1016/j.jsams.2016.10.011



Caries experience in Indian children with cleft lip and palate – an observational study from a tertiary care centre

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ABSTRACT

Introduction and aim. This study aims to assess caries experience in children with cleft lip and palate (CLP).

Material and methods. A total of 127 children (aged 3-12 years) with CLP and 141 non-cleft controls were assessed for dental caries using the decayed-extracted/missing-filled teeth (deft/DMFT) index. Logistic regression analysis was employed to identify factors associated with dental caries. Statistical tests, including t-test, ANOVA, Chi-square, and Fisher's exact test, were used to analyze differences between cleft and non-cleft populations.

Results. In primary teeth, caries prevalence was significantly higher in children with CLP (63.8%) compared to non-cleft controls (40.4%, $p < 0.001$). The deft scores were 3.30 for CLP and 1.63 for non-CLP group ($p < 0.01$). No significant difference was observed in mean DMFT scores ($p = 0.02$). Significant variations in caries prevalence ($p = 0.01$) and mean DMFT values ($p = 0.001$) were noted in permanent dentition among different cleft groups.

Conclusion. Children with CLP show higher caries prevalence and experience, emphasizing the need for targeted dental care interventions in this population. Logistic regression analysis highlights an age-related increase in caries experience among individuals with CLP.

Keywords. cleft lip, cleft palate, dental caries

Introduction

Cleft lip and palate (CLP) rank among the most common craniofacial anomalies in children, affecting nearly 1 in 700 live births globally. This condition can lead to a range of functional, aesthetic, and psychological challenges for affected individuals. Given the complexities involved, children with CLP require specialized care, including dental care. Unfortunately, the appearance of orofacial clefts often overwhelms parents, leading to a tendency to overlook the oral health needs of their children. Children with CLP often show various dental problems, including malocclusion, poor oral hygiene, and dental anomalies.

Reports on the prevalence of dental caries in the CLP population present conflicting findings. The majority of studies suggest a higher caries prevalence in children with CLP compared to non-cleft children.¹⁻⁸ However, Malay et al. and Nagappan et al. reported a lower occurrence of caries in children with CLP, while some studies found no difference in caries experience between children with CLP and the control population.⁹⁻¹² These differences in findings may stem from various reasons such as the multifactorial etiology of dental caries, variations in evaluation periods, methodological disparities, and differences in socio-economic conditions.^{13,14}

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Aim

Epidemiological studies have shown that caries prevalence differs from country to country. Caries experience in a population is influenced by factors such as oral hygiene practices, dietary habits, and ethnicity. Although many studies have explored caries prevalence in India, epidemiological studies on the caries experience of CLP children are scarce. The current study aimed to investigate caries experience in 3–12 years children with CLP and compare them with age- and sex-matched non-cleft children. Additionally, factors such as place of residence, number of siblings, method of tooth cleaning, use of fluoride toothpaste, frequency of brushing, and previous dental visits were investigated to determine their potential influence on caries experience in children with cleft lip and palate.

Material and methods

Ethical considerations

The study protocol adheres to the Declaration of Helsinki and received approval from the Ethics Committee of Dr. R Ahmed Dental College and Hospital, Kolkata (IEC/DCH/089 dated 12/7/2021). Prior to the commencement of the study, informed consent was obtained from the parents or legal guardians of the participating children. The consent process included a detailed explanation of the study's objectives, procedures, potential risks, and benefits. Participants were assured that their involvement was voluntary, and they had the right to withdraw from the study at any stage without repercussions. Confidentiality was maintained throughout the study, with all personal information anonymized and stored securely.

Study subjects

We included all children aged three to twelve years with complete cleft lip and palate (CLP) who were referred from cleft centers, where orofacial cleft surgeries were performed, to the Department of Pediatric and Preventive Dentistry during the study period (October 2021–September 2022). The institute provides free access to dental care for all. Study participants received both preventive and therapeutic dental treatments they needed. Dental treatments carried out in this department include fabrication of obturators, restorative, and orthodontic treatments and teeth extraction. In order to participate in the research, children had to have undergone surgical intervention for cleft lip and palate (CLP) and be free from systemic diseases. Individuals with solely a cleft lip, undergoing orthodontic treatment, having related syndromes, other craniofacial abnormalities or dentofacial deformities were excluded. A total of 127 children aged 3–12 years with cleft lip and palate were selected. We gathered information on cleft types and the age of the patients from these records. According to age children with CLP were further categorized into two groups: the primary dentition group

(3–5 years) and the mixed dentition group (6–12 years). Based on orofacial cleft, children were further grouped into unilateral cleft lip and palate (UCLP), bilateral cleft lip and palate (BCLP), and cleft palate (CP).

We randomly selected 149 healthy children aged 3–12 years without clefts from two local kindergartens and two primary schools situated in Kolkata. Among them, 141 children agreed to participate. These controls, matched for age and sex, shared the same ethnicity and socioeconomic characteristics as the children with CLP. The non-cleft individuals were further divided into two age groups: 3–5 years (62 children) and 6–12 years (79 children).

Clinical examination

Two experienced pedodontists examined all participants, including 20 children (10 with clefts and 10 without) before the main study. The two examiners showed good agreement (kappa scores of 0.89 for deft and 0.91 for DMFT) in assessing teeth with cavities. We recorded dental caries using the decayed (dt/DT), extracted due to caries (et) in case of primary teeth, missed teeth (MT) in case of permanent teeth, and filled teeth (ft/FT) index based on modified WHO criteria (1997). Uppercase letters signify the permanent dentition (DMFT), and lowercase letters (deft) represent primary teeth. Only missing teeth due to caries were recorded; congenitally missing or lost teeth due to other reasons, such as trauma, were not considered. Similarly, only fillings for carious teeth were recorded. Restorations of enamel hypoplasia or hypomineralized teeth were not considered. Details on tooth extraction and filled teeth were gathered from discussions with parents or caregivers.

Before the examination, all participants were asked to brush their teeth. The clinical examinations, conducted at the Department of Pediatric and Preventive Dentistry of Dr. R Ahmed Dental College and Hospital, involved using a mouth mirror and a probe while the participant remained seated in a dental chair. Teeth were dried using compressed air. No X-rays were taken.

Questionnaires

A structured questionnaire was designed to obtain data, including the place of residence, the number of siblings, method of tooth cleaning, use of fluoride toothpaste, frequency of brushing, and previous dental visits. The questionnaire was filled out by the parents at home and collected after the clinical examination by another investigator who did not participate in the clinical examination.

Statistical analysis

Data were analyzed using the software Epi Info version 7.2 (CDC, Atlanta, USA) with a 95% confidence interval for all tests. Descriptive and inferential statistics were performed to analyze the data. The t-test, Chi-

square test, and Fisher's exact test were used to analyze any significant differences between the cleft and non-cleft population. ANOVA test was employed to compare the mean caries score (deft/DMFT) of cleft subgroups. Associated social and behavioral factors such as place of residence, number of siblings, method of tooth cleaning, use of fluoride toothpaste, frequency of brushing, and previous dental visits was assessed using Chi-square tests. Binary logistic regression analysis adjusted by age and sex was used in this study. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from the model. All statistical tests were two-tailed, and the level of significance was set at 0.05.

Results

The mean age of children with cleft lip and palate was found to be 6.52 ± 2.72 years. Initially, 134 children with CLP were selected who met the inclusion and exclusion criteria. However, seven children were excluded due to insufficient data in their medical records, resulting in a final sample size of 127 subjects. Among the cleft population, the caries experience (deft>0) was 63.8% (81/127) in primary dentition, whereas the caries experience (deft>0) was 40.4% (57/141) in the non-cleft population. Similarly, 55.6% (40/72) of the CLP group and 40.5% (32/79) of non-CLP children showed caries experience (DMFT>0) in their permanent teeth.

Table 1. Distribution of CLP according to age, gender, and cleft types and control group*

Age group	BCLP (n=45)		UCLP (n=38)		CP (n=44)		Cleft group (n=127)			Control group (n=141)		
	M	F	M	F	M	F	M	F	Total	M	F	Total
3-5 years (N=55)	8	13	10	9	6	9	24	31	55	29	33	62
6-12 years (n=72)	14	10	10	9	8	21	32	40	72	35	44	79
Total	22	23	20	18	14	30	56	71	127	64	77	141

* n – number, M – male, F – female, BCLP – bilateral cleft lip and palate, UCLP – unilateral cleft lip and palate, CP – cleft palate

Table 2. Caries status of children with CLP according to gender*

	Male	Female	p
deft=0	20 (35.7%)	26 (36.6%)	>0.999
deft>0	36 (64.3%)	45 (63.4%)	
DMFT=0	12 (37.5%)	20 (50%)	0.34
DMFT>0	20 (62.5%)	20 (50%)	
Mean DMFT	2.65 ± 2.82	2.17 ± 2.75	0.46

* deft – decayed extracted and filled primary teeth, DMFT – decayed missing filled permanent teeth

Table 1 shows the distribution of CLP According to age, gender, and cleft types. Among the CLP group,

44.1% were boys, 55.9% were girls, with no significant gender difference in caries experience.

The analysis of caries status in children with CLP based on gender is shown in Table 2 and it reveals no significant differences in both primary and permanent teeth, suggesting that gender may not be a prominent factor influencing caries experience among children with CLP.

Table 3. Caries experience in children with CLP according to cleft types^a

Cleft type	BCLP	UCLP	CP	p
Number (%)	45 (35.4%)	38 (29.9%)	44 (34.6%)	
deft=0	17 (37.8%)	11 (28.9%)	18 (40.9%)	0.51 ^f
deft>0	28 (62.2%)	27 (71.1%)	26 (59.1%)	
DMFT=0	10 (41.7%)	6 (31.6%)	16 (76.2%)	0.01 ^f
DMFT>0	14 (58.3%)	13 (68.4%)	5 (23.8%)	
Mean deft	3.4 ± 3.37	3.21 ± 3.04	3.27 ± 3.252	0.809 ^a
Mean DMFT	2.25 ± 2.54	3.78 ± 3.32	1.58 ± 2.26	0.001 ^a

^a * – ANOVA test, # – Chi square test, deft – decayed extracted and filled primary teeth, DMFT – decayed missing filled permanent teeth, BCLP – bilateral cleft lip and palate, UCLP – unilateral cleft lip and palate, CP – cleft palate

Table 4. Mean caries indices according to age group in children with and without CLP*

Age group	Caries experience	CLP		Without CLP		p
		Mean	SD	Mean	SD	
3–5 years	dt	2.50	2.79	1.45	1.85	0.01
	et	0.2	0.62	0.33	0.69	0.28
	ft	0.09	0.34	0.27	0.72	0.09
6–12 years	deft	2.8	3.17	2.04	2.51	0.15
	dt	3.34	2.95	1.03	1.87	<0.0001
	et	0.30	0.74	0.13	0.38	0.07
	ft	0.08	0.32	0.13	0.47	0.45
	deft	3.68	3.21	1.30	2.23	<0.0001
	DT	1.91	2.44	1.25	1.97	0.06
3–12 years	MT	0.25	0.57	0.14	0.38	0.16
	FT	0.22	0.56	0.08	0.28	0.05
	DMFT	2.38	2.77	1.46	2.19	0.02
	dt	2.98	2.90	1.22	1.87	<0.0001
	et	0.26	0.69	0.23	0.55	0.69
	ft	0.08	0.33	0.20	0.60	0.04
	deft	3.30	3.21	1.63	2.38	<0.0001

* CLP – cleft lip and palate, dt – decayed primary teeth, et – extracted primary teeth due to caries, ft – filled primary teeth, DT – decayed permanent teeth, MT – missing permanent teeth, FT – filled permanent teeth

Table 3 presents the caries experience in children with CLP based on different types of clefts: bilateral cleft lip and palate (BCLP), unilateral cleft lip and palate (UCLP), and cleft palate only (CP). There is no statistically significant difference in the prevalence of caries

among the cleft types ($p=0.51$ for deft and $p=0.01$ for DMFT). The ANOVA test results indicate that there is no statistically significant difference in mean deft scores among the cleft types ($p=0.809$). However, there is a significant difference in mean DMFT scores among the cleft types ($p=0.001$). It is possible that the limited number of children within each cleft group may have contributed to this outcome.

Table 5. Relationship between cleft status and associated factors*

Variables		CLP	Non-CLP	p
Age (mean±SD)	3–5 years	4.02±0.79	4.20±0.87	0.24
	6–12 years	8.44±2.04	8.40±1.95	0.90
	3–12 years	6.52±2.72	6.56±2.60	0.90
deft=0		46 (36.2%)	84 (59.6%)	<0.001
deft>0		81 (63.8%)	57 (40.4%)	
DMFT=0		32 (44.4%)	47 (59.5%)	0.07
DMFT>0		40 (55.6%)	32 (40.5%)	
Residency	Rural	61 (48.03%)	72 (51.1%)	0.62
	Urban	66 (51.97%)	69 (48.9%)	
Number of siblings	one	49 (38.6%)	71 (50.4%)	0.06
	More than one	78 (61.4%)	70 (49.7%)	
Use of fluoride toothpaste	Yes	127 (100%)	141 (100%)	
	No	0 (0%)	0 (0%)	
Method of tooth cleanin	Toothpaste and brush	127 (100%)	141(100%)	0.004
	Finger	0 (0%)	0 (0%)	
Brushing	Once	84 (70%)	108 (76.6%)	0.26
	More than once	36 (30%)	33 (23.4%)	
Previous dental visit	Yes	59 (46.4%)	65 (46.1%)	0.33
	No	68 (53.6%)	96 (53.9%)	

* CLP – cleft lip and palate, deft – decayed, extracted and filled primary teeth, DMFT – decayed, missing and filled permanent teeth

Table 6. Proportion (%) of children with CLP who are free of caries (deft+DMFT=0) and with caries present (deft+DMFT>0) according to their age group, sex, social and behavioral factors, total number of children=127

Characteristics		Caries present n=92	Caries free n=35	p
Age	3–5 years	31 (56.4%)	24 (43.6%)	<0.001
	6–12 years	61 (84.7%)	11 (15.3%)	
Sex	Male	41 (73.2%)	15 (26.8%)	>0.999
	Female	51 (71.8%)	20 (28.2%)	
Place of residence	Rural	45 (73.8%)	16 (26.2%)	0.90
	Urban	47 (71.2%)	19 (28.8%)	
No of siblings	One	32 (65.3%)	17 (34.7%)	0.22
	More than one	60 (76.9%)	18 (23.1%)	
Brushing	Once-daily	68 (71.6%)	27 (28.4%)	0.88
	Twice or more	24 (75%)	8 (25%)	
Previous dental visits	Yes	56 (71.8%)	22 (28.2%)	0.21
	No	58 (81.7%)	13 (18.3%)	

Table 4 presents an evaluation of caries experience in primary and permanent teeth for CLP and non-CLP groups. No significant difference was found in mean

deft values for 3-to-5-year-old CLP and control groups. However, significant differences were observed in the decayed component (dt) for both age groups, with higher values in CLP children. Mean deft for 6–12 years was significantly higher in CLP (3.30) vs. non-CLP (1.63), whereas mean DMFT did not differ significantly (2.38 vs. 1.46; $p=0.02$).

Table 5 indicates a significantly higher prevalence of caries in primary dentition for CLP children (63.8%) compared to non-CLP (40.4%). Although caries experience in the 6–12 age group with CLP was higher than the 3–5 age group, this difference was not statistically significant ($p=0.12$). Permanent teeth did not show significant differences between CLP and non-CLP groups ($p=0.07$).

Logistic regression revealed a significant increase in caries experience with age in individuals with CLP ($p<0.001$, OR 0.66), but no significant differences in residence, siblings, or brushing frequency between CLP and non-CLP children (Table 6).

Discussion

This observational study assessed caries experience in both primary and permanent teeth of 3- to 12-year-old children with CLP, considering factors such as age, gender, and types of clefts. The results were compared with those of an age- and sex-matched non-cleft control population. The cleft populations in this study were drawn from government-run hospitals where treatments are provided free of charge. To ensure homogeneity in ethnicity and socioeconomic conditions among the study samples, non-cleft populations were selected from schools located in the same geographic area as the hospital, where free education is provided.

Examining caries prevalence in the context of the country where the children live is important. Socioeconomic and cultural factors, as well as variations in healthcare systems, can significantly influence oral health outcomes. Overall caries experience in this study in the non-cleft population was found to be 40.4% which is comparable with the findings of a meta-analysis and a recent Indian study carried out on 5- to 12-year-old school-going children of Chandigarh.^{15,16} In this study, children with CLP exhibited higher caries experience, consistent with the findings of numerous previous studies, systematic reviews, and meta-analyses.^{1,2,4,13,17,18} Among the cleft population, 63.8% of children showed caries experience in their primary teeth, a finding comparable to that of Kamble et al.¹⁹

A significant difference in the dt of the deft score between children with CLP and controls suggests that children with CLP may have a higher prevalence of untreated decayed teeth compared to the control group. The low values of missing and filled components in the deft/DMFT score in the CLP group may be a result of

parents or caregivers prioritizing cleft surgeries over dental treatments.

Although the exact cause is not known, possible explanations for higher caries experience in children with CLP include poor oral hygiene, increased oral clearance time, malposition of teeth and presence of dental anomalies, and possible scarring acting as plaque retaining area. The higher occurrence of malocclusion and orthodontic treatment in children with CLP may introduce bias in studies that compares outcomes with controls. Therefore, children undergoing orthodontic treatment were excluded in the current study. In addition, maintaining oral hygiene in CLP patients with obturators is challenging due to increased plaque retention. This can lead to changes in plaque composition, with a rise in cariogenic bacteria like *Streptococcus* and *Lactobacillus*, exacerbating the risk of dental caries.^{3,14}

Among the children with CLP, no correlation was observed between caries experience and gender, implying that gender might not play a primary role in determining caries prevalence among children with CLP. Similar result was observed in other studies.²²

In the 3–5 years age group, there was no significant difference in deft score between cleft and control participants which is consistent with the finding of Zhu et al.⁸ However, in the 6- to 12-year-old group, a significant difference in caries experience was observed possibly attributed to the cumulative increase in deft scores in CLP group with age. Tũaño-Cabrera et al. suggested that children under 6 years brush under parental supervision, while those aged 6–12 years usually brush independently.²³ Lack of supervision, coupled with malocclusions and limited access post-surgery in cleft areas, may contribute to higher caries incidence.²³

Antonarakis et al., in a meta-analysis of five studies, found a mean difference of 1.38 in DMF teeth between individuals with CLP and controls.¹ Another meta-analysis indicated a pooled mean difference in DMFT of 0.28, higher in permanent dentition than mixed dentition.¹³ The present survey provides weak evidence ($p=0.02$) for higher caries experience (DMFT) in children with CLP compared to non-cleft controls, which is consistent with the observations of Tannure et al., Lucas et al. and Freitas et al.^{11,12,18} These studies found no significant DMFT score differences between children with CLP and non-CLP individuals.

Various factors like sample size, cleft types, location, food habits, socio-economic conditions, and oral hygiene practices can influence caries rates. Many studies treat all children with CLP uniformly, limiting exploration of specific correlations between cleft types and caries. The current study classified individuals according to different types of cleft conditions and found no significant difference in the prevalence of dental caries. These results are consistent with previous studies of Chopra et

al., Xiao et al., and Allam et al., but not with the findings of Sunderji et al., Zhu et al., Howe et al., and Gupta et al.^{7,8,17,24–27} It is possible that the limited number of children within each cleft group may have contributed to this outcome.

Previous studies suggest a link between caries experience and oral hygiene practices. In CLP individuals, factors like scar tissue, bleeding, poorly aligned teeth, and cleft anatomy may contribute to reluctance in tooth brushing. However, the present study found no significant difference in brushing frequency between individuals with CLP and the non-cleft control group. The current study also explored the impact of residence, number of siblings, person responsible for tooth cleaning, use of fluoride toothpaste, brushing frequency, and previous dental visits on caries occurrence in children with CLP. No significant association was found between these social and behavioural factors and caries experience. This could be attributed to the problem-centric approach to seeking dental care among the study participants. Bian et al. and Ankola et al., also reported no relationship between brushing frequency and caries experience.^{28,29}

This study has a few limitations. The study's the omission of dietary factors, a smaller sample size, a unicentric design, and the evaluation of only one ethnic group are some of the limitations. In addition, caries experience should be assessed radiographically. We did not take radiographs for caries detection in this prospective study. For ethical reasons, participants did not undergo radiographic evaluation solely for survey purposes. Educational background and family income are known to influence a child's caries experience. Since the participants in this study were selected from the same socioeconomic condition, family income and caregiver's education were not considered separately. Nevertheless, the sample sizes of the CLP and non-CLP groups were matched in the current study, which we consider a strength of this study.

The observational study on children with CLP suggests that these individuals exhibit significantly higher caries experience in primary teeth, emphasizing the importance of oral health interventions. Further research is required to explore sociodemographic and dietary factors that may influence caries risk in this population, potentially informing more comprehensive treatment approaches and improving long-term oral health outcomes for children with CLP.

Conclusion

The following conclusions can be drawn from the findings of this study: Patients with CLP had significantly higher caries experience in the primary dentition. However, no significant difference in DMFT scores for permanent teeth was noted between cases and controls. When we compared caries experience among cleft types, the mean deft scores of BCLP, UCLP, and CP groups did

not differ significantly. By contrast, we observed a significant ($p=0.01$) difference in caries prevalence as well as mean DMFT value ($p=0.001$) in the permanent dentition among different cleft groups. Caries experiences increase significantly with age in individuals with CLP.

Declarations

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Author contributions

Conceptualization, S.M. and P.M.; Methodology, S.M.; Software, S.M.; Validation, P.M.; Formal Analysis, P.M.; Investigation, S.M.; Resources, S.M.; Data Curation, S.M.; Writing – Original Draft Preparation, S.M.; Writing – Review & Editing, S.M., P.M.; Visualization, S.M.; Supervision, P.M.; Project Administration, S.M.; Funding Acquisition, P.M.

Conflicts of interest

The authors declare no competing interests.

Data availability

Data analyzed during the present study and/or are available from the corresponding author upon request.

Ethics approval

The present study was prospectively conducted in a pediatric population between October 2022 and January 2023 after obtaining approval from the Ethics Committee of Dr R Ahmed Dental College and Hospital, Kolkata (IEC/DCH/089 dated 12/7/2021).

Declaration of Generative AI and AI-assisted technologies in English language and grammar editing

During the preparation of this work the author used OpenAI/ ChatGPT in order to check grammar and spelling. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.






References

1. Antonarakis GS, Palaska PK, Herzog G. Caries prevalence in nonsyndromic patients with cleft lip and/or palate: a meta-analysis. *Caries Res.* 2013;47:406-413.
2. Abirami S, Panchanadikar NT, Muthu MS, et al. Dental Caries Experience among Children and Adolescents with Cleft Lip and/or Palate: An Umbrella Review. *Int J Clin Pediatr Dent.* 2022;15(2):261-268. doi: 10.5005/jp-journals-10005-2169
3. Wu Q, Li Z, Zhang Y, Peng X, Zhou X. Dental caries and periodontitis risk factors in cleft lip and palate patients. *Front Pediatr.* 2023;10:1092809. doi: 10.3389/fped.2022.1092809
4. Grewcock RE, Innes NPT, Mossey PA, Robertson MD. Caries in children with and without orofacial clefting: A systematic review and meta-analysis. *Oral Diseases* 2022;28:1400-1411. doi: 10.1111/odi.14183
5. Hazza'a A M, Rawashdeh MA, Al-Nimri K, Al Habashneh R. Dental and oral hygiene status in Jordanian children with cleft lip and palate: A comparison between unilateral and bilateral clefts. *Int J Dent Hygiene.* 2011;9:30-36.
6. Sundell AL, Nilsson AK, Ullbro C, Twetman S, Marcusson A. Caries prevalence and enamel defects in 5- and 10-year-old children with cleft lip and/or palate: A case-control study. *Acta Odontol Scand.* 2016;74(2):90-95. doi: 10.3109/00016357.2015.1044562
7. Sunderji S, Acharya B, Flaitz C, Chiquet B. Dental caries experience in Texan children with cleft lip and palate. *Pediatr Dent.* 2017;39:397-402.
8. Zhu WC, Xiao J, Liu Y, Wu J, Li J Y. Caries experience in individuals with cleft lip and/or palate in China. *Cleft Palate Craniofac J.* 2010;47:43-47.
9. Malay KK, Ravindran V, Kumar J. Dental caries status in children with and without cleft lip and palate: A case control study. *Ann Med Health Sci Res.* 2021;11:422-426.
10. Nagappan N, Madhanmohan R, Gopinathan NM, Stephen SR, Pillai DDM, Tirupati N. Oral Health-Related Quality of Life and Dental Caries Status in Children With Orofacial Cleft: An Indian Outlook. *J Pharm Bioallied Sci.* 2019;11(2):169-174. doi: 10.4103/JPBS.JPBS_285_18
11. Tannure PN, Costa Mde C, Kuchler EC, Romanos HF, Granjeiro JM, Vieira AR. Caries experience in individuals with cleft lip and palate. *Pediatr Dent.* 2012;34(2):127-131.
12. Lucas VS, Gupta R, Ololade O, Gelbier M, Roberts GJ. Dental health indices and caries associated microflora in children with unilateral cleft lip and palate. *Cleft Palate Craniofac J.* 2000;37:447-452.
13. Worth V, Perry R, Ireland T, Wills AK, Sandy J, Ness A. Are people with an orofacial cleft at a higher risk of dental caries? A systematic review and meta-analysis. *Br Dent J.* 2017;223(1):37-47. doi: 10.1038/sj.bdj.2017.581
14. Świtłała J, Sycińska-Dziarnowska M, Spagnuolo G, Woźniak K, Mańkowska K, Szyszka-Sommerfeld L. Oral Microbiota in Children with Cleft Lip and Palate: A Systematic Review. *J Clin Med.* 2023;12(18):5867. doi: 10.3390/jcm12185867
15. Pandey P, Nandkeoliar T, Tikku AP, Singh D, Singh MK. Prevalence of Dental Caries in the Indian Population: A Systematic Review and Meta-analysis. *J Int Soc Prev Community Dent.* 2021;11(3):256-265. doi: 10.4103/jispcd.JISPCD_42_21
16. Prabakar J, Arumugham IM, Sri Sakthi D, Kumar RP, Leelavathi L. Prevalence and Comparison of Dental Caries experience among 5 to 12 year-old school children of Chandigarh using dft/ DMFT and SiC Index: A Cross-sectional study. *J Family Med Prim Care.* 2020;9(2):819-825. doi: 10.4103/jfmpc.jfmpc_781_19
17. Chopra A, Lakhanpal M, Rao N C, Gupta N, Vashisth S. Oral health in 4–6 years children with cleft lip/palate: a case-control study. *N Am J Med Sci* 2014;6:266-269.

18. Freitas AB, de Barros LM, Fiorini J E, Boriollo MF, Moreira AN, Magalhaes CS. Caries experience in a sample of adolescents and young adults with cleft lip and palate in Brazil. *Cleft Palate Craniofac J.* 2013;50:187-191.
19. Kamble S, Hiremath SS, Puranik MP, et al. Dental Caries and Dental Anomalies in Children with Cleft Lip and Cleft Palate in Bengaluru City, India. *World J Dent.* 2017;8(4):304-308.
20. King NM, Wong WL, Wong HM. Caries experience of chinese children with cleft lip and palate. *Cleft Palate Craniofac J.* 2013;50(4):448-455. doi: 10.1597/11-133
21. Mutarai T, Ritthagol W, Hunsrisakhun J. Factors influencing early childhood caries of cleft lip and/or palate children aged 18 to 36 months in southern Thailand. *Cleft Palate Craniofac J.* 2008;45:468-472.
22. Moura AM, André M, Lopez MT, Dias RB. Prevalence of caries in Brazilian children with cleft lip and/or palate, aged 6 to 36 months. *Braz Oral Res* 2013;27(4):336-341. doi: 10.1590/s1806-83242013005000009
23. Tuaño-Cabrera CA, Ildelfonso EC, Palabrica MB. Caries Experience in Filipino Children with Cleft Lip and/or Palate from the Noordhoff Craniofacial Foundation, Philippines. *Acta Medica Philippina.* 2017;51:139-145.
24. Xiao WL, Zhang DZ, Xu YX. The caries prevalence of oral clefts in Eastern China. *Int J Clin Exp Med.* 2015;8:16322-16327.
25. Allam GG, Sobeh IA. Caries experience varies in Egyptian children with different combinations of cleft lip and palate and is related to carbohydrate intake between meals. *Cleft Palate Craniofac J.* 2021;58:414-418.
26. Howe BJ, Cooper ME, Wehby GL, et al. Dental Decay Phenotype in Nonsyndromic Orofacial Clefting. *J Dent Res.* 2017;96(10):1106-1114. doi: 10.1177/0022034517709961
27. Gupta A, Sethi S, Wadhwa J, Batra P, Shick EA. Is caries prevalence site-specific in cleft lip and palate patients? A systematic review and meta-analysis. *Dent Res J (Isfahan).* 2023;20:111.
28. Bian Z, Du M, Bedi R, Holt R, Jin H, Fan M. Caries experience and oral health behavior in Chinese children with cleft lip and/or palate. *Pediatr Dent.* 2001;23(5):431-434.
29. Ankola AV, Nagesh L, Hegde P, Karibasappa GN. Primary dentition status and treatment needs of children with cleft lip and/or palate. *J Indian Soc Paedod Prev Dent.* 2005;23:80-82.



The impact of interpersonal support on quality of life in traumatic brain injury patients – a one-month post-treatment analysis

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ABSTRACT

Introduction and aim. Traumatic brain injuries often result in serious consequences affecting the quality of life of patients, necessitating a profound understanding of influencing factors. This study aims to explore the relationship between interpersonal support and the quality of life in traumatic brain injury patients one month after treatment. The research seeks to identify the extent to which interpersonal support influences the quality of life in traumatic brain injury patients and whether this relationship remains significant one month after hospital treatment.

Material and methods. The research method employed is quantitative, involving sampling of traumatic brain injury patients aged 18–50 years without complications or disabilities who are willing to participate. Data is collected one month post-treatment through questionnaires encompassing scales measuring interpersonal support (ISEL) and post-TBI quality of life (QO-LIBRI). Data analysis is conducted using Pearson's correlation test in SPSS version 26 software.

Results. Statistical analysis revealed that traumatic brain injury patients with good interpersonal support exhibited significantly higher quality of life ($p=0.002$), with a strong correlation between the two variables ($r=0.663$). These findings indicate the crucial role of interpersonal support in enhancing the quality of life in patients.

Conclusion. The study confirms a positive relationship between interpersonal support and the quality of life in traumatic brain injury patients.

Keywords. interpersonal support, post-traumatic brain injury, quality of life

Introduction

Traumatic brain injury (TBI) is a global health issue that poses significant challenges and can have a profound impact on individuals' quality of life. Those suffering from TBI often face complex and diverse challenges, including cognitive, physical, and psychological disturbances. In this context, interpersonal support becomes a critical

element in the recovery of patients, emanating not only from medical professionals but also from family, friends, and the surrounding community.¹

While previous research has highlighted the relationship between interpersonal support and the quality of life for patients with head injury, there is an urgent need to understand in more detail the post-one-month

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treatment impact of this support.^{2,3} After one month, the initial recovery phase may have passed, and it is crucial to identify how the level of interpersonal support correlates with the ongoing development of quality of life.⁴

This study proposes a focus on the post-one-month treatment period, a critical phase in the recovery of patients with head injury. At this point, the challenges faced by patients and their families may have evolved, and interpersonal support relationships can significantly contribute to the improvement or deterioration of the patient's quality of life.^{5,6}

One reason this study is unique is lies in the integration of physical, cognitive, and psychological aspects of the impact of head injuries on quality of life. By considering these various dimensions, the study aims to provide a holistic understanding of how interpersonal support can help enhance these aspects and overall quality of life.⁷ While previous research often emphasized support from medical professionals, this study explored the significant role of support from family and the community. Involving a broader social environment will provide insights into how interpersonal support can be integrated into a larger social structure.^{8,9}

Furthermore, the novelty of this study lies in its comprehensive examination of the multidimensional impact of interpersonal support on TBI patients' quality of life. While previous research has predominantly focused on the role of medical professionals in providing support, this study takes a broader approach by exploring the contributions of familial, social, and community support networks. Additionally, by specifically targeting the post-one-month treatment period, this study fills a crucial gap in the literature and provides timely insights into the ongoing recovery process for TBI patients, ultimately contributing to the advancement of knowledge in this field. By understanding the relationship between interpersonal support and the quality of life for patients with head injury one month after treatment, this research has the potential to lay the foundation for the development of more effective interventions.¹⁰ We have a hypothesis that interpersonal support plays a relevant role in improving the quality of life of patients.

Aim

This research is conducted to explore the relationship of interpersonal support in the recovery of patients with head injury and specify how it can impact their quality of life one month post-treatment.

Material and methods

Study design

The research methodology employed in this study is a quantitative approach aimed at exploring the relationship between interpersonal support and the quality of life in patients with head injury one month post-treat-

ment. The study population focuses on patients with head injury in Indonesia within the age range of 18–50 years. Inclusion criteria involve patients without complications (patient does not have any psychological disorders or degenerative diseases such as Alzheimer's and dementia), disabilities (patient does not experience any disabilities or have any missing or amputated body parts), and those willing to participate as respondents in this study. The initial selection was conducted on 91 respondents who met the inclusion criteria, out of which 19 did not complete the process for one month due to health conditions, including mortality, and could not be contacted again for monitoring during the one-month period as depicted in Fig 1. The sample was selected using a purposive sampling approach, where patients meeting the criteria were invited to participate, resulting in 72 respondents.

Data collection took place one month after the patients underwent treatment at the hospital. Observations and data collection occurred during the patients' routine medical check-up visits to the hospital. Utilizing this method ensures that data is collected at a critical point in the patients' recovery while maintaining the regularity and consistency of data collection.

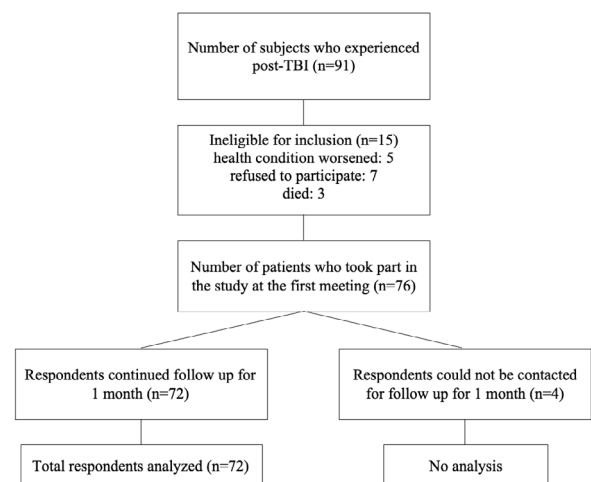


Fig. 1. Flowchart of the sampling process in this study

Instruments

The instruments used to measure interpersonal support and quality of life are structured questionnaires that have undergone validity testing ($p > 0.05$) and reliability testing (Cronbach's alpha $p > 0.361$). The questionnaire was specifically designed to understand the level of interpersonal support received by patients and measure relevant aspects of quality of life in the context of head injuries. The interpersonal support instrument employs the Interpersonal Support Evaluation List (ISEL), while the quality of life instrument utilizes the Quality of Life after Brain Injury (QOLIBRI). Meanwhile, the level of

consciousness is assessed using the Glasgow Coma Scale (GCS), which consists of three parameters: eye opening response, verbal response, and motor response, with scores ranging from 3 to 15.

ISEL consists of 12 items with four response options: definitely wrong, probably wrong, probably right, and definitely right. QOLIBRI comprises 6 parameters, including cognitive abilities (7 items), emotions (7 items), independence (7 items), social relationships (6 items), feelings (5 items), and physical issues (5 items). During medical check-up visits, patients were invited to fill out the questionnaire containing questions related to interpersonal support and aspects of quality of life. Researchers provided guidance to respondents to ensure a clear understanding of the questions and minimize bias in questionnaire completion.

Data analysis

The collected data will be analyzed using the Pearson correlation test in the SPSS statistical software version 26 (IBM, Armonk, NY, USA). The Pearson test was chosen because it is suitable for evaluating linear relationships between two variables. Prior to analysis, data distribution will be checked to ensure conformity with normality assumptions using the Shapiro-Wilk normality test.

Ethical approval

The study has obtained ethical clearance with number 089.6/II.3.AU/F/KEPK/IV/2023 and received permission from the local health authorities. Adequate information for informed consent has been provided, and patient data confidentiality is maintained.

Results

The Adjusted R Square value obtained from the regression test is 0.612, indicating a better fit. Good interpersonal relationships in patients with trauma brain injuries account for 61.2%, while the rest is attributed to other variables that need further investigation. During the initial regression testing phase, variables such as age, GCS score, and ISEL were found to meet the criteria. In the subsequent phase, only age and ISEL variables were considered. It was found that ISEL was the most dominant variable influencing the quality of life in post-TBI patients.

Men in general engage in higher levels of activity and mobility, making them more susceptible to traffic accidents. Particularly for those in their productive years and already married, they bear responsibilities towards both their families and work. In this study, married men are often involved in accidents, as evidenced by the data presented in Table 1. The men involved in the accident in this study amounted to 84% (49 out of 58), all of whom experienced head injuries. Men in their

productive age group are more likely to engage in activities using motorcycles for daily mobility. Educational status also plays a role, with individuals having only elementary, junior high school, and high school education being represented. Men have a strong work ethic. Higher education makes it easier for them to find jobs, often in fieldwork. On average, they have to travel more than 10 km from home to work every day.

Table 1. Characteristic of Participants (n=72)

	n	%
Sex		
Male	58	80.5
Female	14	19.5
Education		
No	12	16.7
Elementary/Middle/Senior High School	46	63.8
College	14	19.5
Marital Status		
Not married	5	6.9
Married	56	77.8
Divorced	11	15.3
Trauma Mechanism		
Accident	42	58.3
Fall	18	25
Other	12	16.7

Table 2. Correlation analysis test results (n=72)

	Median (Min–Max)	Mean±	r	p
Age	47 (24–57)	43.42±	0.385	0.015
GCS	12 (8–14)	11.33±	0.226	0.037
ISEL	32 (25–35)	30.44±	0.663	0.002

Table 3. Regression analysis test results (n=72)

		Coefficients	r	p
Step 1	Age	0.209	0.283	0.016
	GCS Score	0.753	0.180	0.116
	ISEL	-0.529	-0.417	0.005
	Constant	133.741		
Step 2	Age	0.234	0.317	0.017
	ISEL	-0.624	-0.515	0.007
	Constant	141.730		

The common accident that occurs is traffic accidents involving motorcycles. On average, patients are taken to the hospital still conscious if they arrive after the incident. The average age of the respondents is within the productive age range, and those who have experienced accidents show a decrease in consciousness with a Glasgow Coma Scale (GCS) score of 12. The respondents mostly have GCS scores ranging from 12 to 14. The lowest GCS score, which is 8, is only found in one respondent, while GCS scores of 10 are present in two respondents, and GCS scores of 11 are present in three respondents. The rest of the respondents have good GCS scores. Despite this, they exhibit good interpersonal support and a high quality of life, as indicated in Table

2. Statistical results demonstrate a significant correlation between good interpersonal support and the quality of life of patients one month after a head injury, with a strong correlation strength, as depicted in Table 2. Good interpersonal support was identified as a predictive factor for better quality of life, as in Table 3.

Discussion

The data indicates that males are more prone to accidents, possibly due to their higher participation in risky activities and mobility. The fact that married men experience accidents more frequently highlights the impact of family and work responsibilities on accident rates.¹¹ Additionally, the relationship between educational status and accidents provides a more comprehensive picture, emphasizing the importance of health literacy in preventing head injuries.^{12,13}

The average age of the respondents reflects a population still in their productive years, facing a high risk of accidents. A decrease in consciousness with a Glasgow Coma Scale (GCS) score of 12 indicates the serious impact of head injuries, which may require specific attention and recovery efforts.¹⁴ This aligns with previous research findings indicating that the early level of consciousness can predict the prognosis of patients with head injuries.^{15,16}

Statistical test results show that patients with good interpersonal support have a good quality of life ($p=0.002$). The strong correlation ($r=0.663$) emphasizes the positive relationship between these two variables. This suggests that patients with head injury receiving adequate interpersonal support are more likely to experience a positive recovery in terms of their quality of life.

Social interaction and support from the social environment can help individuals cope with stress, reduce the psychological impact of injuries, and enhance overall well-being.^{17,18} Close relationships with family and friends, especially for men with family responsibilities, can provide the emotional and practical resources needed during the recovery process.^{19,20}

Furthermore, strong interpersonal support can help patients overcome the stress, depression, and anxiety often associated with health conditions that require long-term recovery.²¹ Balancing social support and mental health conditions plays a key role in improving the quality of life for patients.²²

The social support model has been recognized as a determinant of quality of life, especially in the context of chronic health conditions.^{23,24} Good interpersonal support is identified as a predictive factor for better quality of life. These findings align with current research, emphasizing the need to consider social support as an integral part of the care for patients with head injury. Although this research proves that interpersonal support has a significant impact on the quality of life of post-

TBI patients, longitudinal studies need to be conducted over a longer period of time to see whether interpersonal support is still the most dominant variable influencing the quality of life of post-TBI patients.

Conclusion

The findings of this research provide a deeper understanding of the relationship between interpersonal support and the quality of life of patients one month after a head injury. Other factors such as gender, marital status, educational status, age, and the level of initial consciousness play a crucial role in patient recovery. These findings are not only relevant in the context of public health but also have practical implications for the planning and implementation of more effective rehabilitation programs.

Declarations

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Author contributions

Conceptualization, P.A.W.S and F.K.; Methodology, A.O. and S.K.D.S; Software, X.X.; Validation, P.A.W.S and A.O.; Formal Analysis, S.K.D.S.; Investigation, F.K.; Resources, P.A.W.S.; Data Curation, M.F.B.; Writing – Original Draft Preparation, P.A.W.S.; Writing – Review & Editing, F.K.; Visualization, P.A.W.S.; Supervision, F.K.

Conflicts of interest

All author declare have no conflict of interest.

Ethics approval

This study was approved by the local ethics committee (Health Research Ethics Committee in Universitas Muhammadiyah Gombong, date: 19.04.2023 decision number: 21124000003).

References

1. Formisano R, Longo E, Azicnuda E, et al. Quality of life in persons after traumatic brain injury as self-perceived and as perceived by the caregivers. *Neurol Sci.* 2017;38(2):279-286. doi: 10.1007/s10072-016-2755-y
2. Tramonti F, Bonfiglio L, Di Bernardo C, et al. Family functioning in severe brain injuries: correlations with caregivers' burden, perceived social support and quality of life. *Psychology, Health & Medicine.* 2015;20(8):933-939. doi: 10.1080/13548506.2015.1009380
3. Salas CE, Rojas-Libano D, Castro O, et al. Social isolation after acquired brain injury: Exploring the relationship between network size, functional support, loneliness and mental health. *Neuropsychological Rehabilitation.* 2022;32(9):2294-2318. doi: 10.1080/09602011.2021.1939062
4. Gordon WA, Cantor J, Kristen DO, Tsousides T. Chapter 27 - Long-term social integration and community support.

- In: Grafman J, Salazar AM, eds. *Handbook of Clinical Neurology*. Vol 127. Traumatic Brain Injury, Part I. Elsevier; 2015:423-431. doi: 10.1016/B978-0-444-52892-6.00027-1
5. Gaertner LHC, Tsur N, Haller CS. Patients' recovery after severe TBI is associated with their close relatives' interpersonal functioning: a 12-months prospective cohort study. *Brain Injury*. 2020;34(6):766-774. doi: 10.1080/02699052.2020.1753241
 6. Mackenzie A, Fountain R, Alfred D, Combs D. EBSCOhost | 110231581 | Quality of Life and Adaptation for Traumatic Brain Injury Survivors: Assessment of the Disability Centrality Model. <https://web-p-ebSCOhost-com.ezproxy.ums.edu.my/abstract?site=ehost&scope=site&jrnl=00224154&AN=110231581&h=u8IDSFo66uc%2brWGrv78buwgNmzWIPqg83D8hyY80vb89q1pRDbcvqDq%2bm0YCo8W9KzXBhZHMAD8vPt5wBsF4wQ%3d%3d&rl=c&resultLocal=ErrCrlNoResults&resultNs=Ehost&crlhashurl=login.aspx%3fdirect%3dtrue%26profile%3dehost%26scope%3dsite%26authtype%3dcrawler%26jrnl%3d00224154%26AN%3d110231581>. Published 2015. Accessed January 28, 2024.
 7. Bosma CM, Mansoor N, Haller CS. Association of Post-traumatic Stress Symptom Severity With Health-Related Quality of Life and Self-Reported Functioning Across 12 Months After Severe Traumatic Brain Injury. *Archives of Physical Medicine and Rehabilitation*. 2018;99(8):1576-1583. doi: 10.1016/j.apmr.2018.02.008
 8. Takada K, Sashika H, Wakabayashi H, Hirayasu Y. Social participation and quality-of-life of patients with traumatic brain injury living in the community: A mixed methods study. *Brain Injury*. 2016;30(13-14):1590-1598. doi: 10.1080/02699052.2016.1199901
 9. Vos L, Poritz JMP, Ngan E, Leon-Novelo L, Sherer M. The relationship between resilience, emotional distress, and community participation outcomes following traumatic brain injury. *Brain Injury*. 2019;33(13-14):1615-1623. doi: 10.1080/02699052.2019.1658132
 10. Mamman R, Grewal J, Garrone JN, Schmidt J. Biopsychosocial factors of quality of life in individuals with moderate to severe traumatic brain injury: a scoping review. *Qual Life Res*. 2024;33(4):877-901. doi: 10.1007/s11136-023-03511-0
 11. Winter L, Moriarty HJ, Short TH. Beyond anger: emotion regulation and social connectedness in veterans with traumatic brain injury. *Brain Injury*. 2018;32(5):593-599. doi: 10.1080/02699052.2018.1432895
 12. Winter L, Moriarty HJ. Quality of relationship between veterans with traumatic brain injury and their family members. *Brain Injury*. 2017;31(4):493-501. doi: 10.1080/02699052.2017.1283534
 13. Ritchie L, Wright-St Clair VA, Keogh J, Gray M. Community Integration After Traumatic Brain Injury: A Systematic Review of the Clinical Implications of Measurement and Service Provision for Older Adults. *Archives of Physical Medicine and Rehabilitation*. 2014;95(1):163-174. doi: 10.1016/j.apmr.2013.08.237
 14. Kitter B, Sharman R. Caregivers' support needs and factors promoting resiliency after brain injury. *Brain Injury*. 2015;29(9):1082-1093. doi: 10.3109/02699052.2015.1018323
 15. Bannon SM, Greenberg J, Goldson J, O'Leary D, Vranceanu AM. A Social Blow: The Role of Interpersonal Relationships in Mild Traumatic Brain Injury. *Psychosomatics*. 2020;61(5):518-526. doi: 10.1016/j.psych.2020.04.003
 16. Lantagne A, Peterson RL, Kirkwood MW, et al. Featured Article: Interpersonal Stressors and Resources as Predictors of Adolescent Adjustment Following Traumatic Brain Injury. *Journal of Pediatric Psychology*. 2018;43(7):703-712. doi: 10.1093/jpepsy/jsy020
 17. Battista AD, Godfrey C, Soo C, Catroppa C, Anderson V. Depression and Health Related Quality of Life in Adolescent Survivors of a Traumatic Brain Injury: A Pilot Study. *PLOS ONE*. 2014;9(7):e101842. doi: 10.1371/journal.pone.0101842
 18. Cutler M, Nelson MLA, Nikoloski M, Kuluski K. Mindful Connections: The Role of a Peer Support Group on the Psychosocial Adjustment for Adults Recovering From Brain Injury. In: *Contemporary Perspectives on Social Work in Acquired Brain Injury*. Routledge; 2018.
 19. McLean AM, Jarus T, Hubley AM, Jongbloed L. Associations between social participation and subjective quality of life for adults with moderate to severe traumatic brain injury. *Disability and Rehabilitation*. 2014;36(17):1409-1418. doi: 10.3109/09638288.2013.834986
 20. Haller CS. Twelve-month prospective cohort study of patients with severe traumatic brain injury and their relatives: Coping, satisfaction with life and neurological functioning. *Brain Injury*. 2017;31(13-14):1903-1909. doi: 10.1080/02699052.2017.1346295
 21. Elliott TR, Hsiao YY, Kimbrel NA, et al. Resilience and Traumatic Brain Injury Among Iraq/Afghanistan War Veterans: Differential Patterns of Adjustment and Quality of Life. *Journal of Clinical Psychology*. 2017;73(9):1160-1178. doi: 10.1002/jclp.22414
 22. Chronister J, Johnson E, Chan F, Tu WM, Chung YC, Lee G. Positive Person-Environment Factors as Mediators of the Relationship Between Perceived Burden and Quality of Life of Caregivers for Individuals With Traumatic Brain Injuries. *Rehabilitation Counseling Bulletin*. 2016;59(4):235-246.
 23. Gould KR, Ponsford JL. A longitudinal examination of positive changes in quality-of-life after traumatic brain injury. *Brain Injury*. 2015;29(3):283-290. doi: 10.3109/02699052.2014.974671
 24. Ashman T, Cantor JB, Tsaousides T, Spielman L, Gordon W. Comparison of Cognitive Behavioral Therapy and Supportive Psychotherapy for the Treatment of Depression Following Traumatic Brain Injury: A Randomized Controlled Trial. *J Head Trauma Rehabil*. 2014;29(6):467. doi: 10.1097/HTR.0000000000000098



ORIGINAL PAPER

Knowledge, risk perception and utilization of hepatitis B vaccine among youths in a semi-urban area in Ibadan, Oyo state, Nigeria

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ABSTRACT

Introduction and aim. Hepatitis B is a chronic liver disease responsible for high morbidity and mortality. Despite the availability of hepatitis B vaccine, the incidence of disease is increasing. This study was designed to investigate the knowledge, risk perception, and utilization of hepatitis B vaccine among youths in the Ido Local Government Area, Oyo state, Nigeria.

Material and methods. A cross-sectional survey design was adapted, and 422 consenting youths were recruited. A pre-tested semi-structured questionnaire was used for data collection. A 19-point knowledge scale was used; scores ≤ 6 , $>6-12$, and $>12-19$ were considered poor, fair and good knowledge, respectively. Risk perception was measured on a 14-point scale, with scores ≤ 7 and >7 as poor and good, respectively. Data were analyzed using descriptive statistics, Chi-square and Fisher's exact at $\alpha_{0.05}$.

Results. Respondents were 26.6 ± 3.5 years, and 56.2% were females. Only 13.7% had good knowledge of hepatitis B, and 53.2% had a good perception of hepatitis B infection. Moreover, 48.9% had received at least one dose of the Hepatitis B vaccine. A significant association existed between knowledge, risk perception and utilization of hepatitis B vaccine.

Conclusion. Knowledge and utilization of hepatitis B vaccine were low among the respondents. Health education programs in the study area are crucial to improving hepatitis B vaccine utilization among youth.

Keywords. hepatitis B, risk perception, vaccine uptake, youths

Introduction

Hepatitis B virus (HBV) affects a large number of people worldwide and accounts for over 820,000 deaths per year. About 90% of infected people with hepatitis B are unaware of their infection and do not seek treatment which contributes to a significant share of hepatitis mortality and morbidity.¹ Although vaccines to prevent the disease have been available since the 1980s, the incidence of hepatitis B is still increasing.² The lack of, or the ineffectiveness of hepatitis management initiatives in the sub-Saharan region of Africa could be responsible for this increase in hepatitis B.³ The high mortality and morbidity that results is because people can live asymptotically

with the virus for up to 30 years. As a result, testing is typically conducted after the disease has progressed to a chronic stage and liver cirrhosis is already severe.³

According to estimates, the burden of hepatitis B infection is highest in the WHO Western Pacific Region and the WHO African Region which comprises 116 million and 81 million chronically infected people, respectively.⁴ This figure accounts for 23% of all cases of the disease worldwide. Hepatitis B prevalence in Nigeria ranges from 7.3% to 24% among different populations and may reach 64% among those with liver cancer.^{1,4,5-8}

Furthermore, 20 million Nigerians are infected with HBV, and about 5 million die as a result of the conse-

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Oyasope BT, Atibioko OP, Dipeolu IO. Knowledge, risk perception and utilization of hepatitis B vaccine among youths in a semi-urban area in Ibadan, Oyo state, Nigeria. *Eur J Clin Exp Med*. 2024;22(3):543–550. doi: 10.15584/ejcem.2024.3.9.



quences.⁹ Seroprevalence studies conducted in different regions among diverse populations in Nigeria have shown that the infection rate varies from 2.3% to 13% among healthcare workers, 11.4% among students in the University of Maiduguri and 12.2% among the general population. According to Oyero and Omoruyi, the prevalence of HBV infection in Oyo State is 22%.^{10,11} Hepatitis B infection is putting an increased economic burden on families, communities, and the country, and is the tenth leading cause of death and is more infectious than the human immunodeficiency virus (HIV).¹² Despite the availability of effective vaccines, low vaccine utilization has been recorded among community members in addition to a lack of information regarding prevalence and awareness among youths in Nigeria.

Thus, the disease is still endemic in the country. Although the vaccine is included in the National Immunization Program (NPI), there is little advocacy on the need for vaccination among the general population. Young adults (18–35 years old) represent 25% of the sexually active population. Nearly 50% of all newly acquired Sexually Transmitted Infections (STIs) are primarily caused by sexual ignorance, sexual abuse, non-use of condoms, increased number of relationships between young persons and older partners, use of psychoactive substances, and poor attitude in the utilization of healthcare services.¹³ In Nigeria, the vaccination of young adults has not had similar implementation success compared to child vaccinations. Scanning through the national HIV/AIDS and STIs Control Program National Policy for the Control of Viral Hepatitis in Nigeria 1st edition 2015, the national policy for the control of viral hepatitis in Nigeria emphasizes the need for public enlightenment on the transmission of viral hepatitis and vaccination, especially among healthcare workers, mothers of infants, and sex workers.¹² However, no information is provided that focuses on youths (young adults) as a high-risk group. Since hepatitis B high-risk groups can serve as reservoirs and carriers of the infection locally and as determinants of its prevalence internationally, the youths must be appropriately identified and monitored if universal prevention and control of disease spread is to be achieved.

Aim

While most studies focus on healthcare workers, medical students, and public safety workers, there are limited studies among the general population, particularly the youth. Hence, this study aimed to investigate the knowledge, risk perception and utilization of hepatitis B vaccine among youths aged 18–35 in the Ido Local Government Area (LGA), Oyo State, Nigeria.

Material and methods

Ethical approval

Ethical approval for the study was obtained from the Oyo State Research Ethical Review Committee (Ref.

No.: A.D. 13/479/304B). Also, written informed consent was obtained from each participant to assure them of voluntary participation and confidentiality associated with the data collection procedures.

Study design and setting

This was a cross-sectional design study that analyzed data of variables collected using a quantitative instrument at one given time across samples of youths from randomly selected wards and communities in Ido LGA in Oyo State.

Study population

The study population was comprised of young residents in the Local Government Area aged 18 to 35 years– as chronologically defined youth in the 2009 National Youth Policy and according to African Youth Charter.¹⁴ This study population was of interest because there has been no research carried out among the population regarding this subject matter. Moreover, the Centers for Disease Control and Prevention have flagged youth to be at risk of hepatitis B and associated diseases.^{15,16} The inclusion criteria considered youths living within the study area who were 18–35 years old and voluntarily participated in the survey. The exclusion criteria were youth visiting the study area at the time of the study, those who were indisposed at the time of the study, those who refused consent to complete the questionnaire, and those who withdrew from completing the questionnaire.

Sample size and sampling procedure

The sample size required for this study was calculated using 50% as a proxy, as no existing research focused on youths in Nigeria. At 5% tolerable error, 95% confidence and adjusting for 10% non-response. A minimum sample size of 422 was calculated. A multistage sampling technique was adopted to select respondents for this study. Oyo State is divided into five zones. Simple random sampling was used to select one Zone in the State. Ibadan Zone 1 was selected, and the Zone has 11 Local Government Areas (LGAs). Five LGAs (Ibadan North, Ibadan North East, Ibadan North West, Ibadan South West and Ibadan South East) are in the city's metropolitan area. Other LGAs (Akinyele, Egbeda, Ido, Lagelu, Oluyole & Ona-Ara) are semi-urban. The Ido Local Government Area was also randomly selected from the six semi-urban LGAs through simple random sampling (balloting). The Ido LGA has ten political wards, of which five were chosen randomly, comprising the study sites.

Data collection

A pre-tested semi-structured interviewer-administered questionnaire developed by the researchers in line with the reviewed literature was used to elicit information from the respondents. The authors used the Cronbach

alpha coefficient as a measure of the instrument's internal consistency. The Cronbach Alpha coefficient for this instrument was 0.74, indicating that the instrument is reliable. The questionnaire comprised five sections with a total of 63 items. The sections were designed to elicit the following information on the sociodemographic characteristics of the respondents (8 items), Awareness of hepatitis B among respondents (2 items), knowledge of hepatitis B among respondents (19 items), risk perception of hepatitis B among respondents (14 items) and the level of utilization of hepatitis B vaccine among respondents (8 items) and barriers to utilization of hepatitis B vaccine (12 items). Seven research assistants were trained on the ethics of research work and procedures essential to conducting the study. Houses in the selected wards were enumerated, and simple random sampling via balloting was used to select respondents from the enumerated houses. In places with more than one eligible respondent, balloting was used to select one of the respondents.

Statistical analysis

Completed questionnaires were coded with the aid of a developed coding guide and entered into the IBM/Statistical Package for Social Science (IBM/SPSS version 26). The sociodemographic information was described using descriptive statistics, showing frequency in frequency distribution tables and charts. Knowledge was measured on a 19-point scale; scores ≤6, >6–12 and >12–19 were considered poor, fair and good knowledge, respectively. Also, the risk perception was measured on a 14-point scale, where ≤7 was considered poor perception and >7 was considered good perception. Quantitative data was analyzed using descriptive statistics, Fisher's exact and Chi-square. Further analysis was also done for significance using multinomial regression to determine the magnitude of association at $\alpha_{0.05}$.

Results

The average respondent's age was 26.6±3.5 years, and 56.2% were females. Respondents with tertiary education accounted for 60.4%, 36% were self-employed, 63% were single, and most (59.5%) earned less than 30,000 Naira as average monthly income (Table 1).

Responses on knowledge of hepatitis B

The respondents' knowledge of hepatitis B is presented in Table 2. For general knowledge of hepatitis B transmission, some of the respondents (35.3%) knew that the disease can be transmitted through unprotected sex. About the signs and symptoms, almost half of the respondents (43.2%) were unaware of the symptoms of the disease, and only 19.8% knew that yellowing of the eyes and skin (jaundice) is one of the symptoms of the infection.

Table 1. Sociodemographic information of the respondents

Variables	n	%
Age (in years)		
≤ 20	75	17.8
21 to 25	104	24.6
26 to 30	131	31
31 to 35	112	26.5
Sex		
Male	185	43.8
Female	237	56.2
Education		
Primary	26	6.2
Secondary	141	33.4
Tertiary	255	60.4
Occupation		
Civil servant	23	5.5
Artisan	42	10
Student	138	32.7
Unemployed	8	1.9
Self-employed	152	36
Private worker	59	14
Marital Status		
Single	266	63
Married	152	36
Divorced	2	0.5
Widowed	2	.5
Average monthly income		
Below 30000	251	59.5
Above 30000	171	40.5

Table 2. General knowledge of HBV (n=278)^a

Statement	n	%
Hepatitis B can be transmitted through *		
Unprotected sex#	98	35.3
I do not know	70	25.2
Through sweat	51	18.3
Blood transfusion	38	13.7
Blood contact#	29	10.4
Body fluid#	26	9.4
Sharing sharp objects#	16	5.8
Mother to child#	14	5.0
Signs and symptoms of hepatitis B *		
Yellowing of eyes and skin#	55	19.8
Weight loss	36	12.9
Dark urine#	28	10.1
Fever#	26	9.4
Abdominal pain	24	8.6
Weakness	19	6.8
Eye redness	8	2.9
Joint pain#	7	2.5
Nausea#	5	1.8
Vomiting#	5	1.8
Bloated stomach	2	0.7
Others	1	0.4
I don't know	120	43.2

^a * – multiple responses, # – correct responses

Respondents level of knowledge of hepatitis B virus infection

Respondents' knowledge level was assessed using 19-item open-ended questions. It was observed that less than a quarter of the respondents (13.7%) had good knowledge of hepatitis B, 5.8% had fair knowledge, and 29.5% had poor knowledge, with a knowledge score of 8.4 ± 3.4 (Fig. 1).

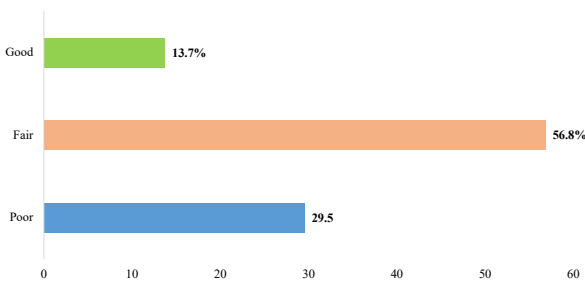


Fig. 1. Respondents' knowledge of hepatitis B

Respondents' risk perception on hepatitis B

The respondents' risk perception is presented in Table 3. Almost half (48.9%) agreed to be at risk of exposure to HBV, while slightly above half (53.6%) disagreed with the statement that since no one has a history of HBV in their family, they are not prone to it, 61.9% agreed that since they do not live with a person that is infected with hepatitis B, they are free from HBV. More than half (51.4%) also agreed that since they do not have multiple sexual partners, they are not prone to HBV. Slightly above half (51.8%) disagreed that since they are not exposed to human blood, they are free from HBV, and 48.2% also agreed that being prayerful persons, they are covered. Finally, 47.1% agreed that HBV is not common but rather over-emphasized.

Table 3. Response on risk perception (n=278)

Statement	Agree Freq. (%)	Disagree Freq. (%)
You are at risk of exposure to HBV	136 (48.9)	142 (51.1)
No one has a history of HBV in my family, so am not prone to it	129 (46.4)	149 (53.6)
Since I do not live with a person who is infected with Hepatitis B, I am free from HBV	172 (61.9)	106 (38.1)
Since I do not have multiple sexual partners, I am not prone to HBV	135 (48.6)	143 (51.4)
Since I am not exposed to human blood, I am free from HBV	134 (48.2)	144 (51.8)
I am a prayerful person, I am covered	134 (48.2)	144 (51.8)
HBV is not common disease; it is just over-emphasized	131 (47.1)	147 (52.9)

Respondents risk perception score on hepatitis B

The risk perception was assessed using a 14-item scale. Findings revealed that more than half of the respondents (53.2%) had a good perception of hepatitis B infection (Fig. 2), with a score of 7.2 ± 3.4 .

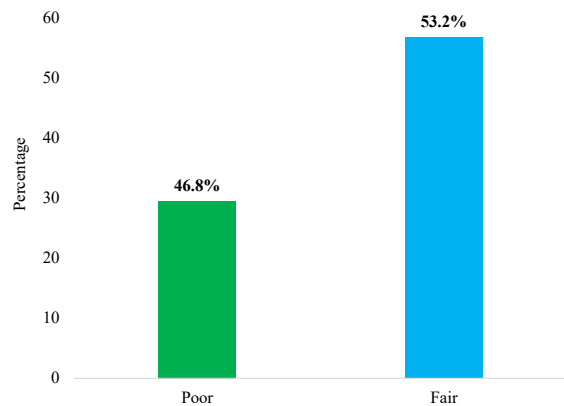


Fig. 2. Respondents' risk perception score on hepatitis B

Level of utilization of hepatitis B vaccine

Almost half (48.6%) of the respondents had been screened for hepatitis B. Less than one-quarter, 23.7%, were vaccinated against hepatitis B, 39.4% received their first dose more than six months before the study, and 33.3% had their first dose between one month and six months before the survey. More than one-third, 39.4%, reported they had received two doses of the vaccine, and 4.5% were unsure of the number(s) of dose (s) they have received so far. About the location where the vaccination was provided, 24.2% received the vaccine from a secondary health facility (Table 4).

Table 4. Respondent's uptake of hepatitis B vaccine

Variable	n	%
Screened against hepatitis B		
No	138	49.6
Yes	135	48.6
Not sure	5	1.8
Ever been vaccinated against hepatitis B (n=135)		
No	69	51.1
Yes	66	48.9
When the first dose was		
More than six months ago	26	39.4
Between one month and six months ago	22	33.3
About one month ago	2	3
Not sure	16	24.2
Point of vaccination		
Private hospital		
Private hospital	13	19.7
Secondary health centre		
Secondary health centre	16	24.2
Tertiary health centre		
Tertiary health centre	16	24.2
Primary health centre		
Primary health centre	15	22.7
Others +	6	9.1
Number of doses received so far		
One	24	36.4
Two	26	39.4
Three	13	19.7
Not sure	3	4.5

A significant association between respondents' level of education, occupation, and knowledge of hepatitis B was found ($p < 0.001$) ($p = 0.005$). However, other

sociodemographic characteristics were not statistically significantly associated with knowledge of hepatitis B infection (Table 5).

Table 5. Relationship between respondents' sociodemographic characteristics and knowledge of hepatitis B infection^a

Variable	Knowledge Category			df	χ^2	p
	Poor n (%)	Fair n (%)	Good n (%)			
Sex						
Male	34 (41.5)	63 (39.9)	10 (26.3)	2	2.813	0.251
Female	48 (58.5)	95 (60.1)	28 (73.7)			
Age						
≤20	10 (12.2)	27 (17.1)	10 (26.3)	6	6.867	0.336
21–25	20 (24.4)	42 (26.6)	9 (23.7)			
26–30	29 (35.4)	46 (29.1)	14 (36.8)			
31–35	23 (28.0)	43 (27.2)	5 (13.2)			
Average monthly income						
Below 30,000	42 (51.2)	97 (61.4)	18 (47.4)	2	3.758	0.164
Above 30,000	40 (48.8)	61 (38.6)	20 (52.6)			
Highest level of education						
Primary	6 (7.3)	5 (3.2)	0 (0)	3	24.648	<0.001**
Secondary	29 (35.4)	36 (22.8)	0 (0)			
Tertiary	47 (57.3)	117 (74.1)	38 (100)			
Marital status						
Single	49 (59.8)	101 (63.9)	29 (76.3)	2	5.445	0.264
Married	32 (39.0)	57 (36.1)	9 (23.7)			
Divorced	1 (1.2)	0 (0.0)	0 (0)			
Occupation						
Civil servant	8 (9.8)	11 (7.0)	0 (0)	10	25.132	0.005**
Artisan	9 (11.0)	7 (4.4)	0 (0)			
Student	17 (20.7)	59 (37.3)	20 (52.6)			
Unemployed	2 (2.4)	3 (1.9)	0 (0.0)			
Self-employed	36 (43.9)	52 (32.9)	9 (23.7)			
Private worker	10 (12.2)	26 (16.5)	9 (23.7)			

^a ** – statistically significant, χ^2 – Chi-square value, df – degree of freedom

Table 6. Relationship between respondents' knowledge of hepatitis B infection and the risk perception of hepatitis B vaccine^a

Variable	Perception Category			df	χ^2	p
	Poor n (%)	Good n (%)				
Knowledge						
Poor	56 (68.3)	26 (31.7)	2	23.125	<0.001**	
Fair	36 (34.6)	95 (60.1)				
Good	11 (28.9)	27 (71.1)				

^a ** – statistically significant, χ^2 – Chi-square value, df – degree of freedom

The study showed a significant association between knowledge of hepatitis B and risk perception of the disease ($p < 0.001$) (Table 6). Similarly, a significant association was also found between knowledge of hepatitis B

infection and the uptake of hepatitis B vaccine among the respondents ($p < 0.001$) (Table 7).

Table 7. Relationship between respondents' knowledge of hepatitis B infection and the uptake of hepatitis B vaccine^a

Variable	Uptake Category		df	χ^2	p
	No uptake, n (%)	Uptake, n (%)			
Knowledge					
Poor	79 (37.3)	3 (4.5)	1	39.827	<0.001**
Fair	116 (54.7)	42 (63.7)			
Good	17 (8.0)	21 (31.8)			

^a ** – statistically significant, χ^2 – Chi-square value, df – degree of freedom

There was a significant association between risk perception of hepatitis B infection and the uptake of the hepatitis B vaccine ($p = 0.007$) (Table 8).

Table 8. Relationship between respondents' risk perception of hepatitis B infection and the uptake of Hepatitis B vaccine^a

Variable	Uptake Category		df	χ^2	p
	No uptake, n (%)	Uptake, n (%)			
Risk perception					
Poor	109 (83.8)	21 (16.2)	1	7.764	0.007**
Good	103 (69.6)	45 (30.4)			

^a ** – statistically significant, χ^2 – Chi-square value, df – degree of freedom

Table 9. Association between respondents' knowledge of hepatitis B infection and the level of uptake of the hepatitis B vaccine^a

Variables	Sig.	OR	95% Confidence interval	
			Lower bound	Upper bound
Knowledge	<0.001**	4.856	2.839	8.305

^a ** – statistically significant, OR – odds ratio

Table 10. Association between respondents' risk perception of hepatitis B infection and uptake of hepatitis B vaccine^a

Variables	Sig.	OR	95% Confidence interval	
			Lower bound	Upper bound
Poor	–	–	–	–
Good	<0.001**	3.016	1.576	5.773

^a ** – statistically significant, OR – odds ratio

Multinomial regression analysis revealed that respondents who have higher knowledge of hepatitis B infection were 4.8 times more likely to uptake the hepatitis B vaccine rather than not uptake the hepatitis B vaccine ($p < 0.001$) (Table 9).

Logistic regression analysis revealed that respondents who have a good risk perception towards hepatitis B infection were 3.0 times more likely to uptake the hepatitis B vaccine ($p < 0.001$) (Table 10).

Discussion

The level of good knowledge (13.7%) reported in this study was lower than the findings in some similar studies. Yakudima et al. recorded 35% good knowledge among respondents in part of Jigawa State, Nigeria.¹⁷ Analyzing the study by Alotaibi et al., it was found that 42% of the respondents had poor knowledge of HBV.¹⁸ Although the majority had received a formal education, our findings suggest that health issues such as HBV may not be adequately emphasized in educational settings and literature within the public domain.

This study revealed that 25.2% of the respondents did not know how hepatitis B can be transmitted, which is lower than the study by Okonkwo et al. among healthy adults, which revealed that 40% of the respondents did not know how HBV can be transmitted.¹⁹ The identified modes of transmission observed in this study, such as blood contact, blood transfusion, infected needles, mother-to-child and unprotected sexual intercourse, align with the findings of Zafrin et al.²⁰

Hassan-Gillani et al. also pointed out that most respondents knew of the existence of the hepatitis B vaccine; however, respondents could not identify the age groups required to take the vaccine and the number of doses.²¹ Furthermore, Adam and Fusheini found a correlation between education level, HBV vaccination, and screening, which can be attributed to at least two factors.²² First of all, hepatitis B is a complicated disease with a range in its natural history, course, and therapeutic therapy such that people with low levels of education may find it challenging to comprehend and digest information on hepatitis B. Second, higher education students are more likely to have a superior understanding because they have easier access to HBV information from various sources. There are two significant consequences of these findings. Firstly, community people with poor educational attainment should be the focus of intervention initiatives to enhance knowledge. Secondly, information related to HBV being used in prevention programs needs to be simplified so that it is easy to understand for households with low academic education. Another important finding is the perceived effect of knowledge on health-seeking behavior, and respondents indicated they would visit the health facility for treatment if they were infected with hepatitis B, which shows they have good health-seeking behavior.

According to Patil et al. study among laboratory technicians, hygienists, laundry workers, and the housekeeping staff in a medical and dental hospital documented 67.2% positive risk perception among respondents, which is slightly higher than the findings of this study.²³ A study by Chingle et al. revealed that respondents had a 76.8% overall risk perception of hepatitis B infection, which is higher than the study findings due to the respondents being medical students with expansive lectures in virology.¹² In another

study by Ochu and Beynon, they recorded 55.3% good perception among the study respondents, and the findings are lower than those in this study.²⁴ This could be a result of the poor knowledge levels among the respondents.

A strong predictor for poor risk perception is poor knowledge. This study found a significant perception gap where most respondents opined they were not at risk of exposure because they did not live with an infected person. The perception gap can also be linked to a lack of understanding of how the hepatitis B virus can be transmitted. In a study conducted among cleaners in a tertiary hospital in Nigeria, among the respondents, 13.5%, 13.5% and 21.3% had low, medium and high-risk perceptions of acquiring hepatitis B infection, respectively, which is slightly lower than the findings of this study.¹⁹ According to a survey conducted in Jos among students at higher institutions, the University of Jos students had a high-risk perception of HBV infection. It was discovered that 76.8% of the students in the survey had a positive risk perception of hepatitis, with 40.7% of medical students and 40.1% of nursing students having a positive risk perception of hepatitis B, respectively. However, among public administration students, the risk perception of hepatitis B was found to be 9.1%, which is lower than the national average.¹²

The ultimate goal of the fight against HBV is to prevent new infections, and the most effective means of achieving zero infections is vaccination against the virus. However, the finding in this study is that there is a very low utilization of the hepatitis B vaccine among the population, which may reflect the true situation in many peri-urban communities in Nigeria.²⁵ The finding of this study showed that only 15.6% of the sampled respondents had received at least one dose of the hepatitis B vaccine, the finding is lower than the study by Tatsilong et al., which revealed that only 19% of the study population had received at least one dose of the hepatitis B vaccine.²⁶ A study conducted by Machmud et al. among the adult population in Indonesia reported that only 15% of the study respondents received at least one dose of the hepatitis B vaccine.²⁷ Another study conducted by Anthony and Babatunde among HCWs similarly reported low uptake of the hepatitis B vaccine, which is worrisome.²⁸

This study also revealed that receiving accurate information about hepatitis B infection and the advantages of vaccination is one of the best preventive measures related to hepatitis B vaccination. Njoroge et al. discovered that direct information from healthcare providers was most closely connected with receiving a hepatitis B vaccination, even though information about hepatitis B and immunization is accessible through the media, including television, scholarly journals, and the internet.²⁹⁻³² Ochu and Beynon revealed that the higher the perceived risk of contracting hepatitis B, the higher the awareness of the need for vaccination, similar to this study.²⁵ According to the Health Belief Model, the person's demograph-

ic traits and level of knowledge are modifying factors. It is hypothesized that various demographic and cognitive characteristics influence a person's perception, which may affect their health-related behavior. For instance, it is thought that educational attainment influences an individual's perception of the benefits-barriers of the action agent (such as the safety, efficacy, and affordability of the vaccine being used to reduce that threat) and perceived threat-agent benefits-barriers of the recommended health action or behavior (such as the susceptibility to and severity of the infection).³³

The implication of this finding for Nigerian youths, in particular, is that many people may still be unvaccinated and unprotected against HBV due to poor risk perception and continue to face the risk of HBV infection. This placed Nigeria on the negative side of progress in meeting sustainable development goal 3 regarding HBV infection control. The low uptake of the HBV vaccine identified in this study population may be because 82.1% of the respondents were born before the mandatory HBV vaccination for all infants was introduced in Nigeria in 2002. Therefore, continuous education is germane to change the negative trend if significant progress is made in preventing HBV among the youth.

Conclusion

There is a significant disparity in knowledge about HBV infection, screening, and vaccination among youths in Ido LGA. The poor level of knowledge and the high risk of HBV infection among the respondents have been highlighted in the findings of this study. The outcome also demonstrates that vaccination against HBV infection was low and consistent with other findings.

The findings of this study are significant in helping to highlight the gaps in the Sustainable Development Goal 3 on reducing infectious diseases, including HBV infection. Indeed, significant progress was reported regarding global HBV incidence and prevalence, whereby newborn infections of chronic HBV have decreased from 4.7% during the pre-vaccination era to 0.8% in 2017. However, there is a gap that needs to be bridged; there are still so many people who were born before the mass vaccination initiation and who continue to face the risk of infection, as found in this study. Therefore, there is a need for a culturally appropriate and evidence-based educational intervention to improve the knowledge of HBV. Additionally, developing and implementing national HBV screening and vaccination programs for the adult population are critical in winning the fight against the increasing morbidity and mortality associated with hepatitis B infections in Nigeria.

Declarations

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Author contributions

Conceptualization, B.T.O., O.P.A. and I.O.D.; Methodology, B.T.O. and I.O.D.; Software, B.T.O. and I.O.D.; Validation, B.T.O., O.P.A. and I.O.D.; Formal Analysis, B.T.O. and I.O.D.; Investigation, B.T.O., O.P.A. and I.O.D.; Data Curation, B.T.O., O.P.A. and I.O.D.; Writing – Original Draft Preparation, B.T.O., O.P.A. and I.O.D.; Writing – Review & Editing, B.T.O., O.P.A. and I.O.D.; Visualization, B.T.O.; Supervision, I.O.D.; Project Administration, B.T.O. and I.O.D.

Conflicts of interest

All authors declare that they have no conflict of interest

Data availability

The data sets generated during and/ or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics approval

Ethical approval for the study was obtained from the Oyo State Research Ethical Review Committee (Ref. No.: A.D. 13/479/304B).




Reference

1. Spearman CW, Afihene M, Ally R, et al. Hepatitis B in sub-Saharan Africa: strategies to achieve the 2030 elimination targets. *Lancet Gastroenterol Hepatol.* 2017;2(12):900-909. doi:10.1016/S2468-1253(17)30295-9
2. World Health Organization. 2017. Global Hepatitis Report, 2017. Geneva; 2017. <http://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455>. Accessed November 20, 2023.
3. Eni AO, Soluade MG, Oshamika OO, Efekemo OP, Igwe TT, Onile-Ere OA. Knowledge and awareness of Hepatitis B Virus infection in Nigeria. *Ann Glob Health.* 2019;85(1). doi:10.5334/aogh.33
4. World Health Organization. Hepatitis B. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>. Accessed November 20, 2023.
5. Forbi JC, Vaughan G, Purdy MA, et al. Epidemic history and evolutionary dynamics of hepatitis B virus infection in two remote communities in rural Nigeria. *PLoS One.* 2010;5(7):e11615. doi: 10.1371/journal.pone.0011615
6. Nwokedinko S, Ijoma UN, Obienu O. Liver Cancer in Enugu, South East Nigeria. *Liver Cancer in Enugu, South East Nigeria Insight Bioinformatics.* 2011;1(1):1-5.
7. Olayinka AT, Nasidi A, Gidado S, et al. Seroprevalence of hepatitis B infection in Nigeria: A national survey. *Am J Trop Med Hyg.* 2016;95(4):902-907. doi: 10.4269/ajtmh.15-0874
8. Akindigh TM, Joseph AO, Robert CO, Okojokwu OJ, Okechalu JN, Anejo-Okopi AJ. Seroprevalence of hepatitis B virus co-infection among HIV-1-positive patients in North-Central Nigeria: The urgent need for surveillance. *Afr J Lab Med.* 2019;8(1):622. doi: 10.4102/ajlm.v8i1.622

9. Okonkwo UC, Ngim OE, Osim H, et al. Knowledge of hepatitis B virus infection among traders. *Niger J Clin Pract.* 2017;20(4):415-420. doi: 10.4103/1119-3077.204404
10. Ijeoma UN, Meka IA, Omotowo B, et al. Sero-prevalence of Hepatitis B virus infection: A cross-sectional study of a large population of health care workers in Nigeria. *Nigerian Journal of clinical Practice.* 2021;24(1):38-44.
11. Oyero O, Omoruyi E. High prevalence of isolated hepatitis B core antibody among adults in oyo state, Nigeria: The need for review of diagnostic and vaccination guidelines. *Int J Trop Dis Health.* 2016;13(1):1-10. doi: 10.9734/ijtdh/2016/21523
12. Chingle MP, Osagie IA, Adams H, Gwomson D, Emeribe N, Zoakah AI. Risk perception of hepatitis B infection and uptake of hepatitis B vaccine among students of tertiary institution in Jos. *Ann Afr Med.* 2017;16(2):59. doi: 10.4103/aam.aam_49_16
13. Oluwole EO, Oyekanmi OD, Ogunyemi DO, Osanyin GE. Knowledge, attitude and preventive practices of sexually transmitted infections among unmarried youths in an urban community in Lagos State, Nigeria. *Afr J Prim Health Care Fam Med.* 2020;12(1):1-7. doi: 10.4102/phcfm.v12i1.2221
14. African youth charter. Youthpolicy.org. <https://www.youthpolicy.org/library/documents/african-youth-charter/>. Accessed April 3, 2024.
15. Masood Z, Jawaid M, Khan RA, Rehman S. Screening for hepatitis B & C: a routine pre-operative investigation. *Pakistan Journal of Medical Sciences.* 2005;21(4).
16. CDC. Hepatitis B - vaccination of adults. Centers for Disease Control and Prevention. <http://www.cdc.gov/hepatitis/hbv/vaccadults.html>. Accessed April 3, 2023.
17. Yakudima II, Magaji Y, Abdulkarim IA. Knowledge, attitude and practice towards Hepatitis B infection of people in part of Jigawa State, Nigeria. *Dujopas.* 2022;8(1a):117-130. doi: 10.4314/dujopas.v8i1a.13
18. Alotaibi BS, Althobaiti MA, Hazazi AY, et al. Exploration of knowledge, attitude, and practice among residents of Saudi Arabia toward hepatitis viruses. *Inquiry.* 2021;58:469580211059965. doi: 10.1177/00469580211059965
19. Okonkwo UC, Ngim OE, Osim H, et al. Knowledge of hepatitis B virus infection among traders. *Niger J Clin Pract.* 2017;20(4):415-420. doi:10.4103/1119-3077.204404
20. Zafrin N, Sarkar MAS, Rahman MM, Salma U, Mahub T, Azhar MA. Hepatitis B virus infection: Knowledge and awareness among the patients admitted in a tertiary care hospital in Bangladesh. *Viral Hepatit Derg.* 2019;25(1):6-13. doi: 10.4274/vhd.galenos.2018.001
21. Hassan-Gillani A, Hayat K, Bakar Ahmed A, Asif M, Azam A. Evaluation of knowledge about hepatitis B, its vaccination and its correlation with the vaccination status of the general population in Bahawalpur, Pakistan. *Med Univ.* 2019;21(3):105-112. doi: 10.24875/rmu.19000084
22. Adam A, Fusheini A. Knowledge, risk of infection, and vaccination status of hepatitis B virus among rural high school students in Nanumba North and South Districts of Ghana. *PLoS One.* 2020;15(4):e0231930. doi: 10.1371/journal.pone.0231930
23. Patil S, Rao RS, Agarwal A. Awareness and risk perception of hepatitis B infection among auxiliary healthcare workers. *J Int Soc Prev Community Dent.* 2013;3(2):67-71. doi: 10.4103/2231-0762.122434
24. Ochu CL, Beynon CM. Hepatitis B vaccination coverage, knowledge and sociodemographic determinants of uptake in high risk public safety workers in Kaduna State, Nigeria: a cross sectional survey. *BMJ Open.* 2017;7(5):e015845. doi: 10.1136/bmjopen-2017-015845
25. Adam A, Fusheini A. Knowledge, risk of infection, and vaccination status of hepatitis B virus among rural high school students in Nanumba North and South Districts of Ghana. *PLoS One.* 2020;15(4):e0231930. doi: 10.1371/journal.pone.0231930
26. Tatsilong N, Chu JJ, Wormann T, et al. Changing epidemiology of Hepatitis B and migration- a comparison of six Northern and North- Western European Countries. *European Journal of Public Health.* 2012;13(7):383-385.
27. Machmud PB, Führer A, Gottschick C, Mikolajczyk R. Barriers to and facilitators of hepatitis B vaccination among the adult population in Indonesia: A mixed methods study. *Vaccines (Basel).* 2023;11(2):398. doi:10.3390/vaccines11020398
28. Anthony M, Babatunde S. Uptake and completion rates of hepatitis b vaccination among health care workers at a referral hospital in Uyo, Akwa Ibom State. *EPRA International Journal of Multidisciplinary Research.* 2023;9(1):168-177. doi:10.36713/epri12227
29. Njoroge J, Hope VD, O'Halloran C, et al. Are there missed opportunities for vaccinating against hepatitis B among people who inject drugs in the UK? *Epidemiol Infect.* 2019;147(e244):e244. doi: 10.1017/S0950268819001353
30. Ghomraoui FA, Alfaqeeh FA, Algadheeb AS, Al-Alsheikh AS, Al-Hamoudi WK, Alswat KA. Medical students' awareness of and compliance with the hepatitis B vaccine in a tertiary care academic hospital: An epidemiological study. *J Infect Public Health.* 2016;9(1):60-65. doi: 10.1016/j.jiph.2015.06.00
31. Machiya T, Burnett RJ, Fernandes L, et al. Hepatitis B vaccination of healthcare workers at the Princess Marina Hospital, Botswana. *Int Health.* 2015;7(4):256-261. doi: 10.1093/inthealth/ihu08
32. Mursy SMEM, Mohamed SOO. Knowledge, attitude, and practice towards Hepatitis B infection among nurses and midwives in two maternity hospitals in Khartoum, Sudan. *BMC Public Health.* 2019;19(1):1597. doi: 10.1186/s12889-019-7982-8
33. Getnet MA, Bayu NH, Abteu MD, W/Mariam TG. Hepatitis B vaccination uptake rate and predictors in health-care professionals of Ethiopia. *Risk Manag Healthc Policy.* 2020;13:2875-2885. doi: 10.2147/RMHP.S286488



Clinical significance of serum interleukin-6 levels in patients with chronic kidney disease

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ABSTRACT

Introduction and aim. Elevated levels of interleukin-6 (IL-6) in serum and kidney tissues are associated with the development and progression of chronic kidney disease (CKD). Although the role of pro-inflammatory cytokines, such as IL-6, in the development of cardiovascular complications is well studied, the relationship between serum IL-6 levels and CKD markers remains unclear. This study investigated the clinical significance of serum IL-6 levels in patients with CKD.

Material and methods. Participants were divided into two groups based on estimated glomerular filtration rate (eGFR): group 1 (n=86) with eGFR >60 mL/min and group 2 (n=74) with eGFR <60 mL/min. The CKD Epidemiology Collaboration equation was used to calculate eGFR from serum creatinine and cystatin C levels to assess CKD severity.

Results. Systolic blood pressure was higher in Group 2 than in Group 1 (138±22 mmHg vs. 129±19 mmHg; p<0.05). Serum IL-6 levels were also higher in group 2 (3.095 [interquartile range: 1.528–6.547] pg/mL) than in group 1 (1.711 [interquartile range: 0.920–3.342] pg/mL; p <0.05). Serum IL-6 levels were strongly correlated with eGFR in multivariable-adjusted linear regression analysis.

Conclusion. IL-6 levels increased in patients with CKD with an eGFR <60 mL/min, and this increase was associated with eGFR and diastolic blood pressure.

Keywords. blood pressure, body mass index, chronic kidney disease, estimated glomerular filtration rate, interleukin, obesity

Introduction

The severity of chronic kidney disease (CKD) and occurrence of cardiovascular and cerebral complications should be assessed in a timely manner for primary and secondary prevention. Changes in interleukin (IL)-6 levels in both serum and kidney tissues are associated with the development and progression of CKD.¹⁻³ IL-6 is absent in healthy kidneys, and its normal level in blood plasma is 1–2 pg/mL.³ Furthermore, it is produced by activated monocytes, macrophages, fibroblasts, endothelial cells, and mesangial and epithelial cells of the renal tubules.^{4,5} It is a major me-

diator of acute inflammation.⁶⁻⁸ Its secretion increases in acute inflammatory diseases, with serum concentrations reaching up to 1,000 pg/mL. In muscle and adipose tissues, it stimulates energy mobilization and increases body temperature. It is the main stimulator of the acute-phase protein synthesis in the liver.

Additionally, IL-6 stimulates the proliferation and differentiation of B and T cells as well as leukopoiesis. Patients with CKD frequently have high levels of IL-6 in their blood,⁹ which occur mostly through increased production as a result of oxidative stress, chron-

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ic inflammation, and excess fluid in the body. Decreased IL-6 clearance, due to compromised renal function, leads to its accumulation. Cardiovascular events are associated with elevated IL-6.^{10,11} Similarly, cardiovascular disease (CVD) is associated with CKD.¹² The relationship between CKD and CVD remains unclear; however, inflammation can be associated with it.¹² Inflammatory activity, as measured by biomarkers, may affect cardiovascular outcomes across renal function. Although the role of proinflammatory cytokines in the development of cardiovascular complications has been extensively studied, the relationship between serum IL-6 levels and CKD markers is not completely understood.

Aim

This study aimed to evaluate the clinical significance of serum IL-6 levels in patients with CKD.

Material and methods

Study design and participants

We enrolled 150 patients with CKD, of whom 64 (42.7%) were men and 86 (57.3%) were women, aged 18–80 years, with a mean age of 55.2 ± 11.9 years at the time of diagnosis. Based on the estimated glomerular filtration rate (eGFR), the participants were divided into two groups: group 1 (n=82) included patients with eGFR >60 mL/min (50 women and 30 men), and group 2 (n=68) included those with eGFR <60 mL/min (32 women and 36 men). CKD was diagnosed based on the presence of signs of damage and/or decreased renal function.¹³ The level of IL-6 was classified as <2 ng/L or ≥ 2 ng/L for categorical analysis, as the study median was 2.1 ng/L. To assess the severity of CKD, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI_{cr-cys}) equation was used to calculate the estimated glomerular filtration rate (eGFR) from serum creatinine and cystatin C, which were obtained prior to dialysis initiation.¹⁴

Inclusion and exclusion criteria

The inclusion criteria were the presence of signs of CKD and the exclusion criteria were the presence of thyroid pathology, fever, or stage 5G CKD; treatment with tocilizumab, itolizumab, sarilumab, satralizumab, siltuximab, and other drugs directed against the IL-6 receptor; diseases characterized by an increase in IL-6 in the blood regardless of kidney function, such as rheumatoid arthritis and systemic lupus erythematosus; and a history of treatment with corticosteroids and immunosuppressants. Body mass index (BMI) was calculated as follows: $BMI (kg/m^2) = \text{mass (kg)}/\text{height (m)}^2$. Systolic and diastolic blood pressure levels (SBP and DBP, respectively; mmHg) and heart rate (beats/min) were measured following the standard guidelines.¹⁵ Participants with a history of any of the following conditions were considered to have CVD: hypertension, myocardial infarction,

stroke, heart failure, angina pectoris, or angina/peripheral artery disease surgery.

Data collection and process

All the patients were tested for serum cystatin C (mg/L) and creatinine ($\mu\text{mol/L}$) levels. Low-weight proteinuria (mg/day) was evaluated by high-performance liquid chromatography (Thermo Fisher Scientific, Waltham, MA, United States). Serum IL-6 samples were obtained and analyzed using a human IL-6 enzyme-linked immunosorbent assay kit (Sigma-Aldrich, Burlington, MA, USA). The results were recorded using a Chromate Microplate Reader (Awareness Technology Inc., Palm City, FL, USA). The normal upper limit for IL-6 level was set to 10 pg/mL.

Ethical approval

Confidentiality of patient data was maintained, and participants provided their informed consent. This study was approved by the Institutional Ethics Committee of Maheshwara Medical College and Hospital, Hyderabad on June 26, 2023 and was performed in accordance with the Declaration of Helsinki.

Statistical analysis

Data are expressed as n (%) or the mean \pm standard deviation. Student's t-test (parametric data) and Mann-Whitney U test (nonparametric data) was used to assess the significance of differences between the groups. Nonparametric data are expressed as the interquartile range (IQR; 25th–75th quartile). Pearson or Spearman correlation coefficients were used to measure the linear relationship between variables depending on the type of distribution. The adjusted odds ratios (ORs) between the highest and lowest tertiles of IL-6 levels in patients with CKD and controls were obtained using multivariate logistic regression. When comparing the groups based on the tertile of IL-6, our study was intended to have 80% statistical power to detect an odds ratio of 1.77 at a 2-sided $p < 0.05$. Furthermore, at a 2-sided $p < 0.05$, we have 80% statistical power to identify a mean difference of 0.3 standard deviations in IL-6 between the groups. In categorical analyses, IL-6 levels <2 ng/L were used as a reference to obtain Cox proportional hazard ratios (HRs) with 95% confidence intervals. Statistical significance was set at two-sided $p < 0.05$. Statistical analyses were performed using Statistica 8.0 software package (TIBCO Software Inc., Palo Alto, CA, USA).

Results

All patients with CKD had comorbidities, including coronary heart disease, overweight or obesity, hypertension, type 2 diabetes mellitus (T2DM), chronic obstructive pulmonary disease, chronic pyelonephritis, and chronic glomerulonephritis. The number of patients with primary kidney pathologies did not differ significantly between

the two groups. Stages G1, G2, G3a, G3b, and G4 were observed in 25 (16.7%), 72 (48.0%), 28 (18.7%), 14 (9.3%), and 11 (7.3%) patients, respectively (Table 1).

Table 1. Number of patients with CKD at different stages*

Stages of CKD	GFR categories (ml/min/1.73 m ²), description and range	n (%)
G1	Normal and high (≥ 90)	25 (16.7%)
G2	Mild reduction related to normal range (60–89)	72 (48.0%)
G3a	Mild-moderate reduction (45–59)	28 (18.7%)
G3b	Moderate-severe reduction (30–44)	14 (9.3%)
G4	Severe reduction (15–29)	11 (7.3%)

* CKD – chronic kidney disease, KDOQI – kidney disease outcomes quality initiative, GFR – glomerular filtration rate

The mean patient age differed significantly between the two groups ($p < 0.05$). The sex distribution differed significantly between the two groups, with a higher female predilection in group 1 than in group 2. BMI, DBP, and heart rate did not differ significantly between the two groups (Table 2). SBP was significantly higher in group 2 than in group 1 (138 ± 22 mmHg vs. 129 ± 19 mmHg; $p < 0.05$). Serum IL-6 levels were significantly higher in group 2 (3.095 [IQR: 1.528–6.547] pg/mL) than in group 1 (1.711 [IQR: 0.920–3.342] pg/mL; $p < 0.05$). Thus, serum IL-6 levels were negatively correlated with eGFR ($r = -0.152$; $p = 0.022$). Additionally, serum IL-6 levels were strongly associated with DBP ($r = 0.125$, $p = 0.048$).

Table 2. Clinical and laboratory parameters in groups 1 and 2^a

Parameters	Group 1	Group 2
Age, years	$54.6 \pm 13.8^*$	$55.2 \pm 11.9^*$
Sex, female:male	61%:39%	47.1%:52.9%
SBP, mmHg	128 ± 18	$139 \pm 23^*$
DBP, mmHg	92 ± 16	91 ± 17
Heart rate, beats/min	81 ± 15	81 ± 14
Presence of CVD, n (%)	42 (28%)	39 (26%)
BMI, kg/m ²	29.3 ± 5.1	29.2 ± 4.6
IL-6, pg/mL	1.703 (IQR: 0.905–3.232)	3.082 (IQR: 1.510–6.458)*
Serum creatinine, $\mu\text{mol/L}$	75.8 (IQR: 61.1–91.3)	196 (IQR: 91.4–296.6)*
Serum cystatin C, mg/L	1.022 (IQR: 0.844–1.192)	2.242 (IQR: 1.436–2.964)*
Proteinuria, mg/d	79.4 (IQR: 70.2–94.1)	85.8 (IQR: 69.4–99.6)
eGFR, mL/min	80.2 (IQR: 73.6–87.9)	33.2 (IQR: 22.3–48.3)*

^a data are expressed as mean \pm standard deviation or number (frequency) for binary variables, * – $p < 0.05$. SBP – systolic blood pressure, DBP – diastolic blood pressure, CVD – cardiovascular disease, BMI – body mass index, IL-6 – interleukin-6, eGFR – estimated glomerular filtration rate, IQR – interquartile range

Multivariate-adjusted logistic regression analysis was used to calculate the ORs (with 95% confidence intervals) for CKD when comparing the two higher tertiles of serum IL-6 levels with the lower tertiles (Table 3). After adjusting for possible confounders, higher IL-6 levels were

associated with the odds of developing CKD. Serum IL-6 levels were strongly correlated with eGFR in multivariable-adjusted linear regression analysis (Table 4).

Table 3. Odds ratios of CKD associated with the higher compared to the lowest tertiles of IL-6*

IL-6 ($\mu\text{g/mL}$)	Multivariable-adjusted ^a	
	OR (95% CI)	p
≤ 1.2	1.0 (ref)	0.03
$> 1.2-2.6$	1.2 (0.5–2.3)	
> 2.6	2.5 (1.1–5.5)	

* CI – confidence interval; IL-6 – interleukin 6, ^a – adjusted for age, sex, systolic blood pressure, diastolic blood pressure, heart rate, presence of cardiovascular disease, body mass index, serum creatinine, serum cystatin C, and estimated glomerular filtration rate

Table 4. Multivariable-adjusted regression coefficients (95% CI) of eGFR associated with a SD difference in IL-6*

SD	eGFR, mL/min/1.73 m ²	
	β (95% CI)	p
IL-6 (Log, 0.8 ng/mL)	-3.95 (-6.56 to -1.22)	0.0015

* SD – standard deviation, eGFR – estimated glomerular filtration rate, CI – confidence interval, IL-6 – interleukin-6

The event rates for major adverse CV events, such as CV death, myocardial infarction, and stroke, associated with the concentration of IL-6 in the CKD strata (eGFR > 60 mL/min and < 60 mL/min) are shown in Figure 1.

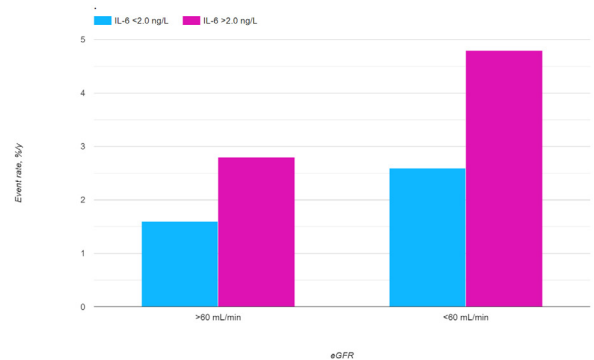


Fig. 1. Event Rates for major adverse CV events by CKD Strata

Discussion

In this study, we considered serum cystatin C in the eGFR assessment as the serum cystatin C level is a better indicator of renal function (GFR) than the serum creatinine level.^{16,17} The prognoses of both CVD and CKD are associated with proinflammatory cytokines.^{7,8} CKD is worsened by pro-inflammatory cytokines including IL-6.¹⁸ Our study demonstrated a notable increase in IL-6 levels in patients with CKD. Furthermore, CKD severity directly correlated with IL-6 levels. These findings align with the results of prior extensive epidemiological investigations.^{19,20} All kid-

ney cell types, such as podocytes, mesangial cells, endothelial cells, and epithelial cells, generate IL-6.²¹ Podocytes, the central cell type involved in IL-6 signaling, express the IL-6 receptor. However, all kidney cells are susceptible to the harmful effects of IL-6 trans-signaling because they express Glycoprotein 130. Studies have shown that podocytes produce IL-6 in response to high glucose levels, and inhibiting IL-6 in rats prevents podocyte damage and death. Mesangial cells also recruit monocytes in response to high IL-6 levels by secreting chemoattractant protein 1. Although the IL-6 signaling pathway appears to be involved in only one type of kidney cell, both this pathway and the trans-signaling pathways are active in the development of diabetic nephropathy.²² Renal abnormalities associated with high IL-6 expression and CKD include increased fibronectin expression in the mesangium, IL-6 mRNA levels, podocyte damage, glomerular hypertrophy, and endometrial alterations.

Elevated IL-6 levels are often linked to CKD because of their harmful effects on kidney cells. Research indicates that IL-6 levels increase in the early stages of CKD and are associated with higher mortality rates in late-stage CKD.^{21,23} Moreover, reduced renal clearance of IL-6 suggests that it may be a symptom of impaired kidney function rather than a cause of the disease.

IL-6 secretion is moderately increased in chronic, mild inflammatory processes, which are characteristic of CKD.⁶⁻⁸ Accordingly, in this study, patients with CKD showed significantly elevated IL-6 levels, and eGFR was significantly associated with serum IL-6 levels. eGFR is also significantly associated with tumor necrosis factor-alpha levels.²⁴

Table 5. Correlation between interleukin-6 levels and clinical and laboratory parameters*

Parameters	IL-6, pg/mL	
	r	p
SBP, mmHg	0.071	0.297
DBP, mmHg	0.125	0.048
BMI, kg/m ²	0.013	0.843
Serum creatinine, mmol/L	0.019	0.695
Serum cystatin C, mg/L	0.041	0.516
Proteinuria, mg/d	0.017	0.604
eGFR, mL/min	0.152	0.022

* SBP – systolic blood pressure, DBP – diastolic blood pressure, BMI – body mass index, eGFR – estimated glomerular filtration rate, IL-6 – interleukin-6

In the present study, the number of overweight or obese patients with T2DM was high. In an Egyptian study, IL-6 levels were elevated in patients with obesity and T2DM.²⁵ IL-6 elevation is accompanied by the proliferation of vascular smooth muscle cells and increased production of platelet growth factor.^{26,27} In this study, proinflammatory cytokines were involved in the occurrence of cardiovascular complications in patients with CKD. IL-6 levels were

not correlated with SBP; however, in group 2, the levels of proinflammatory cytokines and SBP were significantly higher. Furthermore, IL-6 levels were strongly associated with DBP (Table 5). The correlations between serum IL-6 levels and hemodynamic parameters are attributable to the induction of vasoconstriction and increased activity of the sympathetic nervous system caused by IL-6 and the association of elevated tumor necrosis factor-alpha levels with increased vascular stiffness.²⁸ Thus, the pathogenetic mechanisms of CKD progression involving proinflammatory cytokines, particularly IL-6, are extremely complex and diverse and require further research.

Conclusion

The mean patient age differed significantly between the two groups, with a higher female predilection in group 1 than in group 2. The study found that IL-6 levels were significantly higher in patients with CKD than in healthy individuals, and the levels were positively correlated with CKD severity. This study also found that IL-6 levels were significantly associated with cardiovascular events, and the odds of cardiovascular events were higher in patients with higher IL-6 levels.

Declarations

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Author contributions

Conceptualization, R.C.C., P.B., V.R.B. and Y.V.; Formal Analysis, P.B., V.R.B., and Y.V.; Writing – Review & Editing, R.C.C., P.B., V.R.B. and Y.V.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability

Data are available from the corresponding author upon reasonable request.

Ethics approval

This study was approved by the Institutional Ethics Committee of Maheshwara Medical College and Hospital, Hyderabad on June 26, 2023.



References

- Durlacher-Betzer K, Hassan A, Levi R, et al. Interleukin-6 contributes to the increase in fibroblast growth factor 23 expression in acute and chronic kidney disease. *Kidney Int.* 2018;94(2):315-325. doi: 10.1016/j.kint.2018.02.026
- Rops ALWMM, Jansen E, van der Schaaf A, et al. Interleukin-6 is essential for glomerular immunoglobulin A deposition and the development of renal pathology in Cd37-deficient mice. *Kidney Int.* 2018;93(6):1356-1366. doi: 10.1016/j.kint.2018.01.005

3. Boswell RN, Yard BA, Schrama E, et al. Interleukin 6 production by human proximal tubular epithelial cells in vitro: analysis of the effects of interleukin-1 alpha (IL-1 alpha) and other cytokines. *Nephrol Dial Transplant.* 1994;9(6):599-606. doi: 10.1093/ndt/9.6.599
4. Naka T, Nishimoto N, Kishimoto T. The paradigm of IL-6: from basic science to medicine. *Arthritis Res.* 2002;4(3):233-242. doi: 10.1186/ar565
5. Akira S, Taga T, Kishimoto T. Interleukin-6 in biology and medicine. *Adv Immunol.* 1993;54:1-78. doi: 10.1016/s0065-2776(08)60532-5
6. Akchurin O, Patino E, Dalal V, et al. Interleukin-6 Contributes to the Development of Anemia in Juvenile CKD. *Kidney Int Rep.* 2018;4(3):470-483. doi: 10.1016/j.ekir.2018.12.006
7. Hénaut L, Massy ZA. New insights into the key role of interleukin 6 in vascular calcification of chronic kidney disease. *Nephrol Dial Transplant.* 2018;33(4):543-548. doi: 10.1093/ndt/gfx379
8. Scarpioni R, Obici L. Renal involvement in autoinflammatory diseases and inflammasome-mediated chronic kidney damage. *Clin Exp Rheumatol.* 2018;36 Suppl 110(1):54-60.
9. Pecoits-Filho R, Heimbürger O, Bárány P, et al. Associations between circulating inflammatory markers and residual renal function in CRF patients. *Am J Kidney Dis.* 2003;41(6):1212-1218. doi: 10.1016/s0272-6386(03)00353-6
10. Held C, White HD, Stewart RAH, et al. Inflammatory Biomarkers Interleukin-6 and C-Reactive Protein and Outcomes in Stable Coronary Heart Disease: Experiences From the STABILITY (Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy) Trial. *J Am Heart Assoc.* 2017;6(10):e005077. doi: 10.1161/JAHA.116.005077
11. Ridker PM, Rifai N, Stampfer MJ, et al. Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation.* 2000;101(15):1767-1772. doi: 10.1161/01.cir.101.15.1767
12. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med.* 2004;351(13):1296-1305. doi: 10.1056/NEJMoa041031
13. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. *Am J Kidney Dis.* 2012;60:850-886. doi: 10.1053/j.ajkd.2012.07.005
14. Inker LA, Schmid CH, Tighiouart H, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med.* 2012;367:20-29. doi: 10.1056/NEJMoa1114248
15. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension.* 2018;71(6):1269-1324. doi: 10.1161/HYP.0000000000000066
16. Roos JF, Doust J, Tett SE, Kirkpatrick CM. Diagnostic accuracy of cystatin C compared to serum creatinine for the estimation of renal dysfunction in adults and children – a meta-analysis. *Clin Biochem.* 2007;40(5-6):383-391. doi: 10.1016/j.clinbiochem.2006.10.026
17. Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. *Am J Kidney Dis.* 2002;40(2):221-226. doi: 10.1053/ajkd.2002.34487
18. Zoccali C, Vanholder R, Massy ZA, et al. The systemic nature of CKD. *Nat Rev Nephrol.* 2017;13(6):344-358. doi: 10.1038/nrneph.2017.52
19. Gupta J, Mitra N, Kanetsky PA, et al. Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC. *Clin J Am Soc Nephrol.* 2012;7:1938-1946. doi: 10.2215/CJN.03500412
20. Upadhyay A, Larson MG, Guo CY, et al. Inflammation, kidney function and albuminuria in the Framingham Offspring cohort. *Nephrol Dial Transplant.* 2011;26:920-926. doi: 10.1093/ndt/gfq471
21. Su H, Lei CT, Zhang C. Interleukin-6 signaling pathway and its role in kidney disease: an update. *Front Immunol.* 2017;8:405. doi: 10.3389/fimmu.2017.00405
22. Feigerlová E, Battaglia-Hsu SF. IL-6 signaling in diabetic nephropathy: from pathophysiology to therapeutic perspectives. *Cytokine Growth Factor Rev.* 2017;37:57-65. doi: 10.1016/j.cytogfr.2017.03.003
23. Barreto DV, Barreto FC, Liabeuf S, et al. Plasma interleukin-6 is independently associated with mortality in both hemodialysis and pre-dialysis patients with chronic kidney disease. *Kidney Int.* 2010;77(6):550-556. doi: 10.1038/ki.2009.503
24. Murkamilov IT, Sabirov IS, Fomin VV, et al. Correlations between parameters of central hemodynamics and cytokine profile in chronic kidney disease in combination with cerebrovascular diseases. *Zh Nevrol Psikhiatr Im S S Korsakova.* 2019;119(6):65-71. doi: 10.17116/jnevro201911906165
25. Abdelnabi AM, Sadek AM. Role of interleukin 6 and highly sensitive C-reactive protein in diabetic nephropathy. *Egypt J Intern Med.* 2018;30:103-109. doi: 10.4103/ejim.ejim_27_18
26. Klein B, Zhang XG, Lu ZY, et al. Interleukin-6 in human multiple myeloma. *Blood.* 1995;85(4):863-872.
27. Aitbaev KA, Murkamilov Ilkhom T, Fomin VV, et al. Inflammation in chronic kidney disease: sources, consequences and anti-inflammatory therapy. *Klin Med (Mosk).* 2018;96(4):314-320. doi: 10.18821/0023-2149-2018-96-4-314-320
28. Gupta J, Mitra N, Kanetsky PA, et al. Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC. *Clin J Am Soc Nephrol.* 2012;7(12):1938-1946. doi: 10.2215/CJN.03500412



Evaluation of micronuclei in oral squamous cell carcinoma and potentially malignant disorders via different staining techniques

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ABSTRACT

Introduction and aim. Oral squamous cell carcinoma (OSCC) and premalignant disorders (PMDs) are becoming common in India as the use of tobacco in different forms is increasing from a young age, and the prevalence of this disease is becoming more common in middle age. Identifying disease at earlier stages is an important measure for limiting disease incidence and improving patient prognosis. The micronuclei count can be a valid biomarker for screening suspected patients and can be helpful in educating patients about the discontinuation of treatment, diagnosing the disease in its early stages and planning a treatment for a better prognosis. Different stains that are nuclear specific can be used to identify micronuclei. The aim was to establish diagnostic efficacy of various staining techniques in OSCC and potentially malignant disorders on oral brush cytology smears with observation of micronuclei as a valid biomarker for evaluation of the disease.

Material and methods. Exfoliative cytology was done with oral brush and smears are obtained from 25 oral squamous cell carcinoma, 25 leukoplakia, 25 lichen planus, 25 oral sub mucous fibrosis patients and 15 samples with no disease. Each smear was stained with five different stains Papanicolaou (PAP), hematoxylin and eosin (H&E), toluidine blue, Leishman and Giemsa (LG) cocktail and Feulgen and observed for staining efficacy of micronuclei and cellular structures.

Results. The best stain to observe DNA content as micronuclei is Feulgen which gives clear and crisp details of micronuclei without giving any false count as it is nuclear specific stain. PAP can be the second choice stain. Micronuclei count is definitely increased in OSCC and PMDs compared to samples without disease confirming its use as biomarker.

Conclusion. Micronuclei count in oral brush cytology smears is a valid biomarker for evaluation of premalignant disorders and OSCC and can be used for detection of disease in individuals and for screening purposes of large populations at risk. Feulgen stain is best to study DNA content as micronuclei, on the other hand PAP can be used in large sampling investigations where there is lack of armamentarium.

Keywords. Feulgen stain, micronuclei, oral squamous cell carcinoma, potentially malignant disorders

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Introduction

Oral cancer is one of the major threats and economic burdens on the health care system. Oral squamous cell carcinoma (OSCC) is one of the ten most common cancers documented in the world; it accounts for more than 90% of all oral malignant lesions and is three times more common in men than in women, difficult to treat and often unbearable to the patients. According to the International Agency of Research on Cancer, the average yearly mortality rate is 145,000 worldwide.^{1,2} The habits of tobacco chewing, smoking and alcoholism are major factors contributing to the development of potentially malignant disorders and their conversion into OSCC.³ The course of conversion of potentially malignant disorders (PMDs) into malignancies is well documented; if left untreated.⁴⁻⁶ PMDs earlier known as premalignant lesions and conditions were rephrased in combination with potentially malignant disorders by the WHO in 2005.⁷ The prevalence of PMDs is approximately 4.5% worldwide. Among all PMDs, erythroplakia is most often associated with severe dysplasia, carcinoma in situ or frank carcinoma.⁸

The gold standard for diagnosing PMDs and OSCC is histopathological examination of the lesion. However, this approach requires additional armamentarium and time. Oral brush cytology or Exfoliative cytology for oral lesions is a newer and non-invasive methods which is not only equally predictable in diagnosing the severity and prognosis of pre malignant disorders and oral squamous cell carcinoma but also is an economical tool.⁹ To screen a larger population and obtain quick results, sensitive and accurate screening is needed to identify individuals who are at risk for developing oral cancer. Exfoliative cytology or oral brush cytology is a valuable and economical tool for identifying individuals who are at risk and for monitoring lesions that may progress to malignancy.¹⁰ Cytological smears are obtained from lesions in the oral cavity of diseased individuals and stained with different stains and techniques to observe cellular and nuclear changes to study and predict the course of the disease.^{11,12}

The oral mucosa is the first line of defense against irritants inhaled or ingested as carcinogen-bearing substances, consequently causing buccal cells to metabolize carcinogens into reactive products.⁴ These metabolites cause genetic damage, resulting in complex karyotypes that involve chromosomal aberrations and structural abnormalities. The chromosomal alterations appear as separated bodies from the nuclei and are observed in the cytoplasm as micronuclei.¹³ Larger micronuclei result from aneugenic effects where the whole chromosome is excluded following damage to the spindle apparatus; on the other hand, smaller micronuclei result from structural aberrations. Micronuclei serve as effective biomarkers of genetic damage in exfoliated cells.¹⁴

The micronuclei in oral epithelial cells were first proposed as a biomarker in 1983 by Stich et al. It has been observed that micronuclei are significantly increased in individuals who are exposed to polycyclic aromatic hydrocarbons, as in smokers, alcoholics and individuals who habitually use tobacco in any form. The oral epithelium is structured with four layers having a stratum basale, i.e., a basal layer incorporating stem cells that may cause genetic damage. Genetically altered cells migrate to the surface layer during continuous cell renewal, are exfoliated from the superficial layer and are collected in cytological smears.¹⁵

Various stains are used to stain smears obtained from oral mucosa to study micronuclei. They can be DNA specific, as Feulgen is the most widely used for staining chromatin within the cell.¹⁶ The other nonspecific stains used are Giemsa, Papanicolaou (PAP) and, less frequently, hematoxylin and eosin. Toluidine blue is another metachromatic basic dye that is used in oral cytology and fine needle aspiration cytology.¹⁷

Among these stains, PAP is the most widely used stain in exfoliative cytology because it provides promising nuclear and cytoplasmic staining results. Another advantage of PAPs is that they stain cells of different levels of maturity with different colors. With the development of the rapid PAP technique, PAP has gained popularity among pathologists for staining samples obtained via fine needle aspiration cytology (FNAC) and exfoliative cytology.

The Leishman-Giemsa cocktail is another newer staining technique that uses Leishman:Giemsa at a 1:1 ratio, yielding a deep blue color in the nuclear contents and a light blue hue in the cytoplasm.¹⁸ Hematoxylin and eosin are the most easily available stains and are widely used because of their availability and feasibility.

The micronuclei assay is being established as a prognostic marker for oral cancer and potentially malignant disorders. Several studies have been performed to date to prove this fact.¹⁹ The direct correlation between genetic damage and micronuclei makes the micronuclei assay an efficient adjunct to metaphase analysis.¹³

Several studies have confirmed increased micronuclei counts in desquamated oral squamous epithelium in individuals who are exposed to tobacco and other carcinogens encountering the oral cavity. In this study, we investigated the best stain for identifying nuclear anomalies and investigated whether micronuclei can be used as reliable biomarkers for identifying individuals who are at risk of transformation of potentially malignant disorders into malignant lesions.²⁰

Aim

To assess the diagnostic efficiency of the Leishman-Giemsa cocktail, Feulgen stain, toluidine blue, Papanicolaou and hematoxylin and eosin staining of micronuclei

in oral smears of potentially malignant disorders and oral squamous cell carcinoma.

Material and methods

Source of data

The study was conducted in the Department of Oral Pathology and Microbiology at Career Post Graduate Institute of Dental Sciences and Hospital. Patients with oral squamous cell carcinoma, lichen planus, oral submucous fibrosis and leukoplakia were included in the study group of 25 patients with oral squamous cell carcinoma, 25 patients with lichen planus, 25 patients with leukoplakia, 25 patients with oral submucous fibrosis and 15 individuals with normal oral mucosa.

Methodology

Five smears were obtained from each patient with oral submucous fibrosis, lichen planus, leukoplakia or oral squamous cell carcinoma and from the individuals in the normal control group. The smears of each patient were stained with Leishman-Giemsa cocktail, toluidine blue, PAP stain, Feulgen and hematoxylin and eosin.

For each slide 1000 cells were counted to assess micronuclei under 100x magnification oil immersion in zig zag pattern on the prepared slide.

Toluidine blue staining steps

Aqueous 1% toluidine blue solution was prepared by mixing 1 gram of Toluidine Blue powder in 100 ml of distilled water.

The smears are dipped in isopropyl alcohol for fixation for 10 minutes. Then slides are dipped in 50% alcohol for 1 minute, then water washed. Smears are then stained with 1% aqueous Toluidine Blue solution for 45–60 seconds. Slides are water washed, air dried, clear with xylene and to be mount in DPX.¹⁷

Leishman-Geimsa cocktail steps

The unit volume of Giemsa stock is filtered and mixed with an equal unit volume of distilled water to prepare a Giemsa working solution (1:1 dilution from stock) (The dilutions can be changed according to one's preference, up to 1:7.). This cocktail (Garbyal's cocktail) can be used and stored just like Leishman's stain.

Air dried smears are flooded with the LG cocktail and left for 1 minute. An equal volume of buffer (Sorensen's phosphate), distilled water or tap water will be added. The slides were blown on gently and will be kept for 5–7 minutes and are mounted in DPX.²⁰

Rapid PAP staining steps

We used commercially available rapid pap stain kit for staining of the smears.

Smears were fixed with Biofix spray and hydrated in tap water for 3–5 minutes, excess water was blotted out

from the slide. Few drops of nuclear stain were added to the slide for 60 seconds and washed in running tap water. 3–5 drops of wash buffer were added and washed after 20 seconds. Then slides are dehydrated with rapid pap dehydrant for 60 seconds. Few drops of cytoplasm stain added for 60 seconds. Washed in water and dehydrated for 60 seconds, air dried and mounted in DPX.¹⁷

Feulgen staining steps

1N HCL was prepared from concentrated HCL (35–37%) assay, 8.6 ml of HCL mixed with 91.4 ml of distilled water.

Schiff's reagent: 1g basic fuchsin powder mixed in 200 ml of boiling distilled water. Solution is allowed to cool to 50 degrees centigrade and 2g of potassium metabisulphite is added with mixing. This solution is allowed to cool down to room temperature and to this 2 ml conc. HCL added with 2g of activated charcoal and left for overnight in the dark room. Solution is filtered through Whatman filter paper and stored in the dark container.

The slides were immersed in 1 M HCL at 60°C for 5 to 6 minutes, following by placement in 1 M HCL at room temperature for 1 minute. Then they were immersed in Schiff reagent for 30 minutes and then transferred to running tap water for 10 minutes.^{6,10}

Hematoxylin and eosin staining steps

The conventional hematoxylin and eosin used for histopathological staining was used from our lab. Harris hematoxylin for nuclear staining and eosin Y for cytoplasmic staining was used in our study

Total staining procedure is done by following the steps, which included 6 slow dips under tap water, stained with Harris hematoxylin for 30 s, 6 slow dips under tap water, 6 dips in 95% Isopropyl alcohol, stained with EA-36 for 15 s, 6 dips in 95% isopropyl alcohol, 6 dips in 100% Isopropyl alcohol, 10 slow dips in xylene. Dehydrated, cleared and mounted.¹⁴

Scoring criteria

The criteria for assessing micronuclei will be followed as described by Tolbert et al.^{21,22}

1. a rounded smooth perimeter suggested a membrane,
2. the diameter of the associated nucleus was less than one-third, but the nucleus was large enough to discern shape and color,
3. the staining intensity was similar to that of the nucleus,
4. the texture was similar to that of the nucleus,
5. the same focal plane as the nucleus,
6. the absence of overlap with, or bridging to, the nucleus.

Only those structures fulfilling the abovementioned criteria were recorded as micro nuclei.

Inclusion criteria

1. both male and female were included in the study,
2. age group of 20-60 years was considered,
3. cells included in smear counting were those with intact, clear cytoplasm,
4. cells included in smear counting with little or no debris,
5. cells included in smear counting with no overlap with adjacent cells,
6. the main nucleus was normal and intact.

Exclusion criteria

1. structures that resemble micronuclei were not included, as nuclear buds or broken egg (that are connected with main nucleus),
2. bi-nucleated cells that contain a smaller nucleus but has a diameter greater than 1/3 the other nucleus,
3. patients having any chronic diseases,
4. patients with syndromes,
5. child/infant are excluded from the study,
6. patients suffering from gastro esophageal reflux disease,
7. patients who are immune-compromised,
8. over and under stained slides.

Ethical approval

Ethical Ref. No. CPGIDSH/22/280. The duly constituted Ethical Committee for Post Graduate students of Career Post Graduate Institute of Dental Sciences & Hospital, Lucknow has approved and cleared the research project of Dr. Mohammad Imran Khan, Post Graduate Student of Batch 2020-21 in the speciality of Oral Pathology and Microbiology. The topic of the research project is as follows: Evaluation of The Diagnostic Efficiency of Leishman Giemsa Cocktail, Feulgen Stain, Toluidine, Papanicolaou and Hematoxylin & Eosin Stains in Oral Smears of Potentially Malignant Disorders and Oral Squamous Cell Carcinoma”.

Statistical analysis

The results were analyzed using descriptive statistics and making comparisons among various groups. Categorical data were summarized as proportions and percentages (%) and quantitative data were summarized as mean±SD.

The following statistics were calculated in the present analysis: Kruskal-Wallis test (SPSS, IBM, Armonk, NY, USA). The significance level was taken as $p < 0.05$

Results

On the basis of the observations made in the study on the various parameters, the following statistical results were obtained (Table 1, Figures 1–5).

For <1/3rd of the nuclei, the mean staining score for Feulgen was the maximum, while the staining

score for H&E was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as Feulgen>PAP>L-G cocktail>toluidine blue>H&E.

Table 1. Comparison of staining scores among various stains for nucleus in the OSCC group

		L-G cocktail	Toluidine blue	H&E	PAP	Feulgen	p
<1/3rd of nucleus	Mean	4.6	3.7	3.4	7.9	8.9	$z=72.65,$ $p<0.001$
	SD	2.1	1.1	1.2	2.8	2.6	
Smooth texture	Mean	3.2	2.6	2.4	5.6	6.6	$z=58.76,$ $p<0.001$
	SD	1.3	1.0	0.9	2.7	2.8	
Same focal plane	Mean	3.8	3.2	2.9	6.2	7.4	$z=66.33,$ $p<0.001$
	SD	1.5	1.0	1.2	1.9	2.9	
Round shape	Mean	3.2	2.8	2.4	5.7	6.7	$z=61.59,$ $p<0.001$
	SD	1.5	1.1	1.0	2.5	2.9	
Same color	Mean	4.3	3.2	2.9	6.5	7.8	$z=61.52,$ $p<0.001$
	SD	2.2	1.0	0.9	2.3	3.3	
Separated from main nucleus	Mean	4.0	3.3	3.0	6.4	7.5	$z=58.70,$ $p<0.001$
	SD	2.0	0.9	0.9	2.2	3.4	

For the smooth texture, the mean staining score for Feulgen was the highest, while the staining score for H&E was the lowest. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as Feulgen>PAP>L-G cocktail>toluidine blue>H&E.

For the same focal plane, the mean staining score of Feulgen was the maximum, while the staining score of H&E was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as Feulgen>PAP>L-G cocktail>toluidine blue>H&E.

For the round shape, the mean staining score for Feulgen was the highest, while the staining score for H&E was the lowest. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as Feulgen>PAP>L-G cocktail>toluidine blue>H&E.

For the same color, the mean staining score of Feulgen was the maximum, while the staining score of H&E was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as Feulgen>PAP>L-G cocktail>toluidine blue>H&E.

For the separation, the mean staining score of Feulgen was the maximum, while the staining score of H&E was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as Feulgen>PAP>L-G cocktail>toluidine blue>H&E (Table 1).

For <1/3rd of the nuclei, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was

found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>L-G cocktail>toluidine blue.

Table 2. Comparison of staining scores among various stains for nucleus in the leukoplakia group

		L-G cocktail	Toluidine blue	H&E	PAP	Feulgen	p
<1/3rd of nucleus	Mean	2.7	2.6	3.0	5.2	4.5	$z=64.62,$ $p < 0.001$
	SD	0.7	0.8	1.1	1.4	1.2	
Smooth texture	Mean	2.2	2.1	2.6	3.8	3.0	$z=42.97,$ $p < 0.001$
	SD	0.9	0.9	0.9	1.1	1.0	
Same focal plane	Mean	2.6	2.4	2.5	4.2	3.2	$z=40.47,$ $p < 0.001$
	SD	0.6	0.6	0.8	1.2	1.0	
Round shape	Mean	2.4	2.3	2.2	3.8	3.1	$z=37.82,$ $p < 0.001$
	SD	0.7	0.7	0.7	1.3	1.0	
Same color	Mean	2.3	2.0	2.2	3.9	3.5	$z=54.78,$ $p < 0.001$
	SD	0.7	0.6	0.9	1.2	0.9	
Separated from main nucleus	Mean	2.6	2.3	2.5	4.1	3.4	$z=44.91,$ $p < 0.001$
	SD	0.6	0.5	0.8	1.1	1.1	

For the smooth texture, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>L-G cocktail>toluidine blue.

In the leucoplakia group, for the same focal plane, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>L-G cocktail>H&E>toluidine blue.

For the round shape, the mean staining score of PAP was the maximum, while the staining score of H&E was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>L-G cocktail>toluidine blue>H&E.

In the leucoplakia group, for the same color, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>L-G cocktail>H&E>toluidine blue.

In the leucoplakia group, for separation, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>L-G cocktail>H&E>toluidine blue (Table 2).

For <1/3rd of the nuclei, the mean staining score of PAP was the maximum, while the staining score of the

L-G cocktail toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>L-G cocktail=toluidine blue.

Table 3. Comparison of staining scores among various stains for nucleus in the lichen planus group

		L-G cocktail	Toluidine blue	H&E	PAP	Feulgen	p
<1/3rd of nucleus	Mean	1.9	1.9	2.2	3.6	2.6	$z=31.32,$ $p < 0.001$
	SD	1.1	0.9	1.1	1.3	1.0	
Smooth texture	Mean	1.6	1.7	2.0	2.9	2.2	$z=29.96,$ $p < 0.001$
	SD	0.9	0.7	0.9	0.9	0.8	
Same focal plane	Mean	1.7	1.8	1.9	2.8	2.2	$z=21.82,$ $p < 0.001$
	SD	0.9	0.8	0.8	1.0	0.9	
Round shape	Mean	1.4	1.6	1.9	2.7	2.1	$z=29.77,$ $p < 0.001$
	SD	0.9	0.8	0.9	1.0	0.9	
Same color	Mean	1.8	1.7	2.0	2.7	2.3	$z=13.74,$ $p=0.008$
	SD	1.1	0.8	1.0	1.2	0.8	
Separated from main nucleus	Mean	1.8	1.7	2.0	3.1	2.1	$z=26.65,$ $p < 0.001$
	SD	1.1	0.9	1.0	1.0	0.8	

For the smooth texture, the mean staining score of PAP was the maximum, while the staining score of the L-G cocktail was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>toluidine blue>L-G cocktail.

In the lichen planus group, for the same focal plane, the mean staining score of PAP was the highest, while the staining score of the L-G cocktail was the lowest. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>toluidine blue>L-G cocktail.

For the round shape, the mean staining score of PAP was the maximum, while the staining score of the L-G cocktail was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>toluidine blue>L-G cocktail.

In the lichen Planus group, for the same color, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p=0.008$), and the staining scores were calculated as PAP>Feulgen>H&E>L-G cocktail>toluidine blue.

In the lichen Planus group, for separation, the mean staining score of PAP was the maximum, while the staining score of toluidine blue was the minimum. A significant difference was found in the mean staining score for the various stains ($p < 0.001$), and the staining scores were calculated as PAP>Feulgen>H&E>L-G cocktail>toluidine blue (Table 3).

Table 4. Comparison of staining scores among various stains for nucleus in the OSMF group

		L-G cocktail	Toluidine blue	H&E	PAP	Feulgen	p
<1/3rd of nucleus	Mean	2.5	2.5	2.4	3.6	2.8	z=17.39, p=0.002
	SD	0.8	1.0	1.0	1.2	1.5	
Smooth texture	Mean	2.1	2.0	1.8	2.5	2.2	z=8.57, p=0.073
	SD	0.8	0.8	0.8	0.9	1.3	
Same focal plane	Mean	2.2	2.1	2.0	2.9	2.4	z=15.39, p=0.004
	SD	0.6	0.8	0.7	0.8	1.3	
Round shape	Mean	2.0	2.1	2.0	2.6	2.4	z=11.23, p=0.024
	SD	0.8	0.6	0.7	0.7	1.4	
Same color	Mean	2.5	2.3	2.2	2.9	2.5	z=7.62, p=0.107
	SD	0.8	0.9	0.8	0.9	1.1	
Separated from main nucleus	Mean	2.5	2.2	2.1	2.8	2.4	z=8.44, p=0.077
	SD	0.8	0.9	0.8	1.0	1.3	

In the OSMF group, for <1/3 of the cells in the nucleus, the mean staining score of PAP was the highest, while the staining score of H&E was the lowest. A significant difference was found in the mean staining score for the various stains (p=0.002), and the staining scores were calculated as PAP>Feulgen>L-G cocktail=toluidine blue>H&E.

For the smooth texture, the mean staining score of PAP was the maximum, while the staining score of H&E was the minimum. However, no significant difference was found in the mean staining score of the various stains (p=0.073).

In the OSMF group, for the same focal plane, the mean staining score of PAP was the highest, while the staining score of H&E was the lowest. A significant difference was found in the mean staining score for the various stains (p=0.004), and the staining scores were calculated as PAP>Feulgen>L-G cocktail>toluidine blue>H&E.

Table 5. Comparison of staining scores among various stains for nucleus in the control group

		L-G cocktail	Toluidine blue	H&E	PAP	Feulgen	p
<1/3rd of nucleus	Mean	1.3	1.3	1.1	2.0	1.0	z=8.79, p=0.087
	SD	0.9	0.6	1.0	1.0	0.8	
Smooth texture	Mean	1.4	1.3	1.2	1.9	1.1	z=8.26, p=0.082
	SD	0.9	0.6	1.0	0.7	0.7	
Same focal plane	Mean	1.3	1.3	1.1	1.8	0.9	z=7.39, p=0.117
	SD	0.9	0.6	1.0	0.9	0.7	
Round shape	Mean	1.3	1.3	1.1	1.8	1.1	z=5.75, p=0.218
	SD	0.7	0.6	0.9	0.8	0.7	
Same colour	Mean	1.3	1.3	0.9	1.6	0.9	z=6.50, p=0.165
	SD	0.8	0.6	0.8	0.9	0.7	
Separated from main nucleus	Mean	1.3	1.1	0.9	1.5	0.9	z=7.81, p=0.099
	SD	0.9	0.5	0.7	0.7	0.7	

For the round shape, the mean staining score of PAP was the maximum, while the staining scores of the H&E and L-G cocktails were the minimum. A significant difference was found in the mean staining score for the various

stains (p=0.024), and the staining scores were calculated as PAP>Feulgen>toluidine blue>L-G cocktail = H & E.

In the OSMF group, for the same color, the mean staining score of PAP was the highest, while the staining score of H&E was the lowest. However, no significant difference was found in the mean staining score (p=0.107).

In the oral submucous fibrosis group, for the separation, the mean staining score of PAP was the highest, while the staining score of H&E was the lowest. However, no significant difference was found in the mean staining scores of the various stains (p=0.077) (Table 4).

In the control group, no significant differences were observed in various parameters among the strains used in the study (Table 5).

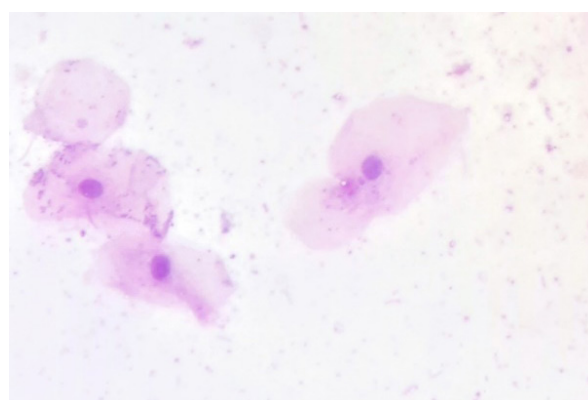


Fig. 1. Feulgen stain

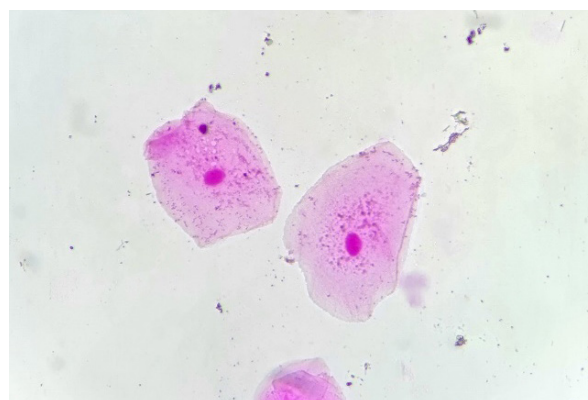


Fig. 2. PAP stain

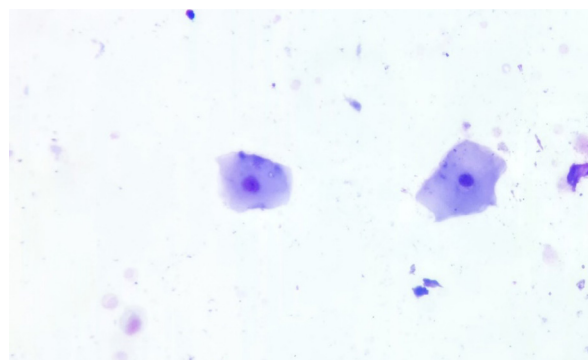


Fig. 3. LG cocktail stain

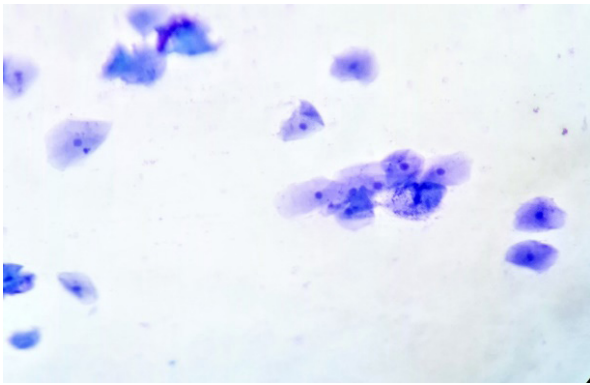


Fig. 4. Toluidine blue stain

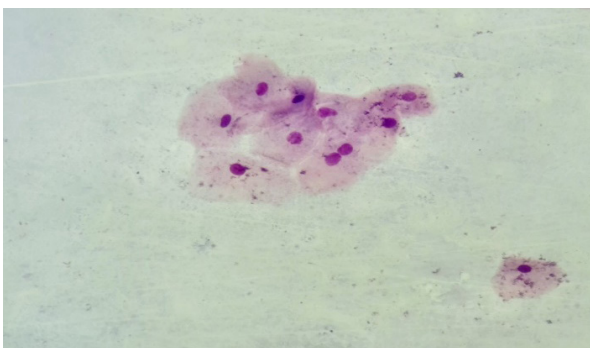


Fig. 5. H&E stain

Discussion

Oral cancer is the sixth most common type of cancer, with INDIA contributing to almost one-third of the total burden, and the second country having the highest number of oral cancer cases.²¹ Studying pre-neoplastic diseases and oral malignancies via Exfoliative cytology is an economical, non-invasive and easy procedure for studying biomarkers of neoplastic changes in oral cells.¹¹ Biomarkers of genetic damage have immense potential to reveal the stage of the disease and are helpful in early diagnosis and progression of the disease. Among the various chairside investigations of lesions at an early stage, the micronuclei assay using Exfoliative cytology is a reliable procedure for diagnosing individuals who are at high risk of developing malignancy.^{21,22}

Buccal cells are the first barrier for carcinogens inhaled or ingested and are capable of metabolizing carcinogens into reactive products. These carcinogens that cause genetic damage to stem cells in the basal layer are referred to as micronuclei during nuclear division. These chromosomal fragments or whole chromosomes that did not reach the spindle pole thus lag behind anaphase during nuclear division and are not incorporated into the daughter nuclei in telophase but are covered by a nuclear membrane resembling a small nucleus. Thus, the cells were termed micronuclei. As the oral epithelium is constantly maintained by cell renewal, which occurs at the basal layer by mitosis, damaged cells with disrupted nuclear division migrate to the surface along

with other cells and are collected via Exfoliative cytology for evaluation.^{23,24}

In our study, we chose nuclear specific stain, Feulgen, and nonspecific DNA stains, such as PAP, H&E, LG cocktail, and toluidine blue, to stain the smears obtained from exfoliative cytology to determine the micronuclei count in each individual smear.²⁰ Our study stands novel to the best of our knowledge as nobody has done study on micronuclei count comparing with five stains and including all three commonly encountered pre malignant disorders as leukoplakia, lichen planus and oral sub mucous fibrosis compared with OSCC. Belgaumiet al. performed a study on 100 patients diagnosed with OSCC and 100 control patients and stained buccal smears with a PAP and LG cocktail. They concluded that, compared with the LG cocktail, PAPs gave almost equivalent results.^{25,26}

Apurva A et al. compared PAP and LG cocktails to study oral neoplastic lesions and found no significant difference in the staining properties of the two agents, but we found a significant difference in the staining score of PAP compared with that of the LG cocktail.^{27,28}

In addition, Gupta et al. conducted a study on 45 patients – 15 with OSCC, 15 with OSMF and 15 with leukoplakia. They found a significant increase in the mean micronuclei count, which was highest in OSCC patients, followed by OSMF and leukoplakia patients. They also concluded that the PAP stain was better than the LG cocktail and H&E stain.²⁹

We found a significant increase in the mean micronuclei count in the PMD and OSCC groups compared with that in the control group as also reported in recent research by Bhatnagar et al. in which they also concluded that there is an increase in micronuclei count suggesting neoplastic changes as malignant changes progresses compared to histologically normal mucosa.³⁰

Sarto et al. considered micronuclei size to be restricted to 1/5th of the parent nucleus.³¹⁻³⁴ Jadhav et al. considered micronuclei to be between 1/3 and 2/3 the size of the nucleus. We used the criteria suggested by Tolbert et al. for a micronuclei size <1/3rd of the parent nucleus.²¹ A larger micronuclei result from the exclusion of the whole chromosome following damage to the spindle apparatus of the cell, whereas smaller micronuclei result from structural aberrations causing chromosomal fragments.³⁵

These findings were consistent with those of studies performed by Sivasanskari et al., Dindgire et al., Grover et al., Saurabh et al., and Gunjan et al. (2019).^{14,20,36-38}

In the OSCC group, as shown in Table 1, all the parameters included micronuclei shape, size, texture, same focal plane, smooth perimeter and separation from the main nucleus. On all of these parameters, in our study, we found the highest mean number of micronuclei with Feulgen, followed by PAP and LG cocktail.

Sharma D et al. performed a cytomorphometric analysis of 125 subjects divided into 25 patient groups, namely, healthy patients, smokers, smokeless tobacco users and OSCC patients, and evaluated variations in cellular area, nuclear area, cellular diameter, nuclear diameter and the nuclear/cytoplasmic ratio. They used Feulgen for staining smears and concluded that cytology was useful for DNA-specific staining for the early diagnosis of OSCC.³⁹

Kumar et al. studied 15 confirmed cases of PMD, 15 confirmed cases of OSCC and 15 control subjects free of any oral lesions. They used PAP staining for the evaluation of smears and reported a stepwise increase in the micronuclei count from the control group to the PMD group, after which the highest increase was observed in the OSCC group.⁴

Chaudhary M et al. studied histopathologically confirmed patients and divided them into three groups of patients with well-differentiated, moderately differentiated and poorly differentiated carcinoma and compared them with 10 patients in the control group.²² They used PAP and Feulgen to study mean micronuclei and found an increased micronuclei count in OSCC in increasing order from well-differentiated to poorly differentiated OSCC. The authors commented that Feulgen is still the gold standard for studying micronuclei and that PAP can lead to misinterpretation of the micronuclei count, as it may not distinguish between true micronuclei and keratohyaline granules, bacterial clumps or artefacts.⁴⁰ (Figure 1 and 2).

The primary step in the Feulgen reaction is hydrolysis, in which purine bases are detached from DNA, exposing free aldehyde groups and leaving the DNA backbone intact; thus, the DNA becomes apurinic. When the cells are reacted with Schiff's reagent, bleached pararosaniline, which is a component of basic fuchsin, binds to free aldehyde groups in apurinic DNA, acquiring a magenta color. The hydrolysis of RNA does not occur, and so RNA rings do not open or are less frequent than DNA rings; moreover, the RNA is degraded and washed off more easily. This is the reason why Feulgen is DNA specific.⁴¹

A statistically significant difference was observed among all of the stains. The mean staining score for Feulgen was the highest, followed by that for PAP, and the lowest mean staining score was for H&E. The increase in the mean micronuclei count in OSCC patients is attributed to increased abnormal nuclear content because of increased mitotic activity, chromosomal aberrations and disturbance of the cell cycle.

In smears obtained from Leucoplakia patients with reference to Table B, PAP staining gave the highest micronuclei count based on all of the criteria for selecting the micronuclei.

In a study comparing leucoplakia patients with those with habits of tobacco and habit-free controls, Mahimkar et al. reported similar results. They concluded

that there is an overall increase in the micronuclei count in leucoplakia patients, indicating increased DNA damage and genetic alterations in the buccal cells of leucoplakia patients.⁴²

This observation has been described by many other researchers, such as Grover et al., who conducted a study on 45 patients with PMD and stained smears with Feulgen, PAP and H&E. These authors found that in potentially malignant disorders, Feulgen had fewer micronuclei than PAP did, which is in correlation with our study on the mean micronuclei count in PMDs.¹⁴

According to Samantha et al., possible explanations for MN formation in preneoplastic conditions include chromosomal loss/breakage, mitotic apparatus dysfunction, aneuploidy and genetic instability. The mean staining score for PAP was the highest, followed by that for Feulgen. Toluidine blue was used to determine the minimum mean staining score.

Patil et al. compared PAP and toluidine blue in cervicovaginal cytology and found that toluidine blue was equivalent to PAP.^{17,24}

Kohli et al. conducted a study on 200 subjects divided into four groups of 50 normal individuals (as controls), 50 with tobacco habits without leucoplakia, 50 with tobacco habits along with leucoplakia and 50 with OSMF. Potentially malignant disorders, including leucoplakia and OSMF, were studied. The authors used Feulgen, PAP and May Grunwald Giemsa stains for smear staining. The authors concluded that the number of micronuclei was greater in PMDs than in the control, and PAP had a greater micronuclei count than did Feulgen, which is in accordance with our study.⁴³ The lichen planus group, with reference to Table 3 and PAP, had the best mean staining scores for all the criteria for micronuclei. PAP was subsequently administered by Feulgen. Buajee et al compared oral lichen planus mucosa with normal mucosa and reported that the mean micronuclei frequency in OLP lesions was significantly greater ($p < 0.01$) than that in normal-appearing mucosa adjacent to lesions and that in normal individuals.²³

Compared with H&E staining, PAP was superior, as was the observation of Balaji et al.⁴⁴ Moreover, they compared PAP to H&E in oral lichen planus patients and found that PAP was better than H&E. Toluidine blue and LG cocktails had nearly the same effects. Figure (3,4&5). Ranjbar et al. performed a study on oral lichen planus and oral lichenoid reaction and reported increased mean micronuclei counts in OLP and OLR patients compared to those in normal mucosa. However, there were no significant differences between OLP and OLR ($p = 0.67$ and $p = 0.36$, respectively).⁴⁵

In the OSMF group, with reference to Table D and PAP, the highest staining score was obtained for the micronuclei count, with PAP indicating the micronuclei size and shape and revealing the location of the focal

plane. No significant differences in texture, color or separation of micronuclei were observed among the strains, but for the evaluation of the mean staining score, PAP was the best stain, with the highest mean, and H&E was the lowest mean. Shreyas Shah et al. studied 60 patients with 30 OSMFs and 30 OSCC patients. They used PAP staining to study micronuclei and found a significantly increased number of micronuclei from the control to the OSMF-treated OSCC patients.⁴⁶

Kumar M et al. studied a total of 90 participants and divided them into groups of 30 individuals each into one group with PMDs, one group with habits of tobacco use with lesions and the other group with habits of tobacco use without lesions. They used Feulgen and PAP for staining smears and found a high number of mean micronuclei in subjects with PMD lesions with PAP compared to Feulgen and suggested that PAP is DNA nonspecific. This high frequency of observation of micronuclei may not be true of micronuclei, as these are actually keratin granules that are found in degenerated cells with nuclear defects. These round cytoplasmic structures do not contain DNA and might resemble micronuclei.²⁶

Kabiraj et al. screened lichen planus, leucoplakia and OSMF lesions with PAP using exfoliative cytology and found that 90% of the leukoplakic lesions were class II cytological features. Sixty-five percent of lichen planus had Class II features. In the oral submucous, 80% of patients had class II features.⁴⁷

PAP had statistically significant effects on the micronuclei count, shape, texture, and separation in the PMD group because nonspecific DNA staining and nuclear anomalies, such as karyorrhexis, karyolysis, condensed chromatin, and binucleates, may be misinterpreted as micronuclei. Keratin granule formation may also be misinterpreted as the presence of micronuclei along with bacteria and small dye granules.¹⁴

Hence, in our study, there was a significant increase in the MN frequency in all the PMD and OSCC groups compared to that in the control group. When the nuclear staining properties were compared, the DNA-specific stain Feulgen was the best stain in the OSCC group, and PAP was the best stain in all the PMD groups, as were leukoplakia, lichen plans and oral submucous fibrosis. We did not find any statistically significant difference in nuclear staining properties in the OSMF group, although the mean staining score for PAP was maximal.

Based on our study, we can say that Feulgen is the best stain for observing MNs in malignant lesions but is technique sensitive. However, rapid PAP staining is less time-consuming than other methods and yields good results in terms of nuclear and cytoplasmic staining.

Conclusion

Facilitating exfoliative cytology to study biomarkers, such as micronuclei, in oral premalignant lesions and

malignant lesions is a great tool for studying and helping in the early diagnosis of any cellular changes because of the presence of any carcinogen leading to the formation of premalignant lesions and the conversion of premalignant lesions into malignant lesions.

The micronuclei count has immense potential to be studied further for its significance in identifying premalignant lesion progress and thus can be a reliable tool for early intervention and treatment to reduce mortality and conversion to malignancy. In addition to PMDs and OSCC, the micronuclei assay has wide applications beyond these lesions to study genotoxicity in other tumors and lesions in humans, the effects of various chemicals or carcinogens on the human body, and the effects of drugs during and after treatment for these pathologies.

DNA specificity is important for studying nuclear content remarkably, and this approach helps to rule out other nuclear anomalies that can be misinterpreted by other non-DNA-specific stains and is still the gold standard for studying DNA-specific abnormalities and cytomorphology.

The staining properties of rapid PAP are good quality and less time consuming, providing satisfactory diagnostic reliability. Although the MN count is increased in PMDs and OSCC, additional studies are needed to determine whether the results of exfoliative cytology are equivalent to those of histopathological biopsy, which is the gold standard for diagnostic purposes.

For counting of micronuclei one has to be skilled enough to differentiate between micronuclei and other nuclear and cytoplasmic abnormalities and inclusion. Failing so can give false results. When doing PAP staining one has to be cautious because PAP stain gives higher micronuclei count which is sometimes false positive. Apart from these limitations micronuclei count is an excellent tool to study neoplastic changes with oral brush cytology. Although a newer technique yields equivalent results to PAP in nuclear and cytoplasmic staining, the LG cocktail can be used as a substitute for PAP for screening purposes. Toluidine blue is used in cervicovaginal cytology and as a vital stain in the oral cavity, its application in oral cytology still needs to be studied.

Declarations

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Author contributions

Conceptualization, M.I.K. and A.K.; Methodology, M.I.K.; Software, M.I.K.; Validation, M.I.K., S.S.K. and A.K.; Formal Analysis, A.K.; Investigation, M.I.K.; Resources, A.N. and K.A.; Data Curation, K.A. and S.L.; Writing – Original Draft Preparation, M.I.K.; Writing – Review & Editing, M.I.K.; Visualization, S.L.; Supervision, S.S.K.; Project Administration, AK.

Conflicts of interest

The authors have no competing interests.

Data availability

The data supporting the findings of this study are available from corresponding author (Mohammad Imran Khan), upon reasonable request.

Ethics approval

The duly constituted Ethical Committee for Post Graduate students of Career Post Graduate Institute of Dental Sciences & Hospital, Lucknow has approved and cleared the research project (ethical ref. No. CPGIDSH/22/280).

References

- Rivera C. Essentials of oral cancer. *Int J Clin Exp Pathol.* 2015;8(9):11884-11894.
- Lewandowska A, Rudzki G, Lewandowski T, et al. Quality of Life of Cancer Patients Treated with Chemotherapy. *Int J Environ Res Public Health.* 2020;17(19):6938. doi: 10.3390/ijerph17196938
- Naderi NJ, Farhadi S, Sarshar S. Micronucleus assay of buccal mucosa cells in smokers with the history of smoking less and more than 10 years. *Indian J Pathol Microbiol.* 2012;55(4):433-438. doi: 10.4103/0377-4929.107774
- Kumar N, Indira AP, David M, et al. Evaluation of Micronucleus Assay in Oral Exfoliated Buccal Cells in Potentially Malignant Disorders and Oral Squamous Cell Carcinoma. *Int J Prev Clin Dent Res.* 2016;3(3):173-177. doi: 10.5005/jp-journals-10052-0038
- Messadi DV. Diagnostic aids for detection of oral precancerous conditions. *Int J Oral Sci.* 2013;5(2):59-65. doi: 10.1038/ijos.2013.24
- Kamboj M, Mahajan S. Micronucleus- an upcoming marker of genotoxic damage. *Clin Oral Investig.* 2007;11(2):121-126. doi: 10.1007/s00784-006-0075-y
- Grover S, Ahmed MB, Telagi N, Shivappa AB, Nithin KP. Evaluation of diagnostic reliability of micronuclei in potentially malignant disorders of oral cavity. *CHRISMED Journal of Health and Research.* 2014;1:15-20. doi: 10.4103/2348-3334.126776
- Iocca O, Sollecito TP, Alawi F, et al. Potentially malignant disorders of the oral cavity and oral dysplasia: A systematic review and meta-analysis of malignant transformation rate by subtype. *Head Neck.* 2020;42(3):539-555. doi: 10.1002/hed.26006
- Wang S, Yang M, Li R, et al. Current advances in noninvasive methods for the diagnosis of oral squamous cell carcinoma: a review. *Eur J Med Res.* 2023;28(1):53. doi: 10.1186/s40001-022-00916-4
- Saraswathi K, Padma M. Evaluation of Cytogenic Damage in the Form of Micronuclei in Oral Exfoliated Buccal Cells in Tobacco Users. *Ind J Dent Res.* 2018;9(6):773-780. doi: 10.4103/ijdr.IJDR_218_17
- Metgud R, Surbhi, Smitha N, Patel S. Spritzer: For diagnostic cytopathology. *J Canc Resear Therap.* 2017;13(6):964-967. doi: 10.4103/0973-1482.174548.
- Kamini K, Agarwal P, Kumar S, et al. Micronuclei as a Predictor for Oral Carcinogenesis. *J Cytol.* 2018;35(4):233-236. doi: 10.4103/JOC.JOC_141_17
- Bansal H, Sandhu VS, Bhandari R, et al. Evaluation of micronuclei in tobacco users: A study in Punjabi population. *Contemp Clin Dent.* 2012;3(2):184-187. doi: 10.4103/0976-237X.96825
- Grover S, Mujib ABR, Jahagirdar A, et al. A comparative study for selectivity of micronuclei in oral exfoliated epithelial cells. *J Cytol.* 2012;29(4):230-235. doi: 10.4103/0970-9371.103940
- Biswas S, Garai B, Banerjee M. Genotoxic Effects of Tobacco on Buccal Epithelium: Cell Nuclear Anomalies as Biomarker. *Asia Pac J Med Toxicol.* 2014;3:157-162.
- Kashyap B, Reddy S. Micronuclei assay of exfoliated oral buccal cells: Means to assess the nuclear abnormalities in different diseases. *J Canc Resear Therap.* 2012;8(2):184-191. doi: 10.4103/0973-1482.98968
- Patil PV, Nikumbh DB. Efficacy of toluidine blue in cervicovaginal cytology over conventional papanicolaou stain. *Arch cytol histopath research.* 2018;3(2):47-51.
- Sidhu K, Ramalingam K, Goyal S, et al. Comparing the Efficacy of Leishman–Giemsa Cocktail Stain, Giemsa Stain, and Papanicolaou Stain in Potentially Malignant Oral Lesions: A Study on 540 Cytological Samples. *J Cytol.* 2018;35(2):105-109. doi: 10.4103/joc.joc_249_16
- Nancy A, Shaaban, Hanaa S, et al. Micronuclei as Biomarkers of Genetic Damage in Oral Squamous Cell Carcinoma. *Alexandria Dental Journal.* 2018;43:28-23.
- Juneja S, Katyal S, Rathore AS, et al. Utility of DNA-Specific Stains in Micronuclei Assay as a Marker of Genotoxicity in Oral Potentially Malignant Disorders and Oral Squamous Cell Carcinoma. *J Cytol.* 2019;36(2):111-115. doi: 10.4103/joc.joc_230_16
- Holland N, Bolognesi C, Kirsch-Volders M, et al. The micronucleus assay in human buccal cells as a tool for biomonitoring DNA damage: The HUMN project perspective on current status and knowledge gaps. *Mutat Res.* 2008;659:93-108. doi: 10.1016/j.mrrev.2008.03.007
- Tolbert PE, Shy CM, Allen JW. Micronuclei and other nuclear anomalies in buccal smears: A field test in snuff users. *Am J Epidemiol.* 1991;134:840-850. doi: 10.1016/0165-1161(92)90033-i
- Buajeeb W, Kraivaphan P, Amornchat C, Triratana T. Frequency of micronucleated exfoliated cells in oral lichen planus. *Mutat Res.* 2007;627:191-196. doi: 10.1016/j.mrgentox.2006.10.010
- Samanta S, Dey P. Micronucleus and its applications. *Diagn Cytopathol.* 2012;40:84-90. doi: 10.1002/dc.21592
- Chieco P, Derenzini M. The Feulgen reaction 75 years on. *Histochem Cell Biol.* 2017;119(6):603-609. doi: 10.1016/j.acthis.2017.07.002

26. Kumar M, Prasad UC, Chandolia B, et al. Can Feulgen Stain be a Reliable Biomarker over PAP Stain for Estimation of Micronuclei Score? *J Clin Diag Res.* 2016;10(10):7-11. doi: 10.7860/JCDR/2016/18859.8630
27. Belgaumi UI, Shetty P. Leishman Giemsa cocktail as a new, potentially useful cytological technique comparable to Papanicolaou staining for oral cancer diagnosis. *J Cytol.* 2013;30:18-22. doi: 10.4103/0970-9371.107507
28. Agrawal A, Kumar K, Chandra SH, Agrawal KC. Comparative Analysis Study of Efficacy of Papanicolaou smear & Leishman-Giemsa Cytological Technique in the Diagnosis of Oral Neoplastic Lesions. *IJSR.* 2019;8:2.
29. Gupta N, Rakshit A, Srivastava S, et al. Comparative evaluation of micronuclei in exfoliated oral epithelial cells in potentially malignant disorders and malignant lesions using special stains. *J Oral Maxillofac Pathol.* 2019;23(1):157. doi: 10.4103/jomfp.jomfp_164_17
30. Bhatnagar A, Madhav N, Kumar S, et al. Evaluation of Micronuclei in Potentially Malignant Disorders and Oral Cancers: A Cytological Assay. *J Ind Acad Ora Medic & Rad.* 2023;35:3:368-372.
31. Shashikala R, Indira AP, Manjunath GS, et al. Role of micronucleus in oral exfoliative cytology. *J Pharm Bioallied Sci.* 2015;7:2:409-413. doi: 10.4103/0975-7406.163472
32. Autrup H, Seremet T, Arenholt D, Dragsted L, Jepsen A. Metabolism of benzopyrene by cultured rat and human buccal mucosa cells. *Carcinogenesis* 1985;6:1761-1765. doi: 10.1093/carcin/6.12.1761
33. Vondracek M, Xi Z, Larsson P, et al. Cytochrome P450 expression and related metabolism in human buccal mucosa. *Carcinogenesis.* 2001;22:481-488. doi: 10.1093/carcin/22.3.481
34. Sarto F, Finotto S, Giacomelli L, Mazzotti D, Toraanin R, Levis AG. The micronucleus assay in exfoliated cells of the human buccal mucosa. *Mutagenesis.* 1987;2:11-17. doi: 10.1093/mutage/2.1.11
35. Jadhav K, Gupta N, Ahmed M. Micronuclei: An essential biomarker in oral exfoliated cells for grading of oral squamous cell carcinoma. *J Cytol.* 2011;28(1):7-12. doi: 10.4103/0970-9371.76941
36. Sivasankari P, Kaur S, Reddy KS, Vivekanandam S, Rao RK. Micronucleus index: An early diagnosis in oral carcinoma. *J Anat Soc India.* 2008;57:8-13.
37. Dindgire SL, Gosavi S, Kumawat R, Ganvir S, Hazarey V. Comparative study of exfoliated oral mucosal cell micronucleus frequency in potentially malignant and malignant lesions. *Int J Oral Maxillofac Pathol.* 2012;3:15-20.
38. Dave GT, Parikh N, Patel N, Joshi H. Evaluation of Micronucleus Frequencies in Exfoliated Buccal Cells of Potentially Malignant Disorder Subjects Using Feulgen Stain. *Indian J Dent Adv.* 2019;11(3):86-92.
39. Sharma D, Sandhu S, Bansal H, Gupta S. Distinct perturbations of oral squamous cell carcinoma patients: A quantitative cytomorphometric analysis. *Int J Health Sci (Qasim).* 2015;9:283-291.
40. Chaudhary M, Venkatapathy R, Oza N, Prashad KV, Malik S. Evaluation of Micronuclei in Oral Squamous Cell Carcinoma: A Cytological Study. *Int J Oral Care Res.* 2017;5:4-8.
41. Greilhuber J. Cytochemistry and C-values: The Less-well-known World of Nuclear DNA Amounts. *Ann Bot.* 2008;101:791-804. doi: 10.1093/aob/mcm250
42. Mahimkar MB, Samant TA, Kannan S, Patil T. Influence of genetic polymorphisms on frequency of micronucleated buccal epithelial cells in leukoplakia patients. *Oral Oncology.* 2010;46:10:761-766.
43. Kohli M, Ahuja P, Mehendiratta M, Sharma M, Dutta J. Micronucleus Assay: An Early Diagnostic Tool to Assess Genotoxic Changes in Patients with Tobacco Use, Oral Leukoplakia and Oral Submucous Fibrosis. *J Clin Diagn Res.* 2017;11(9):28-32. doi: 10.7860/jcdr/2017/27711.10567
44. Hemamalini B. Comparison of Efficacy of Different Stains Used in Exfoliative Cytological Smears From Oral Lichen Planus Patients- A Pilot Study. *IADR, Oral Med & Pathol.* 2016;0529.
45. Ranjbar M, Motalebnejad M, Abbaszadeh H, Gholinia H. Micronuclei Comparison in Lichen Planus and Oral Lichenoid Responses. *Babol Univ Med Sci.* 2018;20:7-12.
46. Shah SN, Manjunatha BS, Shah S, et al. Quantitative evaluation of micronuclei in oral squamous cell carcinoma and oral submucous fibrosis patients: a comparative study. *Rec Pat Anticanc Drug Discov.* 2015;10:2:233-238. doi: 10.2174/1574892810666150317144817
47. Kabiraj A, Khaitan T, Bhowmick D, et al. Screening of Oral Potentially Malignant Disorders Using Exfoliative Cytology: A Diagnostic Modality. *J Cancer Epidemiol.* 2016;2016: 8134832. doi: 10.1155/2016/8134832



The importance of biochemical indicators in determining male infertility

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ABSTRACT

Introduction and aim. Recently, infertility has become a global problem and the frequency of the “male” factor in family infertility has reached 40–50%. The aim of the research is to investigate the role of some biochemical indicators (endocrine factors and fructose) in determining male infertility.

Material and methods. In the study, the spermogram of 101 men aged 20–46 with idiopathic male infertility, the concentration of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin and testosterone hormones in their blood, and the concentration of fructose in their sperm samples were analyzed, and their correlations were determined.

Results. The concentration of FSH in the blood serum of men with asthenozoospermia and oligozoospermia increased statistically significantly by 57.7% and 2.4 times, respectively, compared to the control. More serious endocrinological disorders were recorded in men with azoospermia. In men with non-obstructive azoospermia, the concentration of FSH is 8.8 times, that of LH is 2.9 times; while prolactin increased by 89.0% compared to the control, testosterone concentration decreased by 22.9%. The fructose concentration in the oligozoospermia group compared to the control group increased by 60.8% ($p_{H1} < 0.001$), and in the non-obstructive azoospermia group by 2.0 times ($p_{H1} = 0.001$). A positive correlation between FSH and LH and a negative correlation between fructose concentration and forward motility of spermatozoa were determined in both asthenospermic and oligozoospermic patients ($\rho = 0.544$; $p = 0.002$). In case of non-obstructive azoospermia, FSH and prolactin, in azoospermia, LH and testosterone were directly proportional.

Conclusion. During male infertility, there is a serious relationship between sperm indicators and endocrine disorders. An increase in the concentration of fructose is the main indicator of a decrease in the number and motility of spermatozoa. A high concentration of FSH and LH in men with azoospermia can be considered one of the important indicators in the diagnosis of non-obstructive azoospermia.

Keywords. FSH, LH, male infertility, prolactin and fructose

Introduction

Currently, 14–30% of married couples suffer from infertility, and the share of male infertility in this problem is about 50%. This is explained by the increase in the harmful effects of environmental, industrial and household factors on the human body.^{1,2} Infertility in men is multifactorial, including various endocrine diseases, damage to the testicles for any reason, sexually transmitted infections, varicocele, harmful habits, obstruction of the

genitals and their growth, obesity, environmental factors, chronic stress, sleep disorders, intense office work, physical load, deficiency, vitamin deficiency, etc.³ Under the influence of these factors, the quantitative and qualitative indicators of the spermogram deteriorate, as the number of spermatozoa decreases, their mobility weakens, the number of spermatozoa with fragmented DNA and chromatin disorders increases, and pathological spermatozoa with anomalous structure are formed. Structural-func-

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tional pathology of spermatozoa has a weak ability to fertilize, resulting in infertility in men.^{4,5} Currently, for the purpose of laboratory diagnosis of male infertility, indicators characterizing the general fertilizing ability of sperm – concentration of spermatozoa, motility, proportion of spermatozoa with normal morphology – are studied.^{6–8} Current diagnostic methods for determining male infertility cannot determine its causes in 44–70% of cases. At this time, the treating doctor diagnoses idiopathic male infertility and cannot determine the causes of pathospermia.^{6,9} Although the spermogram is a simple method for examining spermatozoa, it does not provide complete information about the disorders of the spermatogenesis process.^{10,11} In most cases, pathological changes in sperm are non-specific, they cannot accurately determine the type of infertility, they only show any changes in indicators. In this regard, the parallel study of sperm and blood plasma metabolites in the development of male infertility can create greater diagnostic possibilities. In recent years, in the diagnosis of male infertility, the study of hormonal balance, determination of the level of fructose in sperm plasma has been studied more widely.

We believe that determining the level of new effective biochemical markers along with spermogram indicators can provide more accurate information in determining the type of male infertility.

Changes in the endocrine system also play a major role in the disruption of the spermatogenesis process. One of the main causes of male infertility is endocrine disorders.^{12,13} Hormones regulate male reproductive functions based on the principle of well-integrated complex interactions at different developmental stages. In men, sexual development and hormonal functions depend on the functional activity of a complex chain involving the hypothalamus-pituitary-gonadal (HPG) and the central nervous system. The hypothalamic-pituitary-gonadal system consists of three endocrine organs: the hypothalamus, the anterior lobe of the pituitary gland, and the testes, which secrete peptide, protein, and steroid hormones.

Gonadotropin-releasing hormone (GnRH) synthesized in the hypothalamus regulates the secretion of gonadotropins, follicle-stimulating hormone (FSH), luteinizing hormone (LH) in the anterior lobe of the pituitary gland. FSH accelerates the maturation of spermatogonia by acting on Sertoli cells. In Leydig cells, LH ensures the synthesis and release of testosterone.^{14–16} In the presence of testosterone, FSH stimulates Sertoli cells and induces spermatogenesis.¹⁷ Although many hormones play a role in the formation of sperm, testosterone is considered the most important factor in the process of spermatogenesis.¹⁸

Seminal fluid consists of complex organic and inorganic compounds, and although these substances are not of decisive importance in the fertilization process,

they play an important role in the mobility, functional activity and transportation of spermatozoa in the female reproductive organs. Among these substances, fructose is an aerobic and anaerobic energy source for sperm motility, as fructose undergoes metabolism and breaks down into lactate and pyruvate. Metabolism of fructose in spermatozoa takes place through the classical Embden-Meyer glycolysis pathway. Phosphates of hexoses, triose phosphates and pyruvic acid are intermediates in the formation of lactic acid. Lactate is the main carbohydrate source in spermatozoa, and lactic acid is broken down to carbon dioxide and water in the Krebs cycle in the presence of oxygen. Due to the generated energy, the mobility of spermatozoa is ensured. In the presence of glucose, fructose participates in the disintegration of the outer acrosomal membrane - the formation of the acrosomal reaction.^{1,19} Fructose also plays an important role in sperm viscosity and hyaluronidase activation. Determination of fructose in the seminal fluid can allow to determine the state of the seminal vesicles, endocrine anomalies, and obstruction of the seminal ducts. This vital biochemical component not only increases the functional activity of the prostate, but also plays an important role in sperm coagulation and dilution.^{1,20}

Aim

The aim was to investigate the role of some biochemical indicators (endocrine factors and fructose) in determining male infertility.

Material and methods

The study plan was implemented in accordance with the Helsinki Final Act and the protocol was approved by the Ethics Committee Azerbaijan Medical University ICE Committee on Medical Sciences (№8. 28.06.2020).

In the study were analyzed blood and sperm samples of 101 men aged 20–46 years (31.6 ± 0.5 years) with idiopathic male infertility, who had not had children for more than a year and the female cause of infertility was excluded, as well as the presence of antisperm antibodies in the couple. All subjects gave informed consent for inclusion before they took part in the study. The study was conducted in accordance with the Declaration of Helsinki. The study excluded patients with a burdened drug history (androgens or anti-estrogens), chromosomal translocations, hypogonadotropic hypogonadism, as well as other endocrine diseases leading to decreased testosterone secretion: hypothyroidism, thyrotoxicosis (determined based on the levels of thyroid-stimulating hormone, free thyroxine T4), decompensation of diabetes mellitus, hypercortisolism, as well as renal or liver failure, inflammatory and infectious diseases of the urogenital tract in the acute stage, with pituitary adenoma. We studied men who had not had children for more than a year and the reasons were only

the male factor. a female cause of infertility was excluded, as was the presence of antisperm antibodies in the couple 20 fertile men aged 23–40 years (31.1 ± 1.1 years) were included in the control group. The control group was selected among men who had children (fertile) and were practically healthy. After 3–5 days of abstinence from sexual intercourse, sperm samples were collected from each male patient by masturbation, and the samples were poured into dry, clean disposable sterile containers and analyzed morphologically after 30 minutes. Phase-contrast microscopy and special dyes were used to evaluate the structure and functions of spermatozoa. 4 days before the spermogram, alcohol consumption, including beer, as well as hot procedures – going to the bath, sauna, hot bath, unfavorable working conditions are prohibited. Motility was assessed as the proportion of sperm that gradually became motile at 37°C using a Makler chamber. Men were considered azoospermic if no sperm were detected or if sperm were detected only after centrifugation of the semen sample. Men with azoospermia were not included in these analyses.

The number and quality of spermatozoa in the semen was analyzed. The patients included in the study were divided into 3 groups based on the criteria established by the World Health Organization in 2010 according to the number and activity of their spermatozoa: asthenozoospermia (patients with a normal number of spermatozoa and low forward motility) – 56 people; oligozoospermia (number of spermatozoa in 1 ml of sperm <15 million) – 30 people; azoospermia (absence of spermatozoa in ejaculate) – 15 people.⁷ Patients in the azoospermia group were divided into two groups: obstructive ($n=7$) and non-obstructive azoospermia ($n=8$). The morphological structure of spermatozoa was evaluated based on their appearance and compared with Kruger's criteria. Spermatozoa were classified into one of four morphological groups: normal, head pathology, neck pathology, mixed pathology. Thus, spermatozoa with head, neck and tail pathology can be found in the spermogram. In some cases, several pathologies are detected in anomalous cells at the same time (mixed pathology). When the ratio of such spermatozoa is higher than 96%, the sperm loses its ability to fertilize and teratozoospermia occurs. This is caused by chromosomal pathologies, enzyme diseases, viral infections, etc. can be. Asthenozoospermia is diagnosed when the concentration of moving spermatozoa is below 32%. The proportion of morphologically normal spermatozoa that fully meet the Kruger criteria should not be less than 4%.^{20,21}

The concentration of fructose was determined by centrifuging the sperm sample at a speed of 3000 rpm for 10 minutes. The concentration of fructose in sperm fluid was determined by the colorimetric method with the help of B.I.R.D. Diagnostics (Baharafshan institute of Research and development) "semen fructose" reagent kit.

In order to examine the hormonal status, the concentration of FSH, LH, testosterone and prolactin in the blood serum of men was measured using the electrochemiluminescence immunoassay technique with the help of Roche e411 autoanalyzer. The statistical analysis of the obtained results was carried out using the Excel-2017 software package based on Mann-Whitney and Kruskal-Wallis non-parametric criteria. Statistical analysis of the obtained results was carried out using the SPSS-26 software package (IBM, Armonk, NY, USA) based on the t-Student-Bonferroni and H-Kruskal-Wallis tests. Differences between groups were considered statistically significant when $p < 0.05$. Correlation dependence between indicators was determined based on Spearman's statistical criterion. To identify relationships between indicators, a ρ (Rho)-Spearman correlation analysis was carried out. The statistical significance of the ρ -correlation coefficient was assessed using a two-sided test.

Results

According to the results of sperm analysis, the number of spermatozoa decreased by 41,1% ($p_H < 0.001$) in the asthenozoospermia group, and by 7.9 times ($p_{HI} < 0.001$) in the oligozoospermia group compared to the control group. The number of moving spermatozoa decreased by 73,7% ($p_H < 0.001$) in the oligozoospermia group, and by 3.7 times ($p_H < 0.001$) in the asthenozoospermia group compared to the control. As can be seen, the total number of spermatozoa in men with oligozoospermia compared to men with asthenozoospermia decreased by 5.6 times ($p_{H2} < 0.001$), and the number of moving spermatozoa decreased by 2.1 times ($p_{H2} < 0.001$). According to the calculations, a statistically significant difference in the number of moving spermatozoa between the groups was determined ($p_K < 0.001$).

Male infertility can be caused not only by the number of spermatozoa, but also by changes in their morphological structure. In our research work, the number ratio of spermatozoa with head and neck pathology was determined. According to the results of microscopic analysis, there was no statistically significant change in the number of spermatozoa with neck and head pathology in men with asthenozoospermia compared to the control group. In men with oligozoospermia, the ratio of spermatozoa with neck and head pathology was significantly reduced by 10.3% ($p_{HI} = 0.01$) and 41,7% ($p_{HI} = 0.003$), respectively, compared to the control group. A statistically significant difference was determined between the groups in terms of the proportion of spermatozoa with neck ($p_K = 0.031$) and head ($p_K = 0.005$) pathology.

According to the results of microscopic analysis, spermatozoa with mixed pathology prevailed in men with infertility. In asthenozoospermic men, the percentage of spermatozoa with mixed pathology increased by 29.3% ($p_{HI} = 0.014$), and in oligozoospermic men by 61%

($p_{H1} < 0.001$), compared to the control group, statistically significantly increased. The percentage of spermatozoa with mixed pathology in men with oligozoospermia was 24.5% ($p_{H2} = 0.001$) higher than in men with asthenozoospermia. A statistically significant difference in the number of spermatozoa with mixed pathology was determined between the groups ($p_K < 0.001$).

Table 1. Indicators of sperm during idiopathic male infertility*

Sperm index	Groups			p		
	Kontrol (n=20)	Asthenozoospermia (n=56)	Oligozoospermia (n=30)			
Number, (millions)	M	64.6	45.9	7.2	<0.001	
	Median			8		
		63.5	45	$p_{H1} < 0.001$		$p_{H2} < 0.001$
	Q1	61	30	4.5		
	Q2	74	60	10		
Forward movement, (million)	M	34.6	17.9	7.8	<0.001	
	Median			9		
		33	19	$p_{H1} < 0.001$		$p_{H2} < 0.001$
	Q1	32	14	2		
	Q2	35.5	23	11		
Neck pathology, %	M	63.3	60	55.2	0.031	
	Median			58		
		64	61	$p_{H1} = 0.01$		
	Q1	61	55	48		
	Q2	68.5	68	62		
Head pathology, %	M	9.9	8.1	5.3	0.005	
	Median			6		
		8.5	7.0	$p_{H1} = 0.003$		$p_{H2} = 0.041$
	Q1	7	5	3		
	Q2	12	10	7		
Mixed pathology, %	M	21.2	28.2	37.3	<0.001	
	Median			33		
		20.5	26.5	$p_{H1} < 0.001$		$p_{H2} = 0.001$
	Q1	17.5	21	28		
	Q2	24.0	35	48		
Normal, %	M	5.7	3.7	2.2	<0.001	
	Median			2		
		5	3	$p_{H1} < 0.001$		$p_{H2} = 0.016$
	Q1	4	2			
	Q2	7		2		

* M – arithmetic mean, n – number, Q1 – quartile1, Q2 – quartile2, p_{H1} – compared to control, p_{H2} – compared to patients with asthenozoospermia, p – compared between all groups

In men with asthenozoospermia, the percentage of spermatozoa with normal structure is 66.7% ($p_{H1} < 0.001$); in men with oligozoospermia – 2.5 times ($p_{H1} < 0.001$) statistically significantly decreased compared to the control group. The proportion of morphologically normal spermatozoa in men with oli-

gozoospermia was 50% ($p_{H2} = 0.016$) lower than in men with asthenozoospermia. A statistically significant difference was determined between the groups in terms of the proportion of morphologically normal spermatozoa ($p_K < 0.001$) (Table 1).

Thus, during male infertility, the proportion of morphologically normal spermatozoa in sperm samples is significantly reduced, while the number of spermatozoa with mixed pathology is on the contrary increased. This difference was more pronounced in men with oligozoospermia.

Serious disorders in the endocrine system have been identified during male infertility. In the study, the concentration of FSH in the blood of men with asthenozoospermia increased by 57.7% compared to the control, but the result was not statistically significant. There was no significant change in the concentration of LH, testosterone and prolactin in this group compared to the control group.

The concentration of FSH in the blood serum of men with oligozoospermia was statistically significantly increased by 2.4 times ($p_{H1} = 0.046$), the concentration of LH and testosterone tended to increase compared to the control by 39.3% and 17%, respectively, the concentration of prolactin and decreased by 31.7%.

In men with non-obstructive azoospermia, the concentration of FSH – 8.8 times ($p_{H1} < 0.001$), LH – 2.9 times ($p_{H1} < 0.001$); while prolactin increased by 89% compared to the control, testosterone concentration decreased by 22.9%.

In men with obstructive azoospermia, the concentration of FSH – 2.1 times, LH – 32.1%; while prolactin increased by 31.8% compared to the control, testosterone concentration decreased by 10.3%. These results were not statistically significant.

As can be seen from the obtained results, serious endocrine disorders were not recorded in asthenozoospermic patients, unlike other groups, compared to fertile men, only the concentration of FSH increased significantly. In patients with oligozoospermia, compared to men with asthenozoospermia, both FSH (51%) and LH (30%) concentrations increased more, and testosterone (8.7%), prolactin (19.6%) concentrations tended to decrease.

More serious endocrinological disorders were recorded in men with azoospermia. Thus, in men with non-obstructive azoospermia, the concentration of FSH, LH and prolactin was 3.7 times ($p_{H3} < 0.001$), 2.1 times ($p_{H3} < 0.001$) and 2.5 times ($p_{H3} = 0.024$), respectively, compared to men with oligozoospermia. has increased significantly. Testosterone concentration in this group decreased by 43.8% compared to men with oligozoospermia. At the same time, in men with non-obstructive azoospermia, compared to obstructive azoospermia, the concentration of FSH, LH and prolactin increased by 4.2 times ($p_{H4} < 0.001$), 2.2 times ($p_{H4} = 0.033$) and 43.8%, respectively. A statistically sig-

nificant difference was determined between the groups according to the concentration of FSH ($p_K < 0.001$) and LH ($p_K = 0.001$) (Table 2).

Table 2. Changes in the concentration of FSH, LH, testosterone, prolactin hormones in blood, fructose in sperm during idiopathic male infertility*

Index	Groups					p	
	Check (n=20)	Asthenozoospermia (n=56)	Oligozoospermia (n=30)	Azoospermia (non-obstructive) (n=7)	Azoospermia (obstructive) (n=8)		
Age	M	31.1	31.4	32.5	31.4	30.8	0.862
	Median	31.5	30	32.5	31	29.5	
	Q1	28	27.5	28	23	27	
	Q2	3	35.	35	38	35	
FSH mIU/ml	M	3.2	5.2	7.3	24.4	4.9	<0.001
	Median	2.6	4.1	6.2	22.8	5.4	
				$p_{H1} = 0.046$	$p_{H1} < 0.001$	$p_{H2} < 0.001$	
					$p_{H3} < 0.001$	$p_{H4} < 0.001$	
	Q1	2.1	2.2	4	17.5	3.4	
Q2	3.8	5.7	10	32.7	6.1		
LH mIU/ml	M	3.3	3.9	4.3	8.3	4.6	0.001
	Median	2.8		3.9	8.2	3.7	
					$p_{H1} < 0.001$	$p_{H2} < 0.001$	
					$p_{H3} = 0.001$	$p_{H4} = 0.033$	
	Q1	2.1	2.3	2.9	5.6	3.1	
Q2	4.5	4.6	5.3	9.2	5.6		
TST nmol/ml	M	12.4	13.1	14	9	13.7	0.167
	Median	11.8	12.7	13.8	9.6	10.7	
	Q1	10.6	9.3	10.1	6.7	10.2	
	Q2	15	15.5	15.5	10.3	14.7	
PRL mIU/l	M	225.1	228.6	188.1	379.8	300.8	0.196
	Median	208	189	158	394	274	
					$p_{H3} = 0.024$		
	Q1	191	141	127	136	155	
	Q2	225	301	230	507	422	
Fructose, mg/dl	M	241.1	300.5	388.6	412.7	241.8	<0.001
	Median	238.8	284.8	384	476	194.0	
				$p_{H1} < 0.001$	$p_{H1} = 0.001$		
				$p_{H2} < 0.001$	$p_{H2} = 0.024$		
				$p_{H4} < 0.001$	$p_{H4} = 0.004$		
Q1	232.1	244.2	356	408	45.1		
Q2	245.5	350.5	406	496	429		

* FSH – follicle-stimulating hormone, LH – lutein-stimulating hormone, TST – testosterone, PRL – prolactin, M – mathematical average, n – number, Q1 – quartile1, Q2 – quartile2, p_{H1} – compared to control, p_{H2} – compared to patients with asthenozoospermia, p_{H3} – compared to patients with oligozoospermia, p_{H4} – compared to patients with obstructive azoospermia, p – compared between all groups

The obtained results showed that the concentration of fructose did not change significantly in the groups

of asthenozoospermia (19.3% tended to increase) and obstructive azoospermia (23.1% tended to decrease) to the control group. A statistically significant increase of fructose concentration in the oligozoospermia group compared to the control group was observed by 60,8% ($p_{H1} < 0.001$), and in the non-obstructive azoospermia group by 2 times ($p_{H1} = 0.001$). In patients with non-obstructive azoospermia, the concentration of fructose in sperm is 23.9% ($p_{H2} = 0.024$) higher than in patients with asthenozoospermia, and 2.6 times higher ($p_{H4} = 0.004$) than in patients with obstructive azoospermia. A statistically significant difference was determined between the groups for the level of fructose ($p_K < 0.001$).

In the study, correlations between clinical-morphological indicators of spermatozoa, hormonal disorders and fructose concentration were determined in patients diagnosed with male infertility. Based on statistical calculations, it was determined that there was a positive correlation between FSH and LH ($\rho = 0.544$; $p < 0.001$) in the blood of men with asthenozoospermia, which indicates the interdependence of the secretion of both hormones. Thus, LH stimulates spermatogenesis, while FSH plays an important role in the completion of the spermatogenesis process by ensuring the maturation of spermatozoa. A decrease in the total number of spermatozoa ($\rho = -0.388$; $p = 0.003$) and the percentage of spermatozoa with head pathology ($\rho = -0.492$; $p < 0.001$) was observed in this group against the background of an increase in the concentration of FSH. There is a negative relationship between fructose concentration and forward motility of spermatozoa in men with asthenozoospermia ($\rho = -0.542$; $p < 0.001$). Although the number of spermatozoa decreased in this group, the percentage of spermatozoa with mixed pathology increased among them ($\rho = -0.455$; $p = 0.001$). A negative correlation was shown between the ratio of spermatozoa with mixed pathology and the ratio of spermatozoa with neck ($\rho = -0.784$; $p < 0.001$) and head ($\rho = -0.356$; $p = 0.008$) pathology. As the number of spermatozoa with mixed pathology increased, the number of normal spermatozoa decreased ($\rho = -0.769$; $p < 0.001$).

The same trend was recorded in the oligozoospermia group. In the oligozoospermia group, a positive correlation ($\rho = 0.525$; $p = 0.025$) was shown between the age limit of patients and the proportion of spermatozoa with neck pathology. A positive correlation between FSH and LH was determined in this group as well ($\rho = 0.544$; $p = 0.002$). Was found between testosterone levels and sperm count ($\rho = 0.514$; $p = 0.004$) a positive correlation. There is a negative correlation between sperm count and fructose ($\rho = -0.872$; $p < 0.001$). This also shows that when the number of spermatozoa decreases, the consumption of fructose in the seminal fluid decreases. Decreased consumption of fructose results in higher concentration of fructose in sperm. Between the

proportion of sperm with cervical pathology and the proportion of sperm with mixed pathology ($\rho=-0.919$; $p<0.001$) was observed a negative correlation. In case of non-obstructive azoospermia, a direct correlation between FSH and prolactin was determined ($\rho=0.990$; $p=0.017$). That is, of non-obstructive azoospermia an increase in the level of prolactin accelerates the synthesis and secretion of FSH. In obstructive azoospermia, was found between direct correlation between LH and testosterone ($\rho=0.714$; $p=0.047$).

Discussion

As can be seen from the obtained results, only the concentration of FSH increased significantly in asthenozoospermic patients compared to fertile men. In patients with oligozoospermia, although the concentration of FSH increased statistically significantly, the concentration of LH tended to increase, while the concentration of testosterone and prolactin tended to decrease. More serious endocrinological disorders were recorded in men with azoospermia. In both groups of patients with azoospermia, compared to patients with asthenozoospermia and oligozoospermia, the concentration of prolactin increased, while the concentration of testosterone tended to decrease. In the group of non-obstructive azoospermia, the concentration of FSH, LH and prolactin significantly increased compared to all groups.

It is known that FSH and LH are synthesized in the anterior part of the pituitary gland, and their level increases primarily in the gonads – indicating functional disorders of the male gonads, hypogonadism as a result of primary damage to the testicles, as their secretion is regulated based on the feedback mechanism with the level of testosterone. When the level of testosterone in the blood increases, the concentration of gonadotropic hormones decreases. If the production of sperm in the testicles decreases, more FSH is synthesized in the pituitary gland in order to restore the normal function of the testicles.²² Thus, a very high level of FSH indicates an abnormality in the initial stages of spermatogenesis. In addition, elevated levels of FSH during azoospermia and severe oligozoospermia cause damage to the seminiferous tubules. Apparently, in men with non-obstructive azoospermia, an increase in the level of LH, FSH, and a decrease in testosterone, on the contrary, leads to a violation of the spermatogenesis process and a sharp decrease in spermatozoa. It is known that under physiological conditions, high levels of LH and FSH stimulate the secretion of testosterone in Leydig and Sertoli cells, accelerating spermatogenesis. However, at a certain level, they negatively affect the hypothalamus-pituitary-gonadal system and influence the secretion of testosterone through a feedback mechanism. At this time, the concentration of testosterone remains either low or within the norm.²² The increase in the level of FSH is more con-

sistent with the hypothesis of an increase in the secretion of inhibin in the process of spermatogenesis. The increase of LH explains its inhibitory effect on the initial stages of spermatogenesis through a feedback mechanism. However, there are possibilities that feedback factors can inhibit the secretion of LH and FSH.²³

In men with asthenozoospermia, while the concentration of LH, prolactin and testosterone is normal compared to men with normozoospermia, an increase in the level of FSH only indicates the syndrome of Sertoli cells, that is, damage to cells that produce sperm. This is usually recorded more often during serious damage to the testicles and anomalies at the initial stage of spermatogenesis.^{24,25} The results of the study showed that, although the total number of spermatozoa decreases in the oligozoospermia group compared to asthenozoospermia patients, the number of spermatozoa with mixed pathology increases. It is known that with oligozoospermia the number of sperm is predominantly reduced, and in men with asthenozoospermia the number of sperm moving forward is reduced. One of the main reasons for the violation of the forward movement of sperm is a violation of their morphological structure. Patients with asthenozoospermia have many sperm with mixed pathology.

If the level of gonadotropins is elevated ($FSH>LH$) when the sperm count is low or zero, the patient should be investigated for the causes of primary hypogonadism. Deficiency in the first stages of spermatogenesis is observed in such patients.²⁴ In these cases, hypergonadotropic hypogonadism develops, the low level of testosterone leads to a violation of the feedback mechanism and an adequate increase in the concentration of gonadotropins. According to our results, in men with non-obstructive azoospermia, more hypergonadotropic hypogonadism symptoms are observed – high level of gonadotropins, testosterone tends to decrease.

Hyperprolactinemia is one of the main endocrinopathies associated with male infertility. Hyperprolactinemia affects sperm motility in many studies.^{12,26} However, in our study, the effect of hyperprolactinemia on sperm motility was not determined, the concentration of prolactin in men with asthenozoospermia did not change significantly compared to the control group. A significant increase in the level of prolactin in men with azoospermia compared to other groups confirms the important role of hyperprolactinemia in the development of male infertility. As a result of experimental experiments, it was determined that there are prolactin receptors in the prostate gland, and a high concentration of prolactin inhibits the growth of the prostate gland. In addition, the expression of prolactin receptors in the choroidal sheath and hypothalamus proves the role of this hormone in male fertility. Acute hyperprolactinemia inhibits the synthesis of testosterone by

inducing the hypersecretion of corticoids in the adrenal glands or by inhibiting the secretion of GnRH due to the prolactin receptors present in dopamine neurons in the hypothalamus and can cause spermatogenesis disruption.^{12,26-28} In our study, a slight decrease in the level of testosterone against the background of hyperprolactinemia was observed in men with non-obstructive azoospermia. It has been established that endocrine disorders also play an important role in the formation of non-obstructive azoospermia. With non-obstructive azoospermia, a decrease in testosterone levels is also observed. Studies have shown that prolactin also plays a role in reducing testosterone levels, since prolactin suppresses the secretion of GnRH and suppresses testosterone synthesis, resulting in a decrease in testosterone levels leading to suppression of FSH expression.

Fructose and prolactin levels decrease with age in men with obstructive azoospermia. The decrease in the synthesis of LH in this cup leads to the weakening of the synthesis and secretion of testosterone, as a result, the formation of spermatozoa is disrupted, and their number decreases. A decrease in the number of spermatozoa also leads to a decrease in fructose consumption and an increase in its level in sperm.

Fructose is synthesized in seminal vesicles and is considered the main catabolizable energy substrate of seminal fluid.¹ While glucose ensures long-term motility of spermatozoa during their functional activity, fructose is important in their fast and rapid movement in the phase of interaction with the egg cell and in the acrosomal reaction phase.¹⁹ In an environment with high activity of normal spermatozoa, the concentration of fructose decreases due to the high energy demand.²⁹ The concentration of fructose increases as a result of the decrease in the number of spermatozoa. This is primarily due to the fact that fructose is an energy reservoir for spermatozoa. Since only motile spermatozoa use fructose, the determination of fructose is important in the diagnosis of patients with asthenozoospermia. Thus, during idiopathic asthenozoospermia, the number of spermatozoa with mitochondrial defects increases. The increase in the level of fructose in the oligozoospermia and non-obstructive azoospermia group is primarily explained by the decrease in the number of spermatozoa, their anomalous morphology, and their mobility. A decrease in the level of fructose in sperm impairs the movement and coagulation of spermatozoa, which may be associated with inflammation of the genital tract. In patients with asthenozoospermia and oligozoospermia, the ratio of spermatozoa with mixed pathology significantly increases compared to the control group, while the ratio of normal spermatozoa decreases. Pathological spermatozoa consume a small amount of fructose because they are weakly motile or completely immobile.^{1,29,30}

Conclusion

Thus, an increase in the concentration of FSH, LH and prolactin in the blood serum, and a decrease in the concentration of testosterone causes the disruption of the spermatogenesis process, causing male infertility. A high concentration of FSH and LH in men with azoospermia can be considered one of the important indicators in the diagnosis of non-obstructive azoospermia. An increase in the concentration of fructose is the main indicator of a decrease in the number and motility of spermatozoa. Determination of FSH, LH, prolactin, testosterone and fructose concentrations can be of great importance in the differential diagnosis and prediction of male infertility, and can be used to determine the process of spermatogenesis and the biological characteristics of sperm.

Declarations

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Author contributions

Conceptualization, G.E.N.; Methodology, G.E.N.; Software, G.E.N.; Validation, G.E.N.; Formal Analysis, G.E.N.; Investigation, G.E.N.; Resources, G.E.N.; Data Curation, G.E.N.; Writing – Original Draft Preparation, G.E.N.; Writing – Review & Editing, G.E.N.; Visualization, G.E.N.; Supervision, X.X.; Project Administration, G.E.N.

Conflicts of interest

The author assert that they have no conflicts of interest.

Data availability

The author can provide the data upon request.

Ethics approval

Permission to conduct the study was obtained from the Ethics Committee. The study plan was implemented in accordance with the Helsinki Final Act and the protocol was approved by the Ethics Committee Azerbaijan Medical University ICE Committee on Medical Sciences (№8. 28.06.2020).






References

1. Toragall MM, Satapathy SK, Kadavevaru GG, Hiremath MB. Evaluation of Seminal Fructose and Citric Acid Levels in Men with Fertility Problem. *J Hum Reprod Sci.* 2019;12(3):199-203. doi: 10.4103/jhrs.JHRS_155_18
2. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reprod Biol Endocrinol.* 2015;13:37. doi: 10.1186/s12958-015-0032-1
3. Gangwar PK, Sankhwar SN, Pant S, et al. Increased Gonadotropins and prolactin are linked to infertility in males. *Bioinformation.* 2020;16(2):176-182. doi: 10.6026/97320630016176

4. Gamidov SI, Ovchinnikov RI, Popova AY, Naumov NP, Gasanov NG. Role of male infertility in assisted reproductive technology programs (a literature review). *Andrology and Genital Surgery*. 2017;18(3):28-36. doi: 10.17650/2070-9781-2017-18-3-28-36
5. Nguyen HTT, Dang HNT, Nguyen TTT, et al. Correlations between abnormalities of morphological details and DNA fragmentation in human sperm. *Clin Exp Reprod Med*. 2022;49(1):40-48. doi: 10.5653/cerm.2021.04777
6. Pavlov DS, Zubkova AY, Kamaeva IA, Guskova EN. Spermogram as one of the most important laboratory methods for studying male fertility. *Young Scientist*. 2016;26.2(130.2):30-34.
7. World Health Organization. Laboratory manual for the examination and processing of human semen. 5th ed. Geneva: World Health Organization; 2010.
8. Moretti E, Signorini C, Noto D, Corsaro R, Collodel G. The relevance of sperm morphology in male infertility. *Front Reprod Health*. 2022;4:945351. doi: 10.3389/frph.2022.945351
9. Okonofua FE, Ntoimo LFC, Omonkhua A, et al. Causes and Risk Factors for Male Infertility: A Scoping Review of Published Studies. *Int J Gen Med*. 2022;15:5985-5997. doi: 10.2147/IJGM.S363959
10. Agarwal A, Majzoub A, Parekh N, Henkel R. A schematic overview of the current status of male infertility practice. *World J Mens Health*. 2020;38:308-322. doi: 10.5534/wjmh.190068
11. Murgia F, Corda V, Serrenti M, et al. Seminal Fluid Metabolomic Markers of Oligozoospermic Infertility in Humans. *Metabolites*. 2020;10(2):64. doi: 10.3390/metabo10020064
12. Sengupta P, Dutta S, Karkada IR, Chinni SV. Endocrinopathies and Male Infertility. *Life (Basel)*. 2021;12(1):10. doi: 10.3390/life12010010
13. Babakhanzadeh E, Nazari M, Ghasemifar S, Khodadadian A. Some of the Factors Involved in Male Infertility: A Prospective Review. *Int J Gen Med*. 2020;13:29-41. doi: 10.2147/IJGM.S241099.
14. Li X, Zhu Q, Wen Z, et al. Androgen and Luteinizing Hormone Stimulate the Function of Rat Immature Leydig Cells Through Different Transcription Signals. *Front Endocrinol*. 2021;12:599149. doi: 10.3389/fendo.2021.599149.
15. de Mattos K, Pierre KJ, Tremblay JJ. Hormones and Signaling Pathways Involved in the Stimulation of Leydig Cell Steroidogenesis. *Endocrines*. 2023;4:573-594. doi: 10.3390/endocrines4030041
16. Corinne TM, Anatole PC, Jeanne NY. Comparison of Serum Inhibin B and Follicle-Stimulating Hormone (FSH) Level between Normal and Infertile Men in Yaoundé. *International Journal of Reproductive Medicine*. 2020;2020:4765809.
17. Grande G, Barrachina F, Soler-Ventura A, et al. The Role of Testosterone in Spermatogenesis: Lessons From Proteome Profiling of Human Spermatozoa in Testosterone Deficiency. *Front. Endocrinol*. 2022;13:852661. doi: 10.3389/fendo.2022.852661
18. Shirshov V.N. Current state of the male infertility problem: the review of european association of urology clinical guidelines. *Clinical Practice*. 2016;1(25):39-50.
19. Tsujii H, Ohta E, Miah AG, Hossain Sh. Effect of fructose on motility, acrosome reaction and in vitro fertilization capability of boar spermatozoa. *Reproductive Medicine Biology*. 2006;5(4):255-261. doi: 10.1111/j.1447-0578.2006.00150.x
20. Barak S, Baker HWG. Clinical Management of Male Infertility. 2016; Feb 5. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. *South Dartmouth (MA)*: MDText.com, Inc.; 2000.
21. Wald G, Punjani N, Hayden R, Feliciano M, Dudley V, Goldstein M. Assessing the clinical value of the Kruger strict morphology criteria over the World Health Organization fourth edition criteria. *FS Rep*. 2021;2(2):176-180. doi: 10.1016/j.xfre.2021.04.003
22. Gangwar PK, Sankhwar SN, Pant S, et al. Increased Gonadotropins and prolactin are linked to infertility in males. *Bioinformation*. 2020;16(2):176-182. doi: 10.6026/97320630016176
23. Al-Daghistani H, Abdel-Dayem M. Hyperprolactinemia And Hypergonadotropins In Infertile Males With Sever Oligospermia And Azoospermia. *The Internet Journal of Endocrinology*. 2006;3(1):1-6.
24. Hadeel AI, Zhian SR. Impact of Serum Prolactin and Testosterone Levels on Male Infertility in Sulaimanyah City. *Mosul Journal of Nursing*. 2021;7(9):207-214. doi: 10.33899/mjn.2021.168676
25. Palani K, Abdul Jabbar A, Jagannathan N, Babu TT. Association of serum hormone profile and semen quality of infertile males in and around Chennai. *Int J Reprod Contracept Obstet Gynecol*. 2020;9(12):4860-4869. doi: https://doi.org/10.18203/2320-1770.ijrcog20204935
26. Bradley DA. Approach to Male Infertility and Induction of Spermatogenesis. *The Journal of Clinical Endocrinology & Metabolism*. 2013;98(9):3532-3542. doi: 10.1210/jc.2012-2400
27. Oduwole OO, Peltoketo H, Huhtaniemi IT. Role of Follicle-Stimulating Hormone in Spermatogenesis. *Front Endocrinol*. 2018;14(9):763. doi: 10.3389/fendo.2018.00763
28. Raut S., Deshpande S., Balasinar NH. Unveiling the Role of Prolactin and its Receptor in Male Reproduction. *Horm Metab Res*. 2019;51:215-219. doi: 10.1055/a-0859-1144
29. Ndovi TT, Choi L, Caffo B, et al. Quantitative assessment of seminal vesicle and prostate drug concentrations by use of a noninvasive method. *Clin Pharmacol Ther*. 2006;80(2):146-158. doi: 10.1016/j.clpt.2006.04.013
30. Agarwal A, Sharma RK, Gupta S. et al. Sperm Vitality and Necrozoospermia: Diagnosis, Management, and Results of a Global Survey of Clinical Practice. *World J Mens Health*. 2022;40(2):228-242. doi: 10.5534/wjmh.210149



Incidental vs. non-incident gallbladder cancer – a hospital-based clinicopathological study

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ABSTRACT

Introduction and aim. Most gallbladder cancers (GBCs) are discovered incidentally after routine cholecystectomy. The clinicopathological characteristics and prognostic implications of incidental gallbladder cancer (IGBC) versus non-incident gallbladder cancer (NIGBC) is not known.

Material and methods. During this study, clinicopathological details compared between incidental and non-incident GBC groups included age, sex, clinical presentation, preoperative radiological diagnosis, surgical management, and macroscopic and microscopic features. The primary outcome of the study was difference in overall survival (OS) between IGBC and NIGBC.

Results. Among 348 surgically treated patients, 56.6% weren't preoperatively suspected of GBC. Macroscopic examination showed characteristic thickened gallbladder wall without mass lesion (IGBC) vs. clear mass lesion (NIGBC) on imaging. Interestingly, NIGBC had higher LVI (27% vs. 14%) and T stage (68% T2b/T3 vs. 47% T1b/T2a) despite lower margin involvement ($p < 0.001$). The OS for all patients was 12.2 months (median). Among patients who underwent surgery with curative intent, the median survival time was 21.4 months. However, within this group, NIGBC cases had a worse median survival (17 months) compared to IGBC cases (21 months).

Conclusion. Rising incidental GBC necessitates routine microscopic examination of all gallbladder specimens. Surgeons in high-risk areas should remain vigilant for GBC in patients with atypical clinical and ultrasound findings. Early detection and curative resection are paramount for long-term survival in gallbladder carcinoma, with IGBC potentially offering a survival benefit regardless of stage or tumor characteristics. Prospective studies including detailed pathology and molecular analysis are needed to confirm this observation.

Key words. histopathology, incidental gallbladder carcinoma, non-incident gallbladder carcinoma, prognosis, radiology

Introduction

Gallbladder cancers (GBC), the most common cancer of the biliary tract, carries a very poor prognosis when diagnosed at advanced stages due to its aggressive behavior and limited therapeutic options.¹ Surgery remains

the only effective treatment for early GBC; therefore, an accurate preoperative diagnosis is crucial for guiding surgeons to select the most appropriate procedure, minimizing unnecessary surgeries, and optimizing patient outcomes.²

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Unfortunately, despite its significant benefits, accurate preoperative diagnosis of GBC, allowing for a subsequent curative surgical approach, is achievable in only 30% of cases, as documented in the literature. The remaining 50–70% of GBC patients receives an incidental diagnosis postoperatively, typically following laparoscopic cholecystectomy for calculous cholecystitis or acalculous cholecystitis.^{3,4}

Several factors contribute to the difficulty of preoperatively recognizing GBC. These include the non-specific nature of its clinical manifestations and the limitations of radiological diagnosis, particularly in differentiating GBC from other common conditions like calculous cholecystitis or acalculous cholecystitis, especially when presented with a thickened gallbladder wall or a flat tumor type.^{5,6}

The impact of incidental or non-incidental diagnosis on oncological outcomes and the timing of curative-intent resection as a secondary operation in IGBC remain topics of debate. Studies have reported conflicting findings regarding survival outcomes between incidentally and non-incidentally diagnosed GBC.^{7,8}

Aim

We aimed to investigate the clinicopathological characteristics and prognostic factors of IGBC compared to NIGBC cases.

Material and methods

This hospital-based study was conducted on patients who were diagnosed as carcinoma of the gallbladder and came to Acharya Harihar Post-Graduate Institute of Cancer (AHPGIC), Cuttack, Odisha, India, for further management over a period of 5 years from 01.04.2017 to 31.03.2022 were included as study subjects.

This study was approved by the Institutional Ethics Committee of Acharya Harihar Post-Graduate Institute of Cancer, Cuttack, (IEC-AHRCC-066/03.07.2018). All patients provided written informed consent.

The study populations were distributed in two groups: IGBC and NIGBC. IGBC was defined as cancer discovered unexpectedly during routine microscopic examination of a gallbladder specimen removed by laparoscopic cholecystectomy for presumed benign disease. Conversely, NIGBC cases had a preoperative radiological suspicion of gallbladder malignancy. During this study, clinicopathological details compared between IGBC and NIGBC groups included age, sex, clinical presentation, preoperative radiological diagnosis, surgical management, and macroscopic and microscopic features. The primary outcome of the study was the difference in OS between IGBC and NIGBC. OS was calculated from date of surgery to date of last follow up or death.

Categorical data are presented as frequencies and percentages, while continuous data are presented as means

and standard deviations. Chi-square tests were used for comparing categorical variables, with a significance level of 0.05. All statistical analyses were performed using SPSS (version 22, IBM, Armonk, NY, USA).

Results

During this study period, a total of 1,232 GBC cases were referred to our centre, for further management. Of these, only 348 (28.24%) underwent surgical resection, while the remaining 884 cases (71.75%) were deemed inoperable due to advanced disease.

Out of 348 cases, 151 (43.39%) patients preoperatively diagnosed with suspected GBC, only 31 came to our centre for further management, while the others underwent surgery elsewhere. The remaining 197 (56.6%) patients diagnosed with (calculous or acalculous associated inflammatory gallbladder disease by ultrasound underwent laparoscopic cholecystectomy elsewhere (Table 1).

Table 1. The ultrasonographical diagnosis of our included cases

	Preoperative USG diagnosis		Total (n=348)	
	n	%	n	%
Non-suspicious of malignancy	Calculous cholecystitis	169	48.56	
	Acalculous cholecystitis	28	8.04	
Suspicious of malignancy	Gallbladder mass /? GBC	151	43.39	

All patients presented with symptoms, lasting an average of 17 days. Abdominal pain with nausea was the most common complaint in both groups, but non-IGBC patients had a higher prevalence of clinical jaundice (Fig. 1).

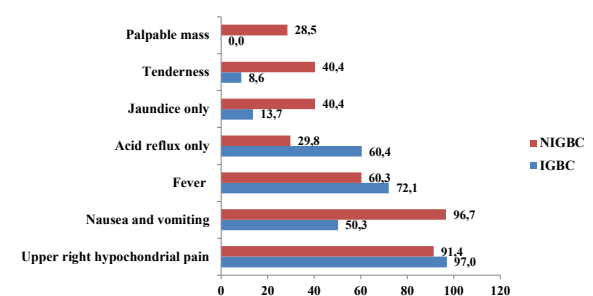


Fig. 1. Sign and symptoms of NIGBC vs. IGBC

For ultrasonographically suspected malignancies (gallbladder mass and/or wall thickening >8 mm), further CT scans were performed to know the disease extension. In USG abdomen and CECT, 13 % patients presented with multiple lymphadenopathies (pericholedochal, peri-pancreatic and para-aortic) and remaining 6% patients presented with either one of the lymphadenopathies. None of the cases showed radiologically regional or distant lymph node metastasis or hepatic or distant organ metastasis (M1 disease). Therefore, all these cases underwent for curative surgery.

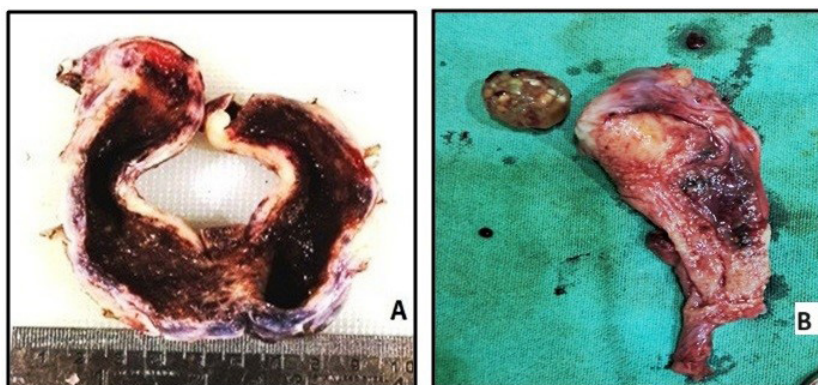


Fig. 2. A: Cut opened gallbladder showing wall thickening (measuring 0.8 cm) with sludge and rugged mucosa, B: GB stone with fundal wall thickening 9 mm.

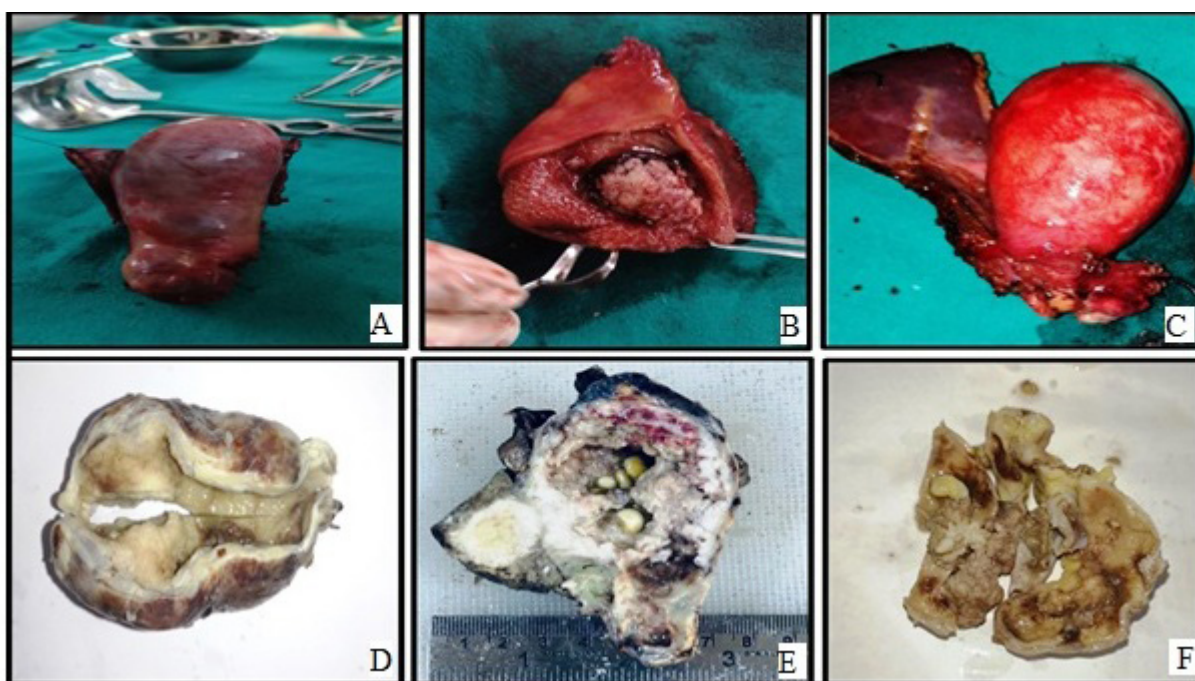


Fig. 3. A: Distended gallbladder measuring 7×4.5 cm, wedge resection; B: Specimen of gallbladder with polypoidal mass measuring 3.6×2.9 cm; C: Resected specimen of gallbladder with wedge of liver; D: Cut opened gallbladder with gallbladder mass (measuring 1.2×0.8cm) with thickened wall; E: Gallbladder (7.6×4.8 cm size) with adherent liver tissue, nodular mass at fundus (measuring 1.9×1.0cm); F: Cut opened gallbladder (6×4 cm size) with ulceroproliferative growth (3.4×2.2 cm at the body)

Macroscopic examination revealed that 78% of non-suspicious GBC cases exhibited a thickened wall without a mass lesion in the cut section, but with a thickened wall and rugged, firm, and sludgy mucosa (Fig. 2).

Mass lesions, such as flat or small nodular growths, were observed in only 20.81% of these cases. In contrast, all radiologically suspicious GBC cases presented with mass lesions during gross examination, including gray-white proliferative masses, cauliflower-like lesions, warty lesions, ulcerative lesions, nodular lesions, and warty polypoidal masses (Fig. 3) (Table 2).

Microscopic examination showed that most non-IGBC cases were classified as T2b/T3 stage tumors (68%), while most IGBC cases were classified as T1b/

T2a stage tumors (47%). This difference was statistically significant ($p < 0.0001$). Non-IGBC also had a higher prevalence of lymphovascular invasion (LVI) (27% vs. 14%; $p = 0.002$). Additionally, IGBC cases had a higher rate of surgical margin involvement compared to NIGBC cases ($p = 0.001$) (Table 3).

Completion surgery was performed in only 38 (19.28%) of the total IGBC cases. The remaining cases could not undergo re-resection due to various reasons, including metastatic disease on staging imaging ($n = 77$, 39%), loss of follow-up after diagnosis ($n = 39$, 19.8%), patient refusal ($n = 22$, 11.1%), and post-surgical complications ($n = 13$, 6.6%). Completion surgery involved exploration of the abdominal cavity, limited liver resection,

Table 2. Age, sex and macroscopic findings of incidental GBC vs. non incidental GBC cases*

Clinical variables	n	Total (n=348)		IGBC (n=197)		NIGBC (n=151)		p
		%	n	%	n	%	n	
Age	<50 years	120	34.4	76	38.6	44	29.1	0.06
	>50 years	228	65.5	121	61.4	107	70.9	
Sex	Male	99	28.4	59	29.9	40	26.5	0.8
	Female	249	71.5	156	79.2	111	73.5	
Gallstone	Present	273	78.4	169	85.78	104	68.8	0.0001
	Absent	75	21.6	28	14.2	47	31.1	
Gallstone numbers	One or two	68	24.9	27	15.9	41	39.4	0.0001
	Multiple	205	75	142	84.0	63	60.5	
Gallstone size	>3cm	86	31.5	49	28.9	37	35.5	0.2
	<3cm	187	68.5	120	71	67	64.4	
Nature of tumor	Only wall thick (0.3–0.7cm)	69	13.7	69	35	0	0	0.0001
	Wall thick only (>0.7) cm	86	24.7	86	43.6	0	0	
Tumor site	Mass/polypoidal growth	193	55.4	42	21.3	151	100	0.2
	Fundus	151	43.3	89	45.2	62	41.1	
	Body	88	25.2	46	23.4	42	27.8	0.2
	Neck	41	11.7	19	9.6	22	14.6	
	Diffuse	68	19.5	43	21.8	25	16.6	

* IGBC – incidental gallbladder cancer, NIGBC – non-incidental gallbladder cancer

Table 3. Histopathological characteristics of IGBC and NIGBC cases*

Histopathological characteristics	n	Total (n=348)		IGBC (n=197)		NIGBC (n=151)		p
		%	n	%	n	%	n	
Tumor type	IAC	297	85.3	167	84.77	130	86.1	0.2
	PAC	16	4.6	13	6.60	3	2.0	
	MAC	15	4.3	7	3.55	8	5.3	
	ASCC	11	3.2	6	3.05	5	3.3	
	SCC	9	2.6	4	2.03	5	3.3	
Tumor grade	G1	121	34.8	72	36.55	49	32.5	0.2
	G2	164	47.1	95	48.22	69	45.7	
	G3	63	18.1	30	15.23	33	21.9	
T stage (pT)	T1b	16	4.6	15	7.61	1	0.7	0.0001
	T2a	127	36.5	79	40.10	48	31.8	
	T2b	139	39.9	83	42.13	56	37.1	
	T3	66	19.0	20	10.15	46	30.5	
PNI	Present	115	33.0	63	31.98	52	34.4	0.6
	Absent	233	67.0	134	68.02	99	65.6	
LVI	Present	69	19.8	28	14.2	41	27.2	0.002
	Absent	279	80.2	169	85.7	110	72.8	
Surgical margin	Positive	76	21.8	67	34.01	9	6.0	0.0001
	Negative	272	78.2	130	65.99	142	94.0	

* IAC – Invasive adenocarcinoma (nos type), PAC – papillary adenocarcinoma, MAC – mucinous adenocarcinoma, ASCC – adenosquamous cell carcinoma, SCC – squamous cell carcinoma, G1 – grade 1, G2 – grade 2, G3 – grade 3, PNI – perineural invasion, LVI – lymphovascular invasion

and dissection of regional lymph nodes. In total, curative surgery (radical/completion surgery following laparoscopiccholecystectomy) were performed in 189 (54.31%) cases. These cases underwent assessment of liver invasion, regional lymph node involvement, and AJCC TNM staging (Table 4). Interestingly, NIGBC patients more frequently had lymph-node-positive disease compared with IGBC patients (23.8% vs. 5.3%; p=0.02) (Table 4).

Table 4. Disease extension and staging status of IGBC and NIGBC cases

Histopathological characteristics	n	Total (n=189)		IGBC (n=38)		NIGBC (n=151)		p
		%	n	%	n	%	n	
Liver invasion	Present	56	29.63	9	23.7	47	31.1	0.3
	Absent	133	70.37	29	76.3	104	68.9	
Lymph node	N1	38	20.11	2	5.3	36	23.8	0.02
	N2	0	0.00	0	0.0	0	0.0	
	N0	151	79.89	36	94.7	115	76.2	
Metastasis	M0	189	100	38	100.0	151	100.0	0.2
	M1	0	0.0	0	0.0	0	0.0	
AJCC (TNM Stage)	IB (T1bN0M0)	3	1.6	2	5.3	1	0.7	0.2
	IIA (T2aN0M0)	55	29.1	8	23.7	47	31.1	
	IIB (T2bN0M0)	56	29.6	13	42.1	43	28.5	
	IIIA (T3N0M0)	31	16.4	7	18.4	24	15.9	
	IIIB (T1-3N1M0)	44	23.3	8	10.5	36	23.8	

Overall follow up time of our study population was 24 months. Median overall survival (OS) among all patients was 12.2 months. Median OS among only patients who underwent curative-intent resections was 21.4 months among which non-IGBC was associated with worse median OS (17 months) compared with IGBC (21 months) (Fig. 4).

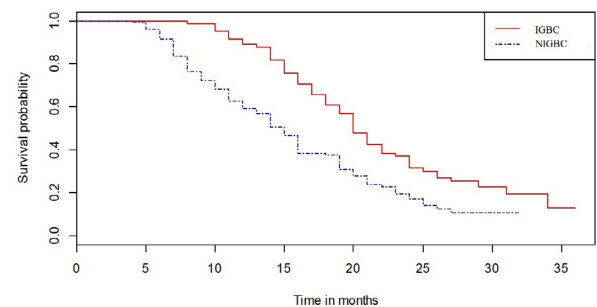


Fig. 4. Comparison the overall survival between IGBC AND NIGBC (Kaplan Meier survival plot)

Discussion

GBC carries a high mortality rate and relatively low 5-year survival rate.⁹ Globally, in 2020, out of 19.3 million total cancer cases, 115,949 new GBC cases were reported, with 84,695 deaths.¹⁰ India accounts for 10% of global GBC cases – approximately one million new cases annually – and experiences a concerning 33% mortality rate. The highest burden of GBC in India occurs

in states like Uttar Pradesh, Bihar, West Bengal, Assam, Delhi, and Odisha.⁹ This regional disparity highlights the need for locally tailored research to understand the high incidence of GBC cases reported in Odisha and determine potential preventive measures.

Another significant challenge is late-stage presentation. In our study, the majority (70%) of patients presented with advanced, unresectable disease. This aligns with studies from the Indian subcontinent, highlighting the importance of early GBC diagnosis to improve surgical outcomes.^{11–13}

Accurate preoperative assessment is crucial for prognosis, selecting appropriate surgery, minimizing unnecessary procedures, and optimizing patient outcomes. However, non-specific symptoms and limitations in diagnostic methods often lead to misdiagnosis and inappropriate surgeries.¹⁴

In our study, only 151 (43.39%) of resectable GBC cases received a preoperative diagnosis suspicious of GBC, allowing for appropriate surgical intervention. The remaining 66% were preoperatively diagnosed as benign and underwent laparoscopic cholecystectomy. World literature suggests 50–70% of gallbladder cancers are diagnosed incidentally, highlighting the limitations of preoperative diagnosis.^{3,4}

Ultrasonography of abdomen is the preferred imaging technique for suspected gallbladder lesions due to its safety, non-invasiveness, real-time capabilities, cost-effectiveness, superior resolution, and ease of use.^{15,16} However, it can sometimes present diagnostic challenges.^{3,15}

In our study, among ultrasonographically unsuspected GBC cases, 169 (85.7%) presented with only a thickened gallbladder wall, often alongside gallstones. This non-specific presentation, common in many gallbladder diseases, makes diagnosis challenging. However, factors like female sex, age over 50, and wall thickening exceeding 3 mm, with or without gallstones, may raise suspicion of malignancy.^{17–19}

Even in macroscopic examination, suspicious cancer features were identified in only 20% of our cases. The remaining 80% showed no suspicious lesions. In these situations, histopathological examination (microscopic) of the cholecystectomy specimen is the gold standard for detecting occult malignancy. It also helps assess invasion depth in IGBC, guiding further management.^{16,17} The Royal College of Pathologists recommends submitting all gallbladder specimens for histopathological examination because significant pathology can present with a normal macroscopic appearance.^{16,17} Several studies support routine histopathological examination of all post-cholecystectomy specimens for increased detection of incidental GBC compared to a selective approach.^{3,16} However, a few authors argue against histopathology for all surgically resected benign gallbladders due to the low IGBC incidence and potential for ear-

ly-stage cases already receiving optimal treatment with simple cholecystectomy.¹⁶

Studies have shown that if GBC is diagnosed symptomatically after cholecystectomy without routine histopathological examination (HPE), the overall resectability rate is only 8%, compared to 70% with early detection based on HPE.²⁰

Pathologists should report crucial factors like surgical margins, histological grade, lymphovascular invasion, perineural invasion, pT stage, and lymph node involvement, all of which are essential for treatment and prognosis of patients incidentally diagnosed with GBC.

Similar to previous reports, our study found that NIGBC cases were associated with indicators of advanced disease and poor prognosis, including clinical jaundice, major hepatectomy, high lymphovascular invasion (LVI) positivity, positive lymph nodes, advanced T-stage, and disease stage.^{8,21} Conversely, IGBC cases exhibited a higher rate of positive cystic duct cut margin. A study suggests that a positive cystic duct margin at initial cholecystectomy is a strong predictor of worse overall survival (OS) even if no further cancer is found at extended radical resection (ERR). Common bile duct resection in patients with a positive cystic duct margin and no recurrence at ERR can lead to improved outcomes.²²

The role of re-resection after incidental GBC diagnosis is to remove residual microscopic local and regional disease from the surgical bed, aiming for an R0 resection, and to perform a complete staging lymphadenectomy. Re-resection is indicated for patients with pathologically confirmed T1b (muscularis layer invasion), T2 (perimuscular connective tissue invasion without serosal or liver involvement), or T3 (serosal perforation or liver invasion) disease without evidence of metastatic disease and adequate performance status to tolerate a potentially more extensive surgery.²³ The optimal timing of re-resection after incidental GBC remains debatable. Some studies suggest that TNM stage, rather than the interval between cholecystectomy and re-resection, is the primary prognostic factor. Others advocate for re-resection within 4 to 8 weeks of initial cholecystectomy, as procedures performed outside this timeframe may be associated with worse outcomes despite similar tumor stages.²⁴

In our study, most patients who did not undergo curative-intent management had metastatic disease on staging imaging. Notably, a majority of patients who underwent re-resection received it after an average of four months following laparoscopic cholecystectomy. This finding emphasizes the importance of early surgical intervention, ideally within 4 weeks of initial cholecystectomy, whenever possible.

Unlike previous reports, we found no statistically significant difference in long-term survival between patients undergoing curative radical resection as a sin-

gle procedure versus those undergoing two procedures (radical re-resection after simple cholecystectomy).^{25,26}

Our study suggests that an IGBC diagnosis may offer a survival advantage, even for patients who receive surgical treatment, regardless of pathological stage and tumor characteristics. Further investigation through prospective studies is needed to explore the reasons behind this observation, including detailed pathological analysis and molecular gene expression analysis.

Conclusion

Rising incidental GBC necessitates routine microscopic examination of all gallbladder specimens. Surgeons in high-risk areas should remain vigilant for GBC in patients with atypical clinical and ultrasound findings. Early detection and curative resection are paramount for long-term survival in gallbladder carcinoma, with IGBC potentially offering a survival benefit regardless of stage or tumor characteristics. Prospective studies including detailed pathology and molecular analysis are needed to confirm this observation.

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Declarations

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Author contributions

Conceptualization, S.S., N.R., and M.R.; Methodology, S.D.; Software, S. D.; Validation, N.R., and S.S.; Formal Analysis, S.S., and P.A.; Investigation, S.S.; Data Curation, S.D.; Writing – Original Draft Preparation, S.S.; Writing – Review & Editing, M.R., S.S., and N.R.; Visualization, S.D.; Supervision, S.S., M.R., and N.R.; Project Administration, N.R.; Funding Acquisition, S.S.

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The data presented in this study are available on request to the corresponding authors.

Ethics approval

This study was approved by the Institutional Ethics Committee of Acharya Harihar Post-Graduate Institute of Cancer, Cuttack, (IEC-AHRCC-066/03.07.2018).





References

1. Roa JC, García P, Kapoor VK, Maithel SK, Javle M, Koshiol J. Gallbladder cancer. *Nat Rev Dis Primers*. 2022;8(1):69. doi: 10.1038/s41572-022-00398-y
2. Cassese G, Han HS, Yoon YS, et al. Preoperative Assessment and Perioperative Management of Resectable Gallbladder Cancer in the Era of Precision Medicine and Novel Technologies: State of the Art and Future Perspectives. *Diagnostics (Basel)*. 2022;12(7):1630. doi: 10.3390/diagnostics12071630
3. Nagarajan G, Kundalia K. Should every cholecystectomy specimen be sent for histopathology to identify incidental gall bladder cancer? *Indian J Cancer*. 2020;57(1):2-3. doi: 10.4103/ijc.IJC_1027_19
4. Wang Z, Xu Y, Hu D, et al. Laparoscopy Versus Open Reoperation for Incidental Gallbladder Carcinoma After Laparoscopic Cholecystectomy. *J Laparoendosc Adv Surg Tech A*. 2020;30(7):764-768. doi: 10.1089/lap.2019.0802
5. Levy AD, Murakata LA, Abbott RM, Rohrmann CA Jr. From the archives of the AFIP. Benign tumors and tumor-like lesions of the gallbladder and extrahepatic bile ducts: radiologic-pathologic correlation. Armed Forces Institute of Pathology. *Radiographics*. 2002;22(2):387-413. doi: 10.1148/radiographics.22.2.g02mr08387
6. Fujiwara K, Masatsugu T, Abe A, Hirano T, Sada M. Preoperative diagnoses and identification rates of unexpected gallbladder cancer. *PLoS One*. 2020;15(9):0239178. doi: 10.1371/journal.pone.0239178
7. Cavallaro A, Piccolo G, Di Vita M, et al. Managing the incidentally detected gallbladder cancer: algorithms and controversies. *Int J Surg*. 2014;12(2):108-119. doi: 10.1016/j.ijssu.2014.08.367
8. Ethun CG, Le N, Lopez-Aguilar AG, et al. Pathologic and Prognostic Implications of Incidental versus Nonincidental Gallbladder Cancer: A 10-Institution Study from the United States Extrahepatic Biliary Malignancy Consortium. *Am Surg*. 2017;83(7):679-686.
9. Kumar A, Ali M, Raj V, et al. Arsenic causing gallbladder cancer disease in Bihar. *Sci Rep*. 2023;13(1):4259. doi: 10.1038/s41598-023-30898-0
10. GLOBOCAN 2020. <https://gco.iarc.fr/today/data/fact-sheets/populations/900-world-fact-sheets.pdf>. Accessed December 11, 2020.
11. Subedi R, Dhimal M, Budukh A, et al. Epidemiologic Pattern of Cancer in Kathmandu Valley, Nepal: Findings of Population-Based Cancer Registry, 2018. *JCO Glob Oncol*. 2021;7:443-452. doi: 10.1200/GO.20.00574
12. Pandit N, Neupane D, Nalbo D, et al. Resectability and prognosis of gallbladder cancer: a cross-sectional study of 100 cases from a tertiary care centre of Eastern Nepal. *Ann Med Surg (Lond)*. 2023;85(5):1755-1760. doi: 10.1097/MS9.0000000000000699
13. Rout N, Hota SK, Dash S, Samantaray S, Mallik RN, Agrawal O. Diagnostic Utility of Ultrasound-Guided Fine-Needle Aspiration Cytology in Gall Bladder Lesions:

- An Experience from a Tertiary Care Cancer Center in Eastern India. *J Cytol.* 2021;38(3):145-150. doi: 10.4103/JOC.JOC_166_20
14. Cassese G, Han HS, Yoon YS, et al. Preoperative Assessment and Perioperative Management of Resectable Gallbladder Cancer in the Era of Precision Medicine and Novel Technologies: State of the Art and Future Perspectives. *Diagnostics (Basel).* 2022;12(7):1630. doi: 10.3390/diagnostics12071630
 15. Fuks D, Regimbeau JM, Le Treut YP, et al. Incidental gallbladder cancer by the AFC-GBC-2009 Study Group. *World J Surg.* 2011;35(8):1887-1897. doi: 10.1007/s00268-011-1134-3
 16. Jha V, Sharma P, Mandal KA. Incidental gallbladder carcinoma: Utility of histopathological evaluation of routine cholecystectomy specimens. *South Asian J Cancer.* 2018; 7(1):21-23. doi: 10.4103/2278-330X.226802
 17. Darmas B, Mahmud S, Abbas A, Baker AL. Is there any justification for the routine histological examination of straightforward cholecystectomy specimens? *Ann R Coll Surg Engl.* 2007;89(3):238-241. doi: 10.1308/003588407X168361
 18. Pyo JS, Son BK, Lee HY, Oh IW, Chung KH. Incidental Carcinoma after Cholecystectomy for Benign Disease of the Gallbladder: A Meta-Analysis. *J Clin Med.* 2020; 9(5):1484. doi: 10.3390/jcm9051484
 19. Rammohan A, Cherukuri SD, Sathyanesan J, Palaniappan R, Govindan M. Incidental gall bladder cancers: Are they truly incidental? *World J Gastrointest Oncol.* 2014; 6(12):441-443. doi: 10.4251/wjgo.v6.i12.441
 20. Agarwal AK, Kalayarasan R, Singh S, Javed A, Sakhuja P. All cholecystectomy specimens must be sent for histopathology to detect inapparent gallbladder cancer. *HPB (Oxford).* 2012;14(4):269-273. doi: 10.1111/j.1477-2574.2012.00443.x
 21. Shih SP, Schulick RD, Cameron JL, et al. Gallbladder cancer: the role of laparoscopy and radical resection. *Ann Surg.* 2007; 245(6):893-901. doi: 10.1097/SLA.0b013e-31806beec2
 22. Vega EA, Vinuela E, Sanhueza M, et al. Positive cystic duct margin at index cholecystectomy in incidental gallbladder cancer is an important negative prognosticator. *Eur J Surg Oncol.* 2019;45(6):1061-1068. doi: 10.1016/j.ejso.2019.01.013
 23. Alarabiyat M, Raza SS, Isaac J, et al. Incidental gallbladder cancer diagnosis confers survival advantage irrespective of tumour stage and characteristics. *World J Gastroenterol.* 2022;28(18):1996-2007. doi: 10.3748/wjg.v28.i18.1996
 24. Zaidi MY, Abou-Alfa GK, Ethun CG, et al. Evaluation and management of incidental gallbladder cancer. *Chin Clin Oncol.* 2019;8(4):37. doi: 10.21037/cco.2019.07.01
 25. Rathanaswamy S, Misra S, Kumar V, et al. Incidentally detected gallbladder cancer- the controversies and algorithmic approach to management. *Indian J Surg.* 2012;74(3):248-254. doi: 10.1007/s12262-012-0592-7
 26. Fong Y, Jarnagin W, Blumgart LH. Gallbladder cancer: comparison of patients presenting initially for definitive operation with those presenting after prior noncurative intervention. *Ann Surg.* 2000;232(4):557-569. doi: 10.1097/00000658-200010000-00011



The importance of ultrasonography examination in renal abscesses in pediatric patients

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ABSTRACT

Introduction and aim. Renal abscess is a rare finding in the pediatric population, estimated at 0.2% of all intra-abdominal abscesses. The most common manifestations are fever, flank pain and simultaneously increased inflammatory markers in laboratory tests. Symptoms of this condition are non-specific and can be dismissed with other pathologies like renal tumor. Although the management is based on widespread antibiotic therapy, some cases need surgical intervention because of poor general condition and major diameter of abscess (>5 cm). We undertook this study to analyze the ultrasonography findings correlated with the clinical manifestations of renal abscesses in children that can potentially improve detecting renal abscesses in children earlier.

Material and methods. We retrospectively studied 9 patients with renal abscesses treated in our hospital.

Results. All patients were diagnosed with renal abscesses based on ultrasonography (US) examination and each of them had elevated inflammatory parameters at the time of admission. For treatment, all patients were treated with intravenous antibiotics and two of them were treated with surgical drainage. All study group recovered completely or received a reduction of abscesses diameters. The renal abscesses were monitored by ultrasonography.

Conclusion. In our study, we assessed the usefulness of the US examination for diagnosis and treatment monitoring in pediatric patients. Ultrasonography is a gold standard due to its wide availability, noninvasiveness and low price. It also allows for immediate diagnosis, which is crucial to institute proper treatment. Treatment of abscesses depends on the clinical condition of the patient, other comorbidities, imaging presentation and the size of the abscess.

Keywords. pediatrics, renal abscess, ultrasonography

Introduction

Renal abscesses are structures composed of purulent and necrotic organic material in the renal parenchyma. It is a rare disease in the pediatric population.^{1,2} Their incidence can be estimated at 0.2% of all intra-abdominal abscesses.³ We can also distinguish perirenal abscesses, which are located outside the renal parenchyma

between the renal capsule and Gerota's fascia and constitute 0.02% of all abdominal abscesses.^{3,4}

Until now, the most common etiologies of renal abscesses were *Escherichia coli* and *Staphylococcus aureus*.^{5,6} An abscess may be a consequence of urinary tract infection, hematogenous spread of pathogens or direct spread from local infection.^{2,7,8} Currently, with

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the widespread use of antibiotic, Gram-negative bacteria, represented by *E. coli* and *Proteus* spp., have gained the advantage.⁵ Conditions identified that are risk factors for renal abscesses, such as: diabetes, immune deficiencies, vesicoureteral reflux, nephrolithiasis and urological abnormalities (duplication of the urinary tract, ureteropelvic junction stenosis, calyceal diverticulum).^{9,10}

Symptoms associated with abscesses are most often non-specific and systemic, which delays proper diagnosis. The most common are fever, general malaise, appetite loss, weight loss, abdominal pain, lumbar pain, painful urination, chills and vomiting.^{4,5,11,12}

It should be noted that prolonged fever after infections in children can be caused by kidney abscesses. Then, with oncological vigilance, a differential diagnosis of the kidney lesion should be made to exclude cancer and make a final diagnosis of an abscess.⁸

In diagnostic imaging are used ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI). A quick and accurate diagnosis and appropriate therapeutic procedures are essential for better treatment results and reduced mortality.

The management of kidney abscesses can be divided into conservative and invasive treatment. The choice of treatment method should be selected individually based on the general condition of the patient, the severity of the infection and the size of the abscess on imaging tests.^{2,5}

Aim

The main purpose of this study is to prove the significance of ultrasonography in prediction of renal abscesses, choice of treatment method and monitoring results. We retrospectively studied 9 patients with renal abscesses treated in our hospital to analyze our experience in the diagnosis and treatment of these rare disorders. Small study group and retrospective character of this paper are the main limitation of our article.

Material and methods

Between 2012 and 2023, nine pediatric patients were admitted to the Pediatric Surgery and Urology Clinic of the Provincial Clinical Hospital No. 2 Saint Jadwiga Queen in Rzeszów with the final diagnosis of a renal abscess. Age, sex, presentation, laboratory test results, imaging diagnostic and treatment were recorded retrospectively. All patients underwent an abdominal ultrasound examination, four patients had CT and one had only MRI. Ultrasound is more readily available than more advanced cross-sectional modalities such as CT or MRI. In laboratory tests we considered white blood cell (WBC) counts, platelet counts, C-reactive protein (CRP) levels and procalcitonin (PCT).

Results

Nine pediatric patients, 3 girls and 6 boys with a median age of 57.4 months (2–147 months) were retrospectively identified. Eight patients (88.89%) had pyuria. Routine urinalysis showed that 88.89% of children had a significant increase in urinary leukocytes. Blood culture was made in 6 patients and was negative in each case. Urine culture was positive in three cases, two *Escherichia coli* and one *Staphylococcus aureus*. The most common symptoms at the time of presentation were fever and flank pain, a patient was admitted because of appendicitis. Moreover, one patient had malformation syndrome with atrial septal defect, cleft palate and epilepsy. All patients were diagnosed with renal abscesses based on US examination. On ultrasound, this was determined by well-defined hypoechoic lesions with a surrounding hypervascularized parenchyma (Fig. 1, 2, 5–8). Color Doppler showed no internal vascular signal (Fig. 4). Contrast-enhanced CT in four patients in the acute phase revealed focal areas with a reduced absorption coefficient and obliteration of the renal calyces with enhancement of normal renal tissue (Fig. 3 and 9). MRI performed in one patient showed hypointense lesion on T1-weighted images and a hyperintense lesion with increasing signal intensity around the lesion (edema) on T2-weighted images (Fig. 10 and 11)

Two patients had a peri-nephric and intra-renal abscess and the remaining patients had intra-renal lesions. In 5 (55.6%) patients, the abscesses were confined to the right kidney and in 3 patients the abscesses were in the left kidney (33.3%). One patient had bilateral abscesses (11.1%). The average size of the abscess was 3.4 cm, with a range of 5 cm to 2.1 cm in our study group. Three of the children had renal lesions suspected of being a tumor during the diagnostic process. In our group of patients, the smallest abscess detected was 2.1 cm. The diagnosis of these changes depends on the experience of the doctor performing the ultrasound and the patient's preparation for the examination and his cooperation.

Table 1. Inflammatory markers

Patient	Age (months)	CRP (H mg/l)	PCT (ng/ml)	WBC (H 10 ³ /μL)	Platelets (10 ³ /μL)
1	2	26.7	0.09	21.63	721
2	26	227.2	26.97	24.64	620
3	2	107.3	1.52	14.76	870
4	147	160.7	1.27	30.63	535
5	26	242.1	2.18	12.48	549
6	142	154.5	8.74	9.95	759
7	24	178.1	–	19.34	561
8	69	71.7	0.12	18.88	700
9	79	74.4	0.12	23.48	691

All patients had elevated inflammatory parameters at the time of admission to the hospital. In all cases CRP, white blood cells were significantly increased. We pres-

ent the results of the laboratory examination of inflammatory markers in Table 1 with its highest value during hospitalisation.

Table 2. Treatment method, antibiotics and time of treatment in our study group

Patients	Treatment method	Antibiotics	Time of treatment (days)	Other information
1	Conservative	Amikacin + cefotaxime	10	
2	Surgical	Amikacin + ceftazidime + metronidazol + vancomycin	8	Malformation syndrome
3	Conservative	Amoxicillin with clavulanic acid + cefotaxime	18	Bilateral abscess
4	Conservative	Amikacin + ceftazidime	17	
5	Surgical	Cefotaxime + vancomycin + cotrimoxazol	14	
6	Conservative	Amikacin + ceftazidime + meropenem + amoxicillin with clavulanic acid	24	Appendectomy
7	Conservative	Cefotaxime	15	Sepsis
8	Conservative	Amikacin + ceftazidime	28	Pyelonephritis
9	Conservative	Amikacin + ceftazidime	14	

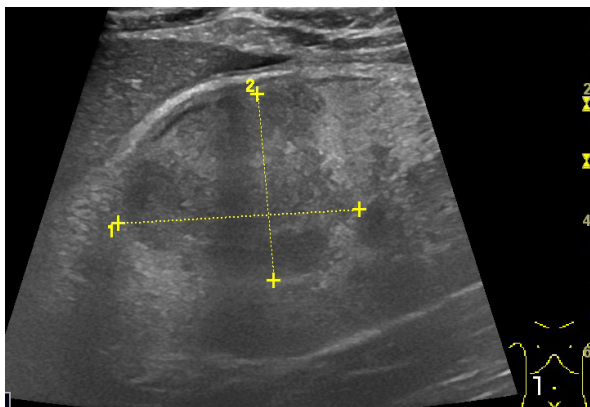


Fig. 1. A heterogeneous hypoechoic area – an abscess with renal parenchyma edema in the vicinity, as well as a narrow layer of fluid around the periphery, subcapsularly, and thickened hyperechoic Gerota's fascia. Blurring of the corticospinal differentiation of the kidney

In our study group, there were two patients who were treated with surgical drainage (22.2%). The procedure was performed under general anesthesia in the theatre by pediatric surgeons. One of them had multiple renal abscesses with the largest 2.6 cm in the US and drainage was performed due to immune disorders and malformation syndrome. The second patient had abscess with diameter 5 cm complicated by urosepsis. Pus culture was performed in one drainage case and was compatible (*S. aureus*) with urine culture. The remaining group of patients were treated with preservative management. All study groups recovered completely or received a reduction of abscesses diameter. The renal abscesses were monitored by US.

For treatment, all patients were treated with intravenous antibiotics mainly as third-generation cephalosporins presented in Table 2.

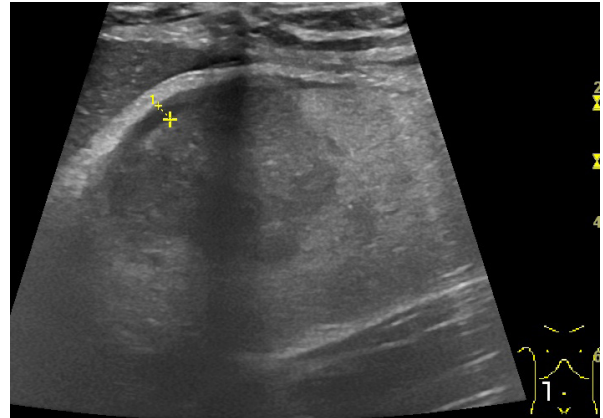


Fig. 2. A heterogeneous hypoechoic area – an abscess with renal parenchyma edema in the vicinity, as well as a narrow layer of fluid around the periphery, subcapsularly, and thickened hyperechoic Gerota's fascia. Blurring of the corticospinal differentiation of the kidney



Fig. 3. CT with contrast, coronal and sagittal

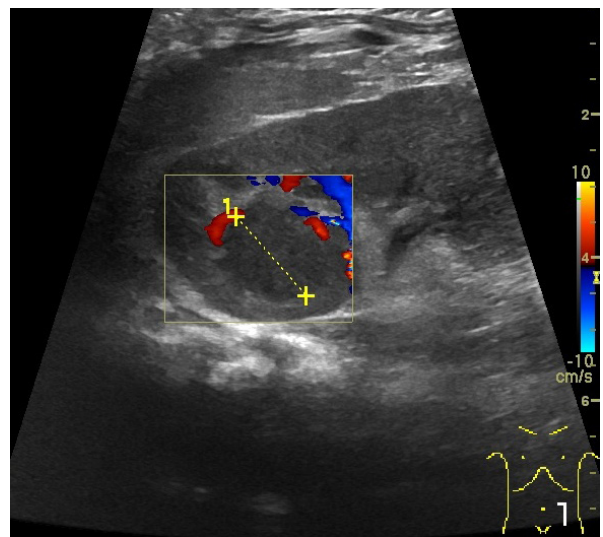


Fig. 4. Image with Color Doppler – no central vascularity, visible vascularization on the periphery of the abscess capsule

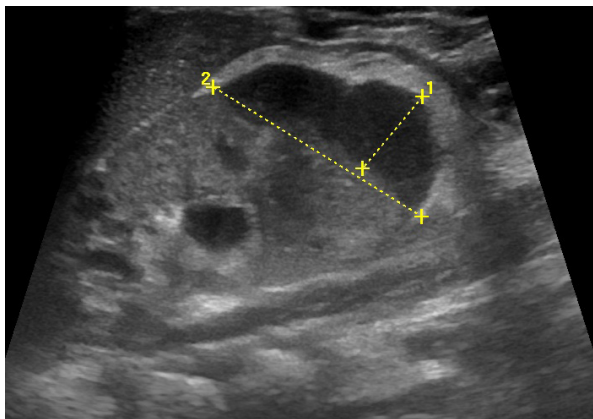


Fig. 5. Hypoechoic banded subcapsular area on the periphery of the renal parenchyma – perirenal subcapsular abscess

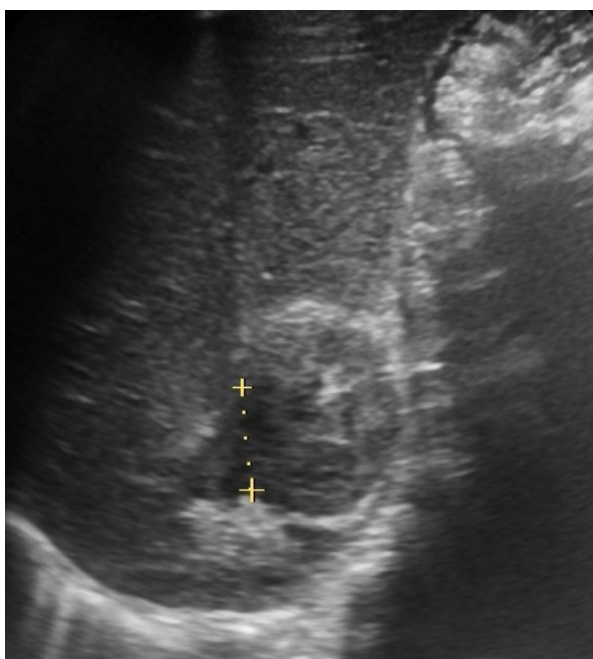


Fig. 6. A heterogeneous and hypoechoic fluid area is visible subcapsularly, organising purulent lesions

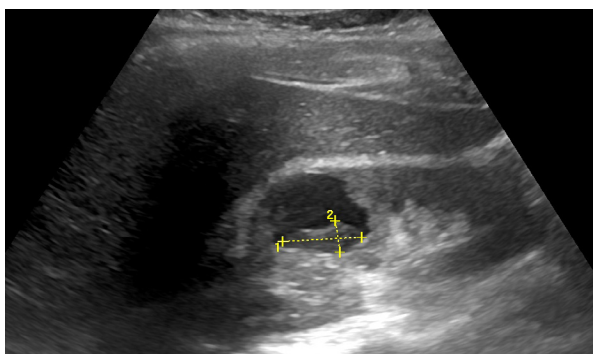


Fig. 7. A single-chamber, anechoic, cystic structure with visible horizontal echogenic bands adjacent to the wall – an abscess that is being cleared

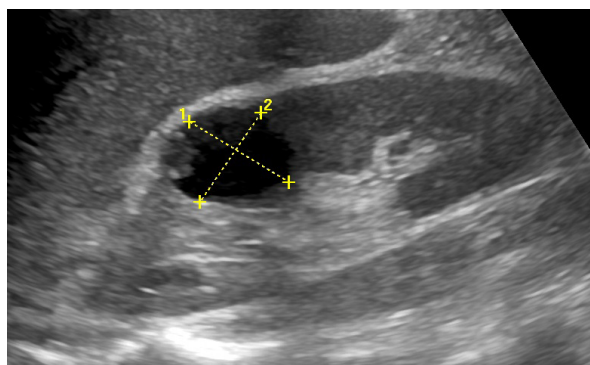


Fig. 8. A single-chamber, anechoic, cystic structure with visible horizontal echogenic bands adjacent to the wall – an abscess that is being cleared

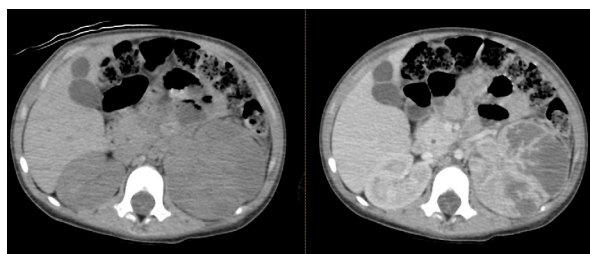


Fig. 9. CT axial

There is limited medial focus at the upper pole of the left kidney, which is enhanced by contrast. The lesion highlights the outline of the kidney, presses the upper renal calyx and reaches into its hilum.

The left kidney has a thin cortical layer with the presence of large, irregular areas of dense fluid density and striated, contrasted parenchyma.

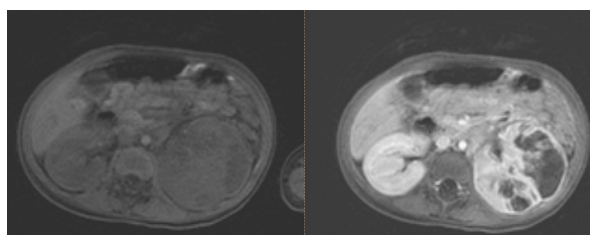


Fig.10. MR T1 axial and axial with contrast

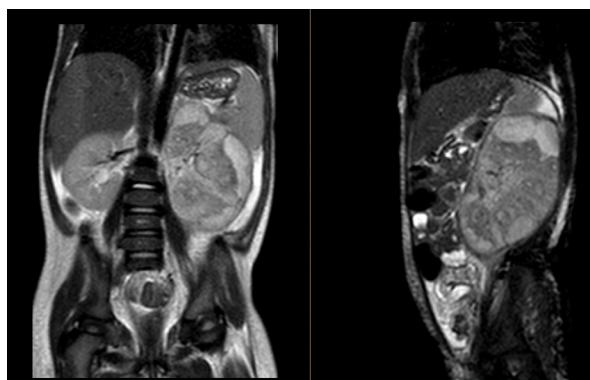


Fig. 11. MR T2 coronal and sagittal

There are bands and areas of fluid space in the left kidney; the fluid signal is moderately increased in T2-weighted images and moderately hypointense in T1-weighted images. After contrast administration, the signal from the distorted renal parenchyma is enhanced.

Discussion

Renal abscesses are infrequent conditions in pediatrics.² Previous research found that there is no obvious gender tendency in children with renal abscess.¹⁰ However Buschel et al. found in their study a predominance of male gender.² Our study also showed that renal abscesses are more likely to occur in males (6/3). Over the years, the etiology of abscesses has changed in favor of Gram-negative bacteria, including *E. coli*, which is also confirmed in our work.^{2,5} Diagnosis and treatment are usually based on guidelines for adults or small sample size data. A small amount of data contributes to the lack of diagnosis or misdiagnosis, that is why early detection and appropriate treatment are important.^{2,10}

US and CT scanning seem to be the most common diagnostic tools.¹ The first-choice examination in case of clinical suspicion of renal abscess is ultrasound examination. One can observe an anechoic fluid reservoir merging with the normal image of fatty tissue inside Gerota's fascia. An abscess is a round lesion with a thick or smooth wall with internal reflections of necrotic changes that move with changes in position. There may be gas inside the abscess, which will give the "comet symptom". It is worth noting that we can also see internal partitions or chambers.¹ Color Doppler and Power-Doppler scans can reveal a well vascularized peripheral ring and no internal vascular signal. Color Doppler in US is an imaging technique that allows obtaining information about blood flow through tissues. This technique generates color maps of flow through tissues that are superimposed on grayscale ultrasound images of anatomical tissues.¹³

The use of intravenous contrast is not required for ultrasound differentiation. One of the possibilities of using US is its use with contrast enhancement (CEUS). The test allows visualization of structures in real time, has a high safety profile and can be performed at the bedside. This method allows for the assessment of renal microvascular perfusion in the case of blood flow disorders, as well as in the case of acute pyelonephritis. It helps differentiate between focal kidney infection and individual stages of kidney abscesses, which determines the decision on the duration of antibiotic therapy. CEUS is also considered a sensitive method for imaging renal post-inflammatory scars in children with reflux nephropathy.¹⁴

However, computed tomography examination can be performed with or without contrast medium administration. In the case without contrast, the most com-

mon image is a single or multiple lesion, unilateral or bilateral, with a round, well-defined shape and a low absorption coefficient. Gas within the collection may also be visible.¹⁵ Abscesses usually have a higher attenuation factor of 10–30 units of H than uncomplicated cysts or the pelvicalyceal system.¹⁶

Contrast-enhanced computed tomography in the acute phase is characterized by the presence of focal areas with a reduced absorption coefficient. In the subacute or chronic phase, strengthening of the abscess wall may be visible as a ring or rim symptom. There is obliteration of the renal sinus or calyces with enhancement of normal renal tissue in the absence of central enhancement of the lesion suspected as a renal abscess. Swelling, obliteration of the perirenal fat tissue and thickening of the perirenal septums and Gerota's fascia may raise the suspicion that the lesions have spread to the perirenal space.¹⁵ In addition, the main advantage of CT is that it provides a distinction between renal and perirenal abscess.⁹ CT also allows to precisely describes small collections (1–2 cm), renal capsule and Gerota's fascia.⁴ Moreover CT can be used to confirm the diagnosis of renal abscesses suggested in US because the method does not always provide a definitive diagnosis.^{2,9} Magnetic resonance imaging can also be used in diagnostics. This examination will show the abscess as a hypointense lesion on T1-weighted images, a hyperintense lesion with increasing signal intensity around the lesion (edema) on T2-weighted images, and peripheral contrast enhancement on T1-weighted images with contrast enhancement.¹⁵

The differential diagnosis should include cystic renal cell carcinoma (especially in the case of chronic, asymptomatic abscesses), metastases or lymphoma, and infected or hemorrhagic cysts. In equivocal cases, a biopsy may be necessary.

Treatment of abscesses depends on the clinical condition of the patient, other comorbidities, imaging presentation and the size of the abscess.⁵ Based on literature data, antibiotic therapy is commonly used in patients with abscesses <3 cm and should last 4–6 weeks.⁸ Lesions between 3 cm to 5 cm in children who are clinically stable may be considered to treat only by preservative management. The method of choice in >5 cm abscess is surgical intervention.^{2,8} In our study group, the above treatment guidelines are also applicable because surgical treatment was used in two patients, one with malformation syndrome, immune disorders and multiple renal abscesses, and the other with an abscess with a diameter of 5 cm complicated by urosepsis.

We analyzed reviews from the literature and present their data on the treatment of renal abscesses in Table 3. This confirms that prolonged antibiotic therapy is generally considered an initial treatment method, preserving drainage for larger renal abscesses or cases refractory to antibiotic course.

Table 3. Review of the literature on kidney abscesses and their treatment

Renal abscesses treatment in children, literature reviews	Number of patients	Surgical treatment	Conservative treatment
Comloj et al. ¹	6	–	6
Linder and Granberg ⁷	16	3 – percutaneous drainage (>3.8 cm)	13
Chen et al. ⁹	17	4 – percutaneous drainage	13
Zhang et al. ¹⁰	17	10 (>4 cm)	7
Buschel et al. ²	14	5 – percutaneous drainage (>5 cm) 2 – surgical drainage	7

It is crucial to remember to always suspect urinary tract infection (UTI) in a febrile child, because approximately 6-8% of febrile infants are ultimately diagnosed with UTI. It is estimated that by the age of 11, 1% of boys and 3% of girls will experience a UTI.⁸ UTI is considered to be the most common etiology of renal abscesses.^{1,9,10}

The main purpose of diagnostic imaging in UTI is to identify disorders that can cause recurrences of UTI and deterioration of kidney function.¹² In the case of UTI with fever, US is not performed routinely, however the Polish Society of Pediatric Nephrology recommends performing an ultrasound examination in all children up to 24 months after the diagnosis of the first episode of UTI, and in children >24 months after the diagnosis of acute UTI, UTI with an atypical course, with risk factors for recurrence or in the event of recurrence of UTI.¹⁷

In our study, we assessed the usefulness of the US examination for diagnosis and treatment monitoring in pediatric patients. The main advantages of US are its low price, high availability, non-invasiveness and lack of exposure of the patient to radiation during the procedure. Other tests used in diagnostics are computed tomography and magnetic resonance imaging, but due to lower availability, costs, and the need for systemic anesthesia of the child, ultrasound is the method of choice.^{4,10,12}

Each patient in our study group with suspected renal abscess based on US had the diagnosis confirmed by subsequent imaging tests, such as CT or MRI. The experience and skills of the radiologist, as well as the cooperation of the pediatric patient and contact with clinicians, play an important role in the correct interpretation of ultrasound images suspected of an abscess. One of the limitations of US is the obesity of patients and the location of pathology in the retroperitoneal or peritoneal space, which requires the experience and skills of the doctor performing this examination.¹²

Our study has several limitations. First, our analysis is a retrospective cohort study. Secondly, our data span eleven years and includes only nine patients, which is why our study group is too small to obtain a diagnostic algorithm.

Conclusion

Ultrasound is the first-choice examination in the case of clinical suspicion of renal abscess. It is crucial to perform the imaging immediately and correct interpretation, due to non-specific symptoms which may delay the diagnosis. Ultrasound also allows us to measure the diameters of the abscess and make decisions about treatment based on the clinical condition and further follow-up of the patient during and after treatment.

Declarations

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Author contributions

Conceptualization, I.K.M. and A.G.; Methodology, I.K.M.; Software, J.K.; Validation, I.K.M., A.G. and J.K.; Formal Analysis, I.K.M.; Investigation, K.K. and K.O.; Resources, I.K.M.; Data Curation, I.K.M.; Writing – Original Draft Preparation, K.K. and K.O.; Writing – Review & Editing, K.K. and K.O.; Visualization, I.K.M.; Supervision, W.G.; Project Administration, I.K.M.;

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

Not applicable.

Declaration of the authenticity of figures

All figures submitted have been created by the authors, who confirm that the images are original without duplication and are the property of the Clinical Department of Radiology and Imaging Diagnostics, Clinical Provincial Hospital No. 2 Saint Jadwiga Queen in Rzeszow.


References

- Comloj E, Cassar W, Farina A, et al. Conservative management of paediatric renal abscess. *J Pediatr Urol.* 2013;9(6 Pt B):1214-1217. doi: 10.1016/j.jpuro.2013.05.016
- Buschel H, Leung P, Stalewski H, Carroll D, Mariyappa-Rathnamma B. Renal abscesses in children: an 11-year retrospective study and review of the literature. *ANZ J Surg.* 2022;92(12):3293-3297. doi: 10.1111/ans.17943
- Jaik NP, Sajuiitha K, Mathew M, et al. Renal abscess. *J Assoc Physicians India.* 2006;54:241-243.
- Coelho RF, Schneider-Monteiro ED, Mesquita JLB, et al. Renal and perinephric abscesses: analysis of 65 consecutive cases. *World J Surg.* 2007;31(2):431-436. doi: 10.1007/s00268-006-0162-x

5. Xia M, Liu J, Hong Y, et al. Renal Abscess: Invasive Treatment or not. <https://www.researchsquare.com/article/rs-56366/v1>. Accessed December 29,2023.
6. Seguias L, Srinivasan K, Mehta A. Pediatric renal abscess: a 10-year single-center retrospective analysis. *Hosp Pediatr*. 2012;2(3):161-166. doi: 10.1542/hpeds.2012-0010
7. Linder BJ, Granberg CF. Pediatric renal abscesses: A contemporary series. *J Pediatr Urol*. 2016;12(2):99.e1-99.e5. doi: 10.1016/j.jpuro.2015.05.037
8. Martonosi ÁR, Pázmány P, Fukász A, et al. Differential diagnostic challenges in the COVID-19 pandemic: renal abscess after SARS-CoV-2 infection in a young adolescent. *Am J Case Rep*. 2022;23:e935190. doi: 10.12659/AJCR.935190
9. Chen CY, Kuo HT, Chang YJ, et al. Clinical assessment of children with renal abscesses presenting to the pediatric emergency department. *BMC Pediatr*. 2016;16(1):189. doi: 10.1186/s12887-016-0732-5
10. Zhang X, Xie Y, Huang G, Fu H. Analysis of 17 children with renal abscess. *Int J Clin Exp Pathol*. 2019;12(9):3179-3184.
11. Kitaoka H, Inatomi J, Chikai H, et al. Renal abscess with bacteremia caused by extended-spectrum β -lactamase-producing *Escherichia coli*: a case report. *Pediatr*. 2020; 20(1):461. doi: 10.1186/s12887-020-02366-5
12. Tamburrini S, Lugarà M, Iannuzzi M, et al. Pyonephrosis ultrasound and computed tomography features: a pictorial review. *Diagnostics (Basel)*. 2021;11(2):331. doi: 10.3390/diagnostics11020331
13. Meola M, Ibeas J, Lasalle G, Petrucci I. Basics for performing a high-quality color Doppler sonography of the vascular access. *J Vasc Access*. 2021;22(1):18-31. doi: 10.1177/11297298211018060
14. Pšeničný E, Glušič M, Pokorn M, Ključevšek D. Contrast-enhanced ultrasound in detection and follow-up of focal renal infections in children. *Br J Radiol*. 2022; 95(1140):20220290. doi: 10.1259/bjr.20220290
15. Caraiani C, Yi D, Petresc B, Dietrich C. Indications for abdominal imaging: When and what to choose? *J Ultrason*. 2020;20(80):e43-e54. doi:10.15557/JoU.2020.0008
16. El-Ghar MA, Farg H, Sharaf DE, El-Diasty T. CT and MRI in Urinary Tract Infections: A Spectrum of Different Imaging Findings. *Medicina (Kaunas)*. 2021;57(1):32. doi: 10.3390/medicina57010032
17. Szczepańska M, Bałasz-Chmielewska I, Grenda R et al. The Polish Society for Pediatric Nephrology (PTNFD) recommendations on the management of children with nephrotic syndrome. *Renal Disease and Transplantation Forum*. 2022;15(1):36-57. doi: 10.5603/RDTF.2022.0001



The relationship between health literacy levels and genital hygiene behaviors in female university students

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ABSTRACT

Introduction and aim. This study investigates the correlation between health literacy levels and genital hygiene behaviors among female university students.

Material and method. A descriptive-correlational study was conducted with 348 female students who voluntarily participated. Data were collected through an online survey comprising participant information forms, the Health Literacy Scale, and the Genital Hygiene Behaviors Scale. Statistical analyses, including descriptive statistics, chi-square test for categorical data, and correlation analyses, were performed using SPSS version 26.0.

Results. The mean age of the participants was 21.92 ± 2.51 years. The average scores on the Health Literacy Scale and Genital Hygiene Behaviors Scale were 106.0 ± 17.9 and 86.73 ± 10.13 , respectively. Significant differences were observed in genital hygiene behavior scores concerning participants' field of study and bathing habits. Furthermore, a moderately significant positive correlation was found between women's health literacy scores and genital hygiene behavior scores.

Conclusion. The study reveals a positive association between high health literacy levels and adequate genital hygiene behaviors among women. As women's health literacy improves, their genital hygiene behaviors also enhance positively. Access to reliable health information resources is crucial to ensure accurate knowledge acquisition regarding genital hygiene practices.

Keywords. genital hygiene, health literacy, university students, women

Introduction

Genital hygiene is crucial for women's health preservation. When genital hygiene is improperly maintained, it can lead to diseases such as glomerulonephritis, cystitis, endometriosis, and oophoritis.¹ These diseases can lead to physiological health problems such as ectopic pregnancy, sepsis, cervical cancer, infertility, and psychological health problems such as fear and anxiety.^{2,3} Among the reasons for women seeking gynecology clinics, urogenital infections are the most common.³ The period between 15 and 24 is crucial for developing gender characteristics and transitioning to adulthood. This pe-

riod is essential in terms of acquiring habits that need to be gained in the health field, and it is also a period at risk for health.^{4,5} Particularly among university-aged students, residing in densely populated environments such as dormitories or shared housing may lead to inadequate attention to genital hygiene, potentially increasing the risk of genital infections.^{2,6} Additionally, individuals' misconceptions, beliefs, practices, values, habits, body perceptions, socio-economic and cultural backgrounds, knowledge gaps, personal preferences, existing health conditions, physiological stages (such as menstruation, pregnancy, postpartum period, etc.),

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familial factors, and the physical and social characteristics of the environment can influence an individual's reproductive health.^{7,8} These factors play a significant role in determining an individual's genital hygiene habits and overall health status. Furthermore, individuals' reluctance to discuss topics related to women's genital health and hygiene can lead to problems being left unaddressed, potentially resulting in serious reproductive health issues.^{2,4,6,7} According to the literature, over the past decade, between 16.5% and 40.3% of university students have been reported to make mistakes in perineal hygiene.^{3-5,8,9,10} Incorrect perineal hygiene increases the risk of urinary tract infections in women.¹⁰ Therefore, individuals should be knowledgeable about and practice proper genital and menstrual hygiene to develop desired health-preserving behaviors and correct misunderstandings.¹¹ The most significant factor in the development of genital infections is incorrect genital hygiene practices due to a lack of knowledge.⁷ Bridging this knowledge gap and accessing accurate information ensures that women have sufficient health literacy levels.⁸

Health literacy refers to the ability of individuals, families, and communities to access, understand, evaluate, and use information and services needed to make effective decisions about health.¹⁴ Having a high level of health literacy at the societal level improves health and increases society's life expectancy.¹⁵ Health literacy is essential in promoting and developing health and preventing diseases and has been proven to be important in various scientific studies.¹⁶⁻¹⁸ Promoting health and preventing diseases requires that individuals understand and use information related to health. A healthy lifestyle promoting health requires control over all behaviors affecting health.¹⁹ Health literacy contributes to developing an individual's ability to participate in activities promoting health. Health literacy enhances the ability of a woman to engage in health-promoting activities.²⁰ The health literacy level of university-aged female students must be high, enabling them to make more informed decisions about their health, adopt healthier behaviors, undergo regular health check-ups, prioritize general and personal hygiene, and keep their vaccinations up-to-date.²¹ Therefore, having a high level of health literacy is crucial for their health and increasing public health awareness. Therefore, it is essential to develop and support health literacy. A study conducted to determine the health literacy level of individuals aged 18 and over living in Turkey with the "Turkey Health Literacy Level and Related Factors Study" reported that 30.9% had inadequate health literacy, and 38% had problematic-limited health literacy.²² Thus, approximately 7 out of 10 people in Turkey were found to have inadequate or limited health literacy levels.²² A study conducted in the United States found that individuals with a high level of health literacy had higher rates of using preventive

health services.²³ Increasing health literacy levels would be beneficial for individuals to use resources correctly and significantly impact both individual and public health in terms of improved health. The effects of increasing the health literacy level of individuals on societal and economic levels are high.²⁴

Studies have shown that women with high health literacy levels are more likely to follow written and visual content related to health and hygiene behaviors, and they have a better understanding of proper hygiene practices.²⁵ Studies have indicated that individuals with a higher level of education tend to exhibit better genital hygiene practices.⁸ When reviewing the literature, it becomes evident that studies emphasize the critical importance of genital hygiene for women's health.²⁻⁶ However, a limited number of studies in the literature have specifically examined the significant association between genital hygiene practices and health literacy in women.^{6-8,24,37} Most of these studies have focused on married women, pregnant women, or those studying in the health field.^{6-8,24,37} Research exploring the relationship between genital hygiene behaviors in female university students and associated factors, as well as their levels of health literacy, remains scarce. Acquiring proper genital hygiene habits during university years can contribute to the prevention of common sexual health issues often encountered during this period. Female students should possess adequate health literacy levels to access and utilize accurate information to enhance their genital hygiene behaviors. Therefore, understanding the impact of health literacy levels on genital hygiene behaviors among female university students is crucial for filling a significant gap in this field.

Aim

This study aims to examine the relationship between the health literacy levels and genital hygiene behaviors of female university students.

Research questions

- What are the health literacy levels of female university students?
- What are the genital hygiene behavior levels of female university students?
- Is there a relationship between the health literacy of female university students and their genital hygiene behaviors?

Material and methods

Study design

This study is a descriptive-correlational research.

Sample

This descriptive study was conducted on female university students at a state university in the Western Black Sea region. A total of 8142 female students studying at

a state university in the Western Black Sea region in the 2022–2023 academic year constitute the research universe. The sample size of the research was calculated as 311 female students using the OpenEpi program with a confidence level of 95%, taking into account that the inadequate health literacy level of Turkish society was 30.9% in the Turkey Health Literacy Level and Related Factors study conducted by the Ministry of Health, Health Development General Directorate.^{22,27} Email addresses, social media accounts, student club groups, and online class groups of students at the university were used to reach out to the participants. A total of 348 female university students who agreed to participate in the study were included in the research.

Inclusion criteria

- being a female student enrolled in undergraduate or associate degree programs at the university where the research was conducted,
- being 18 years of age or older,
- having no verbal communication barrier,
- not having any intellectual disabilities.

Data collection

The research data were collected from 348 female students who met the inclusion criteria and volunteered to participate in the research at a state university in the Western Black Sea region during the 2022–2023 academic year. The data was collected using an online survey form (Google Form) through convenience sampling. The data was collected by sending the link to the study via email to female students' school email addresses, sending the link through instant messaging applications to class representatives of faculties and departments, and sharing the link on the social media pages of university student clubs. Instructions were prepared on topics such as using the data within the scope of the research, keeping their identity information confidential, and obtaining informed consent.

Data collection instruments

Questionnaire form

The questionnaire includes questions about the demographic characteristics of the participants and questions created by the researchers based on the literature.^{19,25,26,28}

Health Literacy Scale

The Turkish validity and reliability of the Health Literacy Scale were established by Aras and Bayık Temel.²⁹ The Health Literacy Scale consists of 25 items and four subheadings: access to information (5 items), understanding of information (7 items), valuing/evaluating information (8 items), and application/usage (5 items). The minimum score for the entire scale is 25, and the maximum is 125. Participants answered the scale items

using a Likert scale as follows: “1: I am unable to do it/ I have no ability at all/ impossible, 2: I have much difficulty, 3: I have some difficulty, 4: I have a little difficulty, 5: I have no difficulty at all.” All items on the scale are positively structured, and there is no reverse item coding. The reliability coefficient of the scale, Cronbach's alpha, was reported as 0.92, and the sub-dimensions alpha values ranged from 0.62 to 0.79.²⁹

Genital Hygiene Behaviors Scale

The scale developed by Karahan was used to assess genital hygiene behaviors in women and consists of 3 sub-dimensions: general hygiene, menstrual hygiene, and awareness of abnormal findings, with a total of 23 items. The Cronbach's alpha value for all items on the scale was found to be 0.80, while the Cronbach's alpha values for the General Hygiene Subscale, Menstrual Hygiene Subscale, and Awareness of Abnormal Finding Subscale were 0.70, 0.74, and 0.81, respectively.³⁰

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee (2023-SBB-0020) and the institution where the study would be conducted (E-12240456-605.01-2300026644). All participants provided both written and verbal consent before their involvement.

Statistical analyses

The data were analyzed using the SPSS 26.0 program (IBM, Armonk, NY, USA). Descriptive statistics (percentage, mean, standard deviation, minimum, and maximum) were used for the questionnaire and the TSOY-32. Data were tested for normality analysis with Kolmogorov–Smirnov tests. Since the data did not show normal distribution due to the analysis, non-parametric tests (Kruskal-Wallis, Mann-Whitney U) and Spearman correlation test were used. The significance level was calculated as $p < 0.05$.³¹

Results

Among the female students who participated in this study, 64.9% are enrolled in undergraduate programs, 29.6% are in health sciences faculties, and 36.5% are in their second year of study (Table 1). Female students have the highest access to health-related information through the Internet (83.9%) and the lowest access through their friends (17.8%) (Table 1).

During their menstrual period, 89.7% of the women use sanitary pads (Table 1). About 50.9% of the participants reported receiving genital hygiene education, with 27% receiving it from their families and 15.5% from healthcare professionals (Table 1). When asked about their bathing habits, 81% of the participants reported taking showers while standing (Table 1).

Table 1. Socio-demographic characteristics of the students (n=348)*

Variables		n	%
Departments of university	Faculty of Health Science	103	29.6
	Faculty of Arts and Sciences	34	9.8
	Faculty of Educational Sciences	26	7.5
	Health Vocational High-School	60	17.2
	Faculty of Economics and Administrative Sciences	17	4.9
	Faculty of Sports Sciences	14	4
	Faculty of Islamic Studies	17	4.9
	Faculty of Engineering	36	10.3
	Vocational High School	41	11.8
Degree	1	79	22.7
	2	127	36.5
	3	58	16.7
	4	84	24.1
Marital status	Single	320	92
	Married	28	8
Level of income	Less	72	20.7
	Middle	226	64.9
	High	50	14.4
Employment status	Employee	55	15.8
	Not employee	293	84.2
Smoking	Yes	95	27.3
	No	253	72.7
Alcohol	Yes	46	13.2
	No	302	86.8
Chronic illness	Yes	38	10.9
	No	310	89.1
Regular use of medication	Yes	44	12.6
	No	304	87.4
Ways to access information [‡]	Internet	292	83.9
	Health Professionals	242	69.5
	Friend	62	17.8
	Book-magazine-brochure	150	43.1
	Family-relatives	152	43.7
	TV-Radio	89	25.6
Daily pad usage	Yes	171	49.1
	No	177	50.9
Material used during menstruation	Sanitary Pad	312	89.7
	Clean Cotton	11	3.2
	Pads	10	2.9
	Menstrual Cup	15	4.3
Status of receiving education on genital hygiene	Yes	177	50.9
	No	171	49.1
Who gave the genital hygiene training?	Friends	17	4.9
	Health Professionals	54	15.5
	Internet	28	8
	Family members	94	27
The ways of taking a bath	Sitting down	56	16.1
	Shower	282	81
	Tub	10	2.9

* [‡] – participants gave more than one answer to this question

In the study, when the sub-dimensions of the Genital Hygiene Behaviors Scale were compared with the total scale scores according to the faculty or department

where students were enrolled, a significant difference was found between the “Menstrual Hygiene Habits” sub-dimension and the total scale score among students from different faculties or departments (Table 2). (KW: 43.606; p<0.001; KW: 21.353, p<0.01).

Table 2. Comparison of the Genital Hygiene Behavior Scale between the departments of the students*

Genital Hygiene Behavior Scale Sub-Dimensions	KW	p
Genital Hygiene Habits Sub-Dimension	9.373	0.312
Menstrual Hygiene Habits Sub-Dimension	43.606	<0.001
Abnormal Finding Awareness Subdimension	12.164	0.144
Genital Hygiene Behaviors Scale Total Score	21.353	0.006

* KW – Kruskal-Wallis test

The sub-dimensions of the Genital Hygiene Behaviors Scale were found as follows: the sub-dimension of genital hygiene habits was 48.05±5.52, the sub-dimension of menstrual hygiene habits was 31.93±4.99, the sub-dimension of abnormal finding awareness was 11.29±2.60, and the total score of the Genital Hygiene Behaviors Scale was 86.73±10.13 (Table 3). The sub-dimensions of the Health Literacy Scale were as follows: SOY information access sub-dimension was 21.77±3.66, SOY information comprehension sub-dimension was 29.68±5.28, SOY value assessment sub-dimension was 33.60±6.44, SOY application usage sub-dimension was 20.96±4.06, and the total score of the Health Literacy Scale was 106.02±17.93 (Table 3).

Table 3. Findings regarding the total and sub-dimension mean scores of female students’ Genital Hygiene Behaviors*

Scale and Sub-Dimensions	Min-Max	X±SD
Genital Hygiene Behaviors Scale	23–115	86.73±10.13
Genital Hygiene Habits Sub-Dimension	33–60	48.05±5.52
Menstrual Hygiene Habits Sub-Dimension	17–40	31.93±4.99
Abnormal Finding Awareness Subdimension	3–15	11.29±2.6
Health Literacy Scale	25–125	106.02±17.93
Access to Information	5–25	21.77±3.66
Understanding Information	7–35	29.68±5.28
Appraisal Evaluation	8–40	33.60±6.44
Using Application	5–25	20.96±4.06

* SD – standard deviation, Min – minimum, Max – maximum

Spearman correlations were used to of between Genital Hygiene Behaviors Scale and Health Literacy Scale There was a significant correlation between the two scales (Table 4). A moderate positive significant relationship exists between the Genital Hygiene Behaviors Scale total scale score and all sub-dimensions of the Health Literacy Scale and the total scale score (p <0.05) (Table 4). There is a moderate positive significant relationship between the Genital Hygiene Habits sub-dimension of the Genital Hygiene Behaviors scale and the

Table 4. Comparison of Genital Hygiene Behaviors Scale and Health Literacy Scale^a

	Min.	SD.	1	2	3	4	5	6	7	8	9
1 Genital Hygiene Habits Sub-Dimension	33	5.52	1								
2 Menstrual Hygiene Habits Sub-Dimension	12	4.68	0.395**	1							
3 Abnormal Finding Awareness Subdimension	3	2.6	0.422**	0.457**	1						
4 Genital Hygiene Behaviors Scale Total Score	62	10.12	0.82**	0.794**	0.688**	1					
5 Access to Information	5	3.66	0.389**	0.323**	0.376**	0.460**	1				
6 Understanding Information	7	5.28	0.407**	0.376**	0.365**	0.489**	0.764**	1			
7 Appraisal Evaluation	8	6.44	0.44**	0.359**	0.349**	0.491**	0.784**	0.839**	1		
8 Using Application	5	4.06	0.421**	0.341**	0.390**	0.491**	0.725**	0.742**	0.843**	1	
9 Health Literacy Scale Total Score	25	17.93	0.45**	0.368**	0.393**	0.517**	0.852**	0.915**	0.956**	0.894**	1

^aMin – minimum, SD – standard deviation, ** – correlation is significant at the 0.01 level (2-tailed)

“Understanding Information, Appraisal Evaluation, Using Application” sub-dimensions of the Health Literacy scale and the total scale score of the Health Literacy Scale ($p < 0.05$) (Table 4).

Discussion

It is crucial for a significant portion of the population, especially young women, to adopt proper genital hygiene practices in order to prevent urogenital infections. The community must have adequate knowledge to embrace these hygiene behaviors, and therefore, genital hygiene practices and health literacy should be examined in conjunction.

When evaluating the sources of health-related information for the participants in this study, it was determined that they primarily accessed such information from the Internet (83.9%), television and radio (25.6%), healthcare professionals (69.5%), books, magazines, and brochures (43.1%), and family members and relatives (43.7%). Literature reports that individuals primarily obtain health-related information from online websites, healthcare professionals, and family/friends, aligning with findings from various studies.^{26,38,39} The rapid increase in internet usage and the ease of access to online health-related information have facilitated the availability of a wealth of health information online. However, individuals must possess adequate health literacy levels to interpret the reliability and accuracy of online health information.

The study revealed that most female students participating in the research preferred to use sanitary pads during their menstrual periods. Sanitary pads are considered hygienic and beneficial for menstrual periods due to their single-use nature and absorbent properties. Similarly, the literature reports that participants mostly use sanitary pads during their menstrual periods.^{12,32} Considering the ease and accessibility of sanitary pads in Turkey, the majority is believed to prefer them.

Eighty-one percent of the female students participating in the study reported taking showers while standing. Similarly, in the literature, it is reported that most women take showers while standing.^{11,18} Because

most students stay in state or private dormitories, they can only take showers while standing. Therefore, it is thought that students mostly take showers while standing. Showering while standing may be a preventive factor for vaginal or urethral infection in women compared to showering while sitting.

The total scale score average of female students on the Genital Hygiene Behaviors Scale was determined to be 86.73 ± 10.13 . This result indicates that the genital hygiene behaviors of the female students participating in the study are at a good level. Similarly, in studies conducted in the literature, the total scale score averages for women's genital hygiene behaviors vary between 85 and 95.^{6,25,33,40} When looking at the sub-dimensions of the Genital Hygiene Behaviors Scale, an average score of 48.05 ± 5.52 was obtained for the “Genital hygiene habits” sub-dimension, 31.93 ± 4.99 for the “Menstrual hygiene habits” sub-dimension, and 11.29 ± 2.6 for the “Awareness of abnormal findings” sub-dimension. The average scores obtained from the sub-dimensions of the scale also indicate a good level. When compared with previous studies, it can be observed that the participants in this study have a sufficient level of genital hygiene behavior scores. It is thought that the high total scale score and sub-dimension scores may be related to the region where the sample group resides, their level of education, income status, and awareness of health behaviors. The research indicates that students in health-related fields demonstrate higher scores in overall hygiene behavior, awareness of abnormal findings, and genital hygiene than students in other departments.⁷ Additionally, students in health-related fields notably differed in average scores for menstrual hygiene habits compared to students in other faculties. It is believed that the professional courses taken by health students from their first year onwards contribute to their knowledge and awareness of genital hygiene.

Educating women on proper genital hygiene practices and dispelling misconceptions are crucial in preventing urogenital infections. An individual's access to accurate health information and translating it into behavior is closely linked to their level of health literacy.^{34,35}

The number of studies on health literacy is increasing, with recommendations to enhance it, as it plays a vital role in improving individuals' quality of life, enabling access to health information during illness, understanding one's health conditions, and adopting appropriate behaviors based on this information.^{34,35}

Health literacy is crucial for maintaining and improving health. In this study, the sub-dimensions of the Health Literacy Scale were determined as follows: "Access to health information" sub-dimension scored 21.77 ± 3.67 , "Understanding health information" sub-dimension scored 29.69 ± 5.28 , «Appraisal of health information» sub-dimension scored 33.6 ± 6.44 , «Application of health information» sub-dimension scored 20.97 ± 4.07 , and the total score of the Health Literacy Scale was 106.03 ± 17.93 .

The health literacy levels of female students in this study were found to be satisfactory, with an average score of around 125 on a scale of 25 to 125. This is in contrast to a previous study involving university students, where the average health literacy scores were lower.¹⁵ This study's higher total health literacy score is likely due to their knowledge and experience in health, access to health services, and attitudes toward health.^{15,41}

Women with higher health literacy levels demonstrate better genital hygiene practices. A study revealed a positive correlation between health literacy and genital hygiene behaviors, with participants scoring higher on hygiene scales when possessing higher literacy levels.²⁴ Moreover, a moderate association was found between gynecological cancer awareness and health literacy.⁴¹ As health literacy improves, women prioritize genital hygiene, leading to enhanced practices. This aligns with research suggesting that higher health literacy contributes significantly to improved genital hygiene behaviors among women.

Study limitations

The study's limitations include its exclusive reliance on data from female students at a single university, with 30% enrolled in health-related fields, and the use of convenience sampling, all of which hinder the generalizability of its findings.

Conclusion

The research has shown a moderately significant and positive relationship between health literacy and genital hygiene behaviors among female university students. In this context, recommendations are proposed for developing a healthy societal consciousness and raising healthy generations. Firstly, various educational activities aimed at enhancing health literacy should be organized. These activities may include courses, lectures, seminars, peer education, and project work. Furthermore, the effective utilization of social media is suggest-

ed for awareness and enlightenment campaigns. Social media platforms, widely used by a significant portion of the younger generation, present a potential avenue for increasing health awareness.

Professional nurses can address deficiencies by designing specialized education programs encompassing health literacy and proper genital hygiene behaviors. These programs, accessible to girls from the onset of menarche, can facilitate acquiring accurate information and skills early.

In conclusion, the findings of this study indicate a positive correlation between increasing levels of health literacy among women and the enhancement of genital hygiene behaviors. Therefore, more comprehensive efforts in health education and awareness campaigns employing innovative methodologies are warranted.

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Conflicts of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Vocational Technical Education Strengthening Project (MEGEP). Health Services Urogenital System Diseases. Web site: https://megep.meb.gov.tr/mte_program_modul/moduller/Üro-Genital%20Sistem%20Hastahklari.pdf. Accessed December 23, 2023.

2. Timur S. Genital hygiene behaviors of female university students living in a dormitory. *E-Journal of New World Sciences Academy*. 2010;5:39-48.
3. Ünsal A. Genital hygiene behaviors of female university students. *Fırat Sağlık Hizmetleri Dergisi*. 2010;5:79-93.
4. Topuz Ş, Duman NB, Güneş A. Genital hygiene practices of first-year female students in the faculty of health sciences. *Turkish Journal of Clinics and Laboratory*. 2015;6:85-90. doi: 10.18663/tjcl.80899
5. Türkmen H, Karagüzel EN. Factors influencing young people's genital hygiene attitudes. *Sürekli Tıp Eğitimi Dergisi*. 2021;30(3):190-199. doi: 10.17942/sted.767685
6. Bulut A, Yiğitbaş Ç, Çelik G. Genital hygiene behaviors from the perspective of nursing students. *Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi*. 2019;52(3):227-232. doi: 10.31067/0.2019.199
7. Parlas M, Eryılmaz G. The effects of the PRECEDE-PROCEED model-based educational program on genital hygiene behaviors: A randomized controlled trial. *Health Care Women Int*. 2023. doi: 10.1080/07399332.2022.2164582
8. Uzun A, Ozturk GZ, Aksu SB. Evaluation of the genital hygiene behavior and related factors of women aged 15-49. *Eurasian Journal of Family Medicine*. 2022;11(1):35-42. doi: 10.33880/ejfm.2022110105
9. Koyun A, Özpulat F, Özvarış ŞB. Developing and evaluating an education program: "genital hygiene" education program for high school female students. *Gümüşhane University Journal of Health Sciences*. 2013;2(4)443-459.
10. Ardahan M, Bay L. Knowledge levels of nursing school students in the first and fourth grades about vaginal discharge and individual hygiene. *Ege Tıp Dergisi*. 2009;48:33-43.
11. Ergün S, Gök G, Karlıdağ E, Er Güneri S. Determination of women's genital hygiene behaviors. *TJFMPC*. 2020;14(4):540-547. doi: 10.21763/tjfm.706830
12. Demirağ H, Hintistan S, Cin A, Tuncay B. Investigation of genital hygiene behaviors of health services vocational school students. *Bozok Tıp Dergisi*. 2019;9(1):42-50. doi: 0.16919/bozoktip.446246
13. Arıkan D, Tortumluoğlu G, Özyazıcıoğlu N. The impact of planned education given to the students to the menstruation hygiene behaviors. *JHS*. 2004;1:1-15.
14. WHO. World Health Organization Web. <https://apps.who.int/iris/handle/10665/205244>. Accessed December 23, 2023.
15. Sørensen K, Van den Broucke S, Fullam J, et al. Health literacy and public health: a systematic review and integration of definitions and models. *BMC Public Health*. 2012; 12(1)1-13. doi: 10.1186/1471-2458-12-80
16. Beauchamp A, Buchbinder R, Dodson S, et al. Distribution of health literacy strengths and weaknesses across socio-demographic groups: a cross-sectional survey using the Health Literacy Questionnaire (HLQ). *BMC Public Health*. 2015;15:678. doi: 10.1186/s12889-015-2056-z
17. Biçer EB, Malatyalı İ. Determination of health literacy level: the example of Sivas Cumhuriyet University. *Ankara Sağlık Hizmetleri Dergisi*. 2018;17(2):1-15.
18. Sevil S, Özdemir K, Aleattin U, Dilek A, Tijen N. An Evaluation of the relationship between genital hygiene practices, Genital Infection. *Gynecology and Obstetrics*. 2013; 3(6):3-5. doi: 10.4172/2161-0932.1000187
19. Uysal N, Yıldız G. Examination of health literacy levels of nursing students. *BAUN Sağ Bil Derg*. 2021;10(1):43-48.
20. Ghorbani-Dehbalaei M, Loripoor M, Nasirzadeh M. The role of health beliefs and health literacy in women's health-promoting behaviors based on the health belief model: a descriptive study. *BMC Women's Health*. 2021; 21:421. doi: 10.1186/s12905-021-01564-2
21. Luo Y, Yang S, Chen A, Chiang C. Associations of e-health literacy with health services utilization among college students: Cross-sectional study. *J Med Internet Res*. 2018;20(10):e283. doi: 10.2196/jmir.8897
22. Ministry of Health General Directorate of Health Promotion. <https://dosyamerkez.saglik.gov.tr/Eklenti/39699/0/soya-rapor-1pdf.pdf>. Accessed December 25, 2023.
23. Scott TL, Gazmararian JA, Williams MV, Baker DW. Health literacy and preventive health care use among Medicare enrollees in a managed care organization. *Medical Care*. 2002;40: 395-404. doi: 10.1097/00005650-200205000-00005
24. Sezgin D. Understanding health literacy. *Galatasaray University Journal of Communication*. 2014:73-92.
25. Özkan E, Tosun H. Examination of genital hygiene behaviors and related factors in women applying to the gynecology clinic. *Sürekli Tıp Eğitimi Dergisi*. 2022; 31(6):418-427.
26. Filiz E, Bodur S. Evaluation of the relationship of health literacy and health perception in pregnant and non-pregnant women. *Journal of Selcuk Health*. 2022;3(1):17-33.
27. OpenEpi. <https://www.openepi.com/SampleSize/SSPropor.htm>. Accessed April 10, 2023.
28. Çelik S, İstek Z, Kızkın A, Yiğit MC, Kaçan H. Examination of health literacy levels of university students: the example of Bartın University. *IGUSABDER*. 2021;15:593-605. doi: 10.38079/igusabder.976692
29. Bayık-Temel A, Aras Z. Evaluation of the validity and reliability of the Health Literacy Scale Turkish form. *Florence Nightingale Journal of Nursing*. 2017;25(2):85-94. doi: 10.17672/fnhd.94626
30. Karahan N. Development of the Genital Hygiene Behaviors Scale: A validity and reliability study. *İstanbul Tıp Dergisi*. 2017;18:157-162. doi: 10.5152/imj.2017.82957
31. McShane BB, Gal D, Gelman A, Robert C, Tackett JL. Abandon statistical significance. *The American Statistician*. 2019;73(1):235-245. doi: 10.1080/00031305.2018.1527253
32. Bilgiç D, Yüksel P, Gülhan H, Şirin F, Uygun H. Genital hygiene behaviors and health outcomes of female university students living in dormitories. *AUHSJ*. 2019(3):478-485. doi: 10.31067/0.2018.86

33. Yağız Altıntaş R, Bakır S, Gül İ, Süer N, Kavlak O. The Effect of Menstrual Attitude on Genital Hygiene Behaviors in Nursing Students. *TJFMPC*. 2021;15(3):568-575. doi: 10.21763/tjfmpe.931262
34. Yılmaz M, Tiryaki Z. What Is Health Literacy? How Is It Measured? *JNEF*. 2016;9(4):142-147.
35. Pete PMN, Biguioh RM, Izacar AGB, Adogaye SBB, Nguemo C. Genital hygiene behaviors and practices: A cross-sectional descriptive study among antenatal care attendees. *JPHIA*. 2019;10:1. doi: 10.4081/jphia.2019.746
36. Yalçın B. The effect of health literacy level on health perception: a study on university students. *Göbeklitepe Sağlık Bilimleri Dergisi*. 2020;3:23-33.
37. Çankaya S, Yılmaz S. Factors associated with genital hygiene behaviours in pregnant and non-pregnant women in Turkey. *International Journal of Human Sciences*. 2015; 12(1):920. doi: 10.14687/ijhs.v12i1.3126
38. Kelley MS, Su D, Britigan DH. Disparities in health information access: results of a county-wide survey and implications for health communication. *Health Communication*. 2016;3(5):575-82.
39. Póinhos R, Oliveira BM, Van Der Lans IA, et al. Providing personalised nutrition: consumers' trust and preferences regarding sources of information, service providers and regulators, and communication channels. *Public Health Genomics*. 2017;20(4):218-228.
40. Ozkan E, Tosun, H. Investigation of genital hygiene behaviors and related factors in women applied to gynecology polyclinic. *Journal of Continuing Medical Education*. 2022;31(6):418-427. doi: 10.17942/sted.1021695
41. Uslu-Sahan F, Mert-Karadas M, Yıldız T, et al. Effect of health literacy on the awareness of gynecological cancer among women in Turkey. *Indian Journal of Gynecologic Oncology*. 2023;21:15. doi: 10.1007/s40944-022-00690-5



Surgery experiences of patients with hematologic cancer, individual applications for the symptoms due to chemotherapy and determination of the anxiety levels

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ABSTRACT

Introduction and aim. The aim of the study was to determine the surgical experiences of patients with hematologic cancer, their anxiety levels, and their individual practices regarding the symptoms they experience.

Material and methods. The study was conducted by face-to-face interviews with 74 patients followed up in a hematology clinic. The “Patient information form” and “Beck Anxiety Scale” were administered to the patients before chemotherapy, and the “Questionnaire Form Including Patients Practices for Symptoms” was administered after chemotherapy.

Results. The mean age of the participants was 63.76 ± 15.1 years, 47.3% were female, 47.3% were diagnosed with lymphoma, 67.6% had undergone surgery, and 32% received education. The mean Beck Anxiety Scale score was 11.36 ± 7.99 and was considered mild anxiety. A significant difference was observed between education and employment status and postoperative education status, gender and hair loss, employment status and anorexia, scale score and employment status, and the effect of COVID-19 on chemotherapy ($p < 0.05$).

Conclusion. It was determined that patients with hematological cancer had a low levels of knowledge about surgical procedures and they did not perform any negative practice due to chemotherapy. Their anxiety levels were mild and the pandemic process was effective on anxiety.

Keywords. anxiety, chemotherapy, hematological cancer, surgical experience

Introduction

Cancer is “a disease in which cells multiply uncontrollably and rapidly, disrupting the normal functioning of the body.”¹ Despite many inspiring advances in medicine, cancers affect human health biologically, physically and psychologically, with high mortality rates. According to the 2018 data from World Health Organization, cancer is the second deadliest disease in the world and is the cause of death for one in six people.² Although mortality rates are low for some types of cancer, overall high mortality rates can be a source of fear and despair for patients and their relatives. Two studies of people with

hematologic cancers found that young people and older adults were more prone to depression.³ Hematological cancers are cancers that start in the tissues that make up the blood or the cells that make up the immune system. Hematological cancers include leukemia, lymphoma, multiple myeloma, and their subtypes.⁴ In 2018, hematological cancers ranked second among cancer-related deaths in Turkey with a ratio of 8.2%.⁵

Anxiety is “fear and uneasiness caused by undefinable or unknown things.”⁶ According to definition, cancer is a disease that affects the diagnosed individual and his/her family throughout the entire treatment

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process as an unknown condition.⁷ Like other patients diagnosed, the majority of patients with hematological cancer experience anxiety. Therefore, anxiety complicates the adherence to treatment and prolongs hospitalization.⁸ Surgery, chemotherapy and radiotherapy are used in cancer treatment. Immunotherapy, hormone therapy and biological treatment methods are less preferred.¹ Chemotherapy, which can be combined with other treatment methods, is a method that uses drugs prevent cancer cells from multiplying rapidly. While chemotherapy drugs prevent cancer cells from growing, they can also damage human cells. The most common side effects of chemotherapy include nausea, loss of appetite, weight loss, anemia, wounds, pain, fatigue, sleeping disorders and hair loss.⁹ Patients who want to reduce side effects and complete the treatment with minimal damage resort to individual methods. When the alternative method preferences of patients undergoing chemotherapy were investigated, it was found that 19.7% used phytotherapy and 19.3% used vitamins.¹⁰ In a similar study, it was observed that half of patients diagnosed with Myeloma preferred complementary and alternative medicine methods in addition to medical treatment.¹¹

Although access to information has become easier with the advancement of technology, the resulting information pollution has made it difficult to access accurate information. Patients diagnosed with cancer can resort to individual and complementary practices in addition to medical treatments.

Aim

Based on reasons such as the scarcity of studies and the lack of sufficient evidence-based data on this subject, it was aimed to determine the surgical experiences of patients with hematologic cancer, their anxiety levels, and their practices for the symptoms that occur.

Material and methods

All patients gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Sakarya University (Document Date-Number: 20/10/2020-E.9543) and written permission was obtained from the institution where the study was conducted.

This descriptive study was conducted to determine the surgical experiences of patients followed in the hematology clinic of a training and research hospital, their anxiety levels before chemotherapy, and their practices for the symptoms experienced by patients after chemotherapy. Data were collected using face-to-face interview technique between November 16, 2020 and May 17, 2021 after ethics committee approval and

institutional permissions were obtained. The scope of the study consisted of 77 patients who received inpatient treatment in a hematology clinic between the specified dates. It was aimed to reach all patients who applied to the hematology clinic and met the inclusion criteria without sampling, and the study was completed with 74 people. Of the three patients receiving chemotherapy, one was excluded because he had a major psychiatric diagnosis, the other because he had communication problems, and the third because he refused to participate in the study.

In this two-stage study, “Patient Information Form” and “Beck Anxiety Scale” were administered to the patients before chemotherapy, and “Questionnaire Form Including Patients’ Applications for Their Symptoms”, which was created by the researchers using literature information, was administered after chemotherapy.^{7,11-13} The questions included questions about the surgical history of the patients. In the Questionnaire for Patients’ Applications for Their Symptoms, patients’ hematologic diseases, type of chemotherapy they received, duration and information about chemotherapy were questioned.

The Beck Anxiety Scale (BAS) developed by Beck et al. in 1998, is a Likert-type scale consisting of 21 items scored between 0-3, used for determining the severity of anxiety experienced by individuals. Scale values are scored between 0-63 and higher scores indicate more severe anxiety. Scores between 0-7 are interpreted as “no anxiety symptoms”, scores between 8-15 as “mild anxiety”, scores between 16-25 as “moderate anxiety”, and scores between 26-63 as “severe anxiety”. Ulusoy et al. conducted the Turkish validity and reliability study of the scale in 1998 and calculated Cronbach’s alpha value as 0.93. Permission to use the scale in this study was obtained from Hüsnü Erkmen via e-mail.¹⁴

Data were evaluated using SPSS 25.0 (Statistical Package for the Social Sciences). Study data were evaluated by frequency distribution (number, percentage) for categorical variables and descriptive statistics (mean, standard deviation) for numerical variables. Independent sample t-test, One Way ANOVA, Levene Test, Bonferroni or Tamhane’s T2, Chi-squared Test, Pearson Correlation Analysis were also used. A p-value of $p < 0.05$ was accepted for significance.

Results

The mean age of chemotherapy patients was 63.76 ± 15.1 years, 47.3% were female, 92.2% were married, 94.6% had children, 78.4% were primary school graduates and 39.2% were housewives. 81.1% lived in the district for the longest time, 97.3% had an income equal to their expenses, 25.7% had hypertension, 77% did not smoke, and 95.9% did not drink alcohol (Table 1).

Table 1. Examination of descriptive features and operative conditions

		n	%
Age	(mean±SD)	63.76±15.1	
Gender	Male	39	52.7
	Female	35	47.3
Marital status	Married	69	93.2
	Single	5	6.8
Child	Yes	70	94.6
	No	4	5.4
Education	Primary school	58	78.4
	High school	10	13.5
	Associate-bachelor	6	8.1
Occupation	Housewife	29	39.2
	Employed	23	31.1
	Retired	20	27
	Other	2	2.7
Place of Longest Residence	District	60	81.1
	Province	12	16.2
	Village-town	2	2.7
Income Situation	Income equals expenses	72	97.3
	Income less than expenses	2	2.7
Disease	Absent	33	44.6
	Hypertension (HT)	19	25.7
	Diabetes (DM)	11	14.9
	DM+HT	10	13.5
	Other	1	1.4
Current Medical Diagnosis	Lymphoma	35	47.3
	Leukemia	20	27
	MM	17	23
	MDS	2	2.7
Had Operation Before	"Yes I did"	50	67.6
	"No. I did not"	24	32.4
Operations had	Urology-gynecology	16	32
	Other	13	26
	Gastrointestinal system surgery	8	16
	Brain-nerve surgery	7	14
Being Informed During Operation	KVC	6	12
	"No. not informed"	25	50
	"Yes. by physician and nurse"	19	38
Pre-operative Education Status	"Yes. by a physician"	6	12
	"No. I had not"	34	68
Surgery Experience Satisfaction Level (VAS; 0–10) (mean±SD)	"Yes I had"	16	32
	Other	33	67.3
The most worrying situation for the patient during the operation	Fear of not being able to wake up	11	22.4
	Not being informed	4	8.2
	Fear of telling secrets	1	2

The proportion of participants with a medical diagnosis of lymphoma was 47.3%. When the previous hospitalization and surgical experiences of chemotherapy patients were questioned, 91.9% had been hospitalized in the past, 67.6% had undergone surgery, and the rate of urology/gynecology surgeries (32%) was high among these surgeries. Again, 38% of these patients stated that they were

informed during the previous surgery and 32% stated that they received trainings such as exercise etc. after surgery. The mean score of satisfaction with the surgical experience was 6.12±2.05, which is moderate. 22.4% of the participants stated that the thing that worried them the most during surgery was the fear of not waking up (Table 1).

Table 2. Postoperative complaints and ways of coping (n=74)

		n	%
Post-operative complaints	Pain	35	70
	Physical problem	22	44
	Fatigue	7	14
	Loss of appetite	4	8
	Fever	1	2
	No complaints	4	8
	Weight loss	3	6
	Nausea, vomiting	3	6
	Constipation	2	4
	Sleep problems	2	4
	Diarrhea	1	2
	Respiratory problems	1	2
Fatigue	"I took time to rest during the day."	6	85.7
	"I restricted my daily activities."	1	12.5
Nausea-vomiting	"I used drugs."	2	100
	Other	14	63.6
Physical problems	"I did not do anything."	5	22.7
	"I paid attention to the choice of clothes."	3	13.6
Weight loss	Other	2	66.7
	"I ate my favorite foods."	1	33.3
Pain	"I used painkillers."	35	100
Fever	"I used antipyretics."	1	100
Constipation	Other	2	100
Diarrhea	Other	1	100
Respiratory problems	"I received oxygen."	1	100
Sleep problems	"I rested during the day."	2	100

After surgery, 70% of the patients reported feeling pain and 44% reported physical problems. 85.7% of the participants reported that they took time to rest during the day for fatigue-weakness, 22.7% of those with physical problems did nothing, 33.3% of those with weight loss ate their favorite foods, all patients with pain and high fever used painkillers and antipyretics, and in cases of constipation and diarrhea, they used non-drug methods (apricot juice, olive oil, etc.) (Table 2).

A correlation was found between education and employment status and postoperative training on breathing-cough, rotation-body exercises. Accordingly, the rate of receiving education about surgery was significantly higher in those with higher education level and those who were employed ($p<0.05$, Table 3).

85.1% of the participants stated that intravenous treatment (IV; intravenous) was the method of administration for the type of chemotherapy, 52.7% stated that

they were informed by the doctor and nurse, 43.2% stated that the question “What will be the result, will I recover?” was a worrying situation, 51.4% stated that COVID-19 did not affect chemotherapy. Complaints after chemotherapy; 51.4% felt tired and 97.3% of those who felt tired took time to rest during the day, 71.4% of those who had mouth sores after chemotherapy gargled, 64% of those who experienced nausea and vomiting after chemotherapy, 7% used medication, 60% of those who experienced hair loss after chemotherapy wore scarves and bonnets, 33.3% of those who lost weight after chemotherapy ate less and more frequently, 3% of those who experienced pain after chemotherapy used painkillers, It was determined that 60% of those with fever used antipyretics and monitored fever, 43.5% of those with constipation after chemotherapy used medication, 25% of those with diarrhea ate a fiber-free diet and drank two liters of fluid a day, 90% of those with anorexia ate little and often, 60% of those with respiratory problems took oxygen, and 95.5% of those with sleep problems after chemotherapy rested during the day.

Table 3. Examination of the correlation between demographical information and operative conditions, postoperative complaints, and methods of coping (n=74)^a

		Gender		Education status				Working situation					
		Female		Male		Primary school		High school		Employed		Unemployed	
		n	%	n	%	n	%	n	%	n	%	n	%
Had operation	Yes	27	77.1	23	59	41	70.7	9	56.3	15	65.2	35	68.6
	No	8	22.9	16	41	17	29.3	7	43.8	8	34.8	16	31.4
Test/p¹		2.779/0.096				1.193/0.275				0.084/0.772			
Got educated	Yes	8	29.6	8	34.8	10	24.4	6	66.7	9	60.0	7	20
	No	19	70.4	15	65.2	31	75.6	3	33.3	6	40.0	28	80
Test/p¹		0.152/0.697				6.062/0.022*				7.721/0.009*			
Surgery experience	Yes	5.89	6.39	6±2.09		6.67±1.87		6.47±2.07		5.97±2.05			
	No	±2.10	±1.99										
Test/p²		-0.863/0.393				-0.883/0.382				0.781/0.439			
Beck Anxiety Scale	Yes	12.97	9.92	11.38		11.31		8.48±6.22		12.67±8.40			
	No	±7.72	±8.04	±7.82		±8.84							
Test/p²		1.659/0.101				0.027/0.978				-2.139/0.036*			
Medical diagnosis	Leukemia	9	25.7	11	28.2	16	27.6	4	25.0	8	34.8	12	23.5
	Lymphoma	16	45.7	19	48.7	26	44.8	9	56.3	10	43.5	25	49.0
	Mds	1	2.9	1	2.6	2	3.4	0	0.0	0	0.0	2	3.9
	Mm	9	25.7	8	20.5	14	24.1	3	18.8	5	21.7	12	23.5
Test/p		-				-				-			

^a 1 – Chi-square test, 2 – independent sample t-test, * – p<0.05

A significant difference was noted between gender and hair loss and between employment status and anorexia. Accordingly, the rate of hair loss was significantly higher in women than in men, and the rate of anorexia was significantly higher in non-working patients than in working patients (p<0.05, Table 4). Although there was no significant difference, 41.7% of patients

with 0 Rh-positive blood group and 48.4% of patients with A Rh-positive blood group were diagnosed with lymphoma. The mean BAS total score was 11.36±7.99 and was evaluated as mild anxiety. It was determined that 40.5% of the patients had low to no anxiety, 32.4% had mild anxiety, 21.6% had moderate anxiety and 5.4% had severe anxiety. BAS score showed a significant difference according to employment status. In other words, the BAS score of those who were not working was significantly higher than those who were working (p<0.05, Table 5). The difference between BAS score and the effect of COVID-19 on chemotherapy symptoms was found to be significant. Those who thought that COVID-19 prolonged the duration of chemotherapy had significantly higher BAS scores than those who did not think so, and those who experienced fatigue, mouth sores, pain, loss of appetite and constipation had significantly higher BAS scores than those who did not (p<0.05, Table 5). Anxiety scores for receiving chemotherapy during COVID-19 were significantly higher in those who thought “What will be the outcome?” compared to those who did not worry (p<0.05).

Table 4. Examination of the correlation between demographical information and post-chemotherapy complaints (n=74)^a

		Gender		Education status				Working status					
		Female		Male		Primary school		High school		Employed		Unemployed	
		n	%	n	%	n	%	n	%	n	%	n	%
Informed about chemotherapy	Physician	1	2.9	2	5.1	3	5.2	0	0	2	8.7	1	2
	Nurse	2	5.7	4	10.3	5	8.6	1	6.3	3	13	3	5.9
	Physician+nurse	18	51.4	21	53.8	27	46.6	12	75	13	56.5	26	51.0
No		14	40.0	12	30.8	23	39.7	3	18.8	5	21.7	21	41.2
Test/p¹		-				-				-			
Hair loss	Yes	8	22.9	2	5.1	8	13.8	2	12.5	2	8.7	8	15.7
	No	27	77.1	37	94.9	50	86.2	14	87.5	21	91.3	43	84.3
Test/p¹		4.961/0.040*				0.018/1.000				0.663/0.715			
Pain	Yes	12	34.3	8	20.5	16	27.6	4	25.0	5	21.7	15	29.4
	No	23	65.7	31	79.5	42	72.4	12	75.0	18	78.3	36	70.6
Test/p¹		1.774/0.183				0.043/1.000				0.473/0.492			
Anorexia	Yes	19	54.3	13	33.3	27	46.6	5	31.3	6	26.1	26	51.0
	No	16	45.7	26	66.7	31	53.4	11	68.8	17	73.9	25	49.0
Test/p¹		3.299/0.069				1.196/0.274				4.002/0.045*			

^a 1 – Chi-square test, * – p<0.05

When hematologic cancer patients were asked about their suggestions regarding the chemotherapy process and surgical process, some of the remarkable responses can be summarized as follows; “The information given to patients and their relatives should be improved and detailed, early diagnosis should be made, the chemotherapy process should be eased, access to the physician should be facilitated, and results should be obtained faster.”

Table 5. Examination of correlation between the variables and BAS score^a

		Beck Anxiety Scale		Test/p
		Ave	SD	
Had operations	Yes	11.9	6.96	0.830/0.409 ¹
	No	10.25	9.87	
How did COVID-19 affect chemotherapy?	"The process took longer"	16.86 [†]	11.82	3500/0.012 ^{*2}
	"We have been careful"	11.14	5.37	
	"We were afraid of the hospital/contamination"	9.57	4.89	
	"Did not affect"	8.92 [^]	5.80	
	Other	15.13	8.39	
Fatigue	Yes	13.26	8.1	2.153/0.035 ^{*1}
	No	9.36	7.45	
Mouth sores	Yes	18.43	6.7	2.551/0.013 ^{*1}
	No	10.63	7.78	
Hair loss	Yes	17.4	11.87	1.812/0.100 ¹
	No	10.42	6.86	
Pain	Yes	14.75	9.05	2.282/0.025 ^{*1}
	No	10.11	7.25	
Anorexia	Yes	13.94	8.44	2.505/0.015 ^{*1}
	No	9.4	7.11	
Weight loss	Yes	17.5	10.88	1.998/0.073 ¹
	No	10.41	7.08	
Constipation	Yes	14.67	10.5	2.123/0.042 ^{*1}
	No	9.78	5.95	
Respiratory problems	Yes	14.4	6.31	0.879/0.382 ¹
	No	11.14	8.09	

^a #, ^ – shows the differences between the means of the groups (#=highest percentage), 1 – independent sample t-test, 2 – one-way ANOVA test, 3 – Pearson correlation analysis, r – Pearson correlation coefficient, * – p<0.05

Discussion

Rates of hematologic cancers are increasing year by year. Various treatment methods are being developed to achieve positive results. All treatment methods cause anxiety in patients and affect treatment outcomes. In the study, most of the patients (91.9%) had been hospitalized before and more than half (67.6%) had undergone surgery. In a study by Buldan and Kurban, the rate of anxiety was found to be high in those who stayed in the hospital for 11 days or longer.¹⁵ The literature supporting our study shows that the duration of hospitalization and uncertainty in the treatment process significantly affect the lives of cancer patients and their families.

It was determined that more than one third of the patients with hematologic cancer were informed and trained during surgery, and these patients gave their surgical experience a moderate score out of ten (6.12±2.05). In addition, patients reported that their most common concern during surgery was "fear of not waking up". Similar to our study, Özşaker et al. found that more patients (43.9%) had undergone surgery before; 90% of the patients thought that the information provided during the process was sufficient; and 41.4% experienced "fear

of not waking up" after surgery.¹⁶ In another study, while the proportion of patients who received preoperative information was higher (68.6%), 40.2% of those who provided information were physicians, and similar to our study, 36.3% of patients received training on postoperative exercises.¹⁷ In South Korea, 91% of patients reported receiving preoperative education and counseling for gastric cancer surgery.¹⁸ The reasons for the lower rate of being informed in our study compared to other studies can be listed as the lack of patients who had undergone surgical intervention during the period when the study data were collected, and the inability of individuals to express information they forgot due to the questioning of their past surgical experiences.

Patients often experience pain and physical problems after surgery. In a study of 12,276 patients from all surgical disciplines, the most common postoperative complaints were nausea and vomiting, sore throat and hoarseness.¹⁹ In another study, postoperative pain, nausea and dry mouth were among the common complaints. In the same study, postoperative complaints were found to be more common in women than in men (p<0.05).²⁰ Another study reported that the most common complaint after urogynecology surgery was pain.²¹ In this study, the proportion of patients who underwent urology-gynecology surgery was high. The results in the literature are similar to the findings of our study; it is known that different complaints may come to the fore in patients depending on the type of surgery and the treatment methodology applied. The results in the literature are similar to the findings of our study; it is known that different complaints may come to the fore in patients depending on the type of operation and the treatment methodology applied.

More than half of the patients reported that they felt tired after chemotherapy and took time to rest during the day. It was observed that they did not have alternative practices to cope with other complaints. In a study by Sarıtaş and Büyükbayram, it was determined that patients felt fatigue, sadness and anxiety the most.⁷ In another study, 54.5% of the relatives of individuals receiving chemotherapy reported fatigue.²² This draws attention to the need for holistic evaluation of patients together with their families. Unlike the results of our study, Karakoç's study on oncology patients found that 31.5% of patients used complementary and alternative medicine methods during chemotherapy.¹¹ In Bıçaklı and Yılmaz's study, 19.7% of patients used phytotherapy, 19.3% used vitamins, and 47.6% used products or drugs without consulting a doctor-nurse-dietitian.¹⁰ Although it was determined that the patients did not use any alternative methods in our study, as the results of other studies in the literature show, the determination of alternative methods used by patients during the treatment process; their effects, side effects and contra-

indications should be closely monitored. Among the complaints seen after chemotherapy, the rate of anorexia in unemployed patients was significantly higher than in employed patients ($p=0.045$).

In a study conducted, fatigue, shortness of breath, insomnia, and loss of appetite were among the most common complaints in cancer diagnosis and treatment.²³ In another study, changes in the dietary habits of patients before and after cancer diagnosis were examined and an increase in healthy eating behaviors of patients was found after diagnosis.²⁴ No literature directly supporting or contradicting our study findings was found. In unemployed patients, it is thought that in addition to living introverted due to limited social activities, inability to access adequate and balanced food due to financial inadequacies may also be effective in the rate of anorexia.

According to the Beck Anxiety Scale, the anxiety levels of the patients were evaluated as “mild anxiety”. The rate of participants without anxiety was 40.5%. In a study, it was found that the majority of patients with hematological cancer experienced distress, and anxiety and depression levels increased as the level of distress increased.⁸ It is very important for healthcare professionals to monitor anxiety and depression in all cancer patients and to provide the necessary medical treatment and care.

In the BAS administered before chemotherapy, the anxiety score of those who were not working was significantly higher than those who were working ($p=0.036$). In contrast to our findings, Ustaalioglu et al. evaluated the presence of depression in patients receiving chemotherapy and found no significant relationship between employment status and depression.²⁵ In a study in which the findings were parallel to our findings, anxiety was found to be significantly higher ($p<0.001$) in the unemployed.²⁶ In unemployed individuals who experience uncertainty about the future, the diagnosis of a severe disease such as cancer, the onset of a challenging treatment process such as chemotherapy, and the socioeconomic difficulties of being unemployed may play a role in increasing the level of anxiety.

In the study, the BAS scores of those who thought that COVID-19 prolonged the chemotherapy process were significantly higher than those who thought that it did not. In a previous study, the rate of those who stated that they did not have difficulty in coping with their diseases during the pandemic period was 70.5%, while the rate of those who thought that delay in diagnosis-treatment would negatively affect their health status was 55%.²⁷ COVID-19 has had an impact on hematologic cancers as in other diseases and has negatively affected patients. It is reported that there were patients whose diagnosis was delayed due to the decrease in hospital admissions during the pandemic.²⁸ Health managers took

various measures during the pandemic to prevent and minimize this situation. Within the scope of these measures, the process of starting treatment was left to the doctor's decision.¹

Anxiety levels of those who thought “What will be the outcome?” while receiving chemotherapy were higher in those who received chemotherapy during the COVID-19 pandemic. The study supporting our findings was conducted by Amelia et al. and reported that 48.9% of cancer patients receiving chemotherapy experienced moderate stress during the COVID-19 period.²⁹ In a study conducted in Indonesia, three different cancer patients and their chemotherapy processes were examined; it was emphasized that the cases disrupted their chemotherapy and did not receive their treatment during the COVID-19 period.³⁰ The pandemic process, which has affected the whole world, has also negatively affected the chemotherapy process. The aim of nursing care should be to reduce anxiety, prevent complications, minimize loss of function, improve quality of life and maintain well-being in patients.³¹

In this study, surgical history, anxiety levels and individual practices during treatment were examined in patients receiving chemotherapy and the change in the covid-19 period was evaluated. We think that this study will contribute to improving the quality of patient care, raising the awareness of healthcare professionals working in clinics, performing necessary medical tests, asking adequate questions to patients and making patients aware of their wrong practices.

Conclusion

As a result, it was determined that patients with hematological cancer had low levels of information about the surgical processes, did not have alternative applications for chemotherapy and experienced mild anxiety.

In line with the results obtained from the study; It is thought that expressing the anxiety of the patients and eliminating the fears of the patients will positively affect the compliance with the chemotherapy process and the treatment. Healthcare professionals should be careful in this process, the subjects such as “hematological cancers, chemotherapy process” etc. should be well constructed and well-designed, randomized controlled studies with appropriate sample size should be conducted to contribute to the evidence-based literature.

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Declarations

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Author contributions

Conceptualization, G.Y. and D.A.; Methodology, G.Y. and D.A.; Software, G.Y. and D.A.; Validation, G.Y. and D.A.; Formal Analysis, G.Y. and D.A.; Investigation, G.Y. and D.A.; Resources, G.Y.; Data Curation, G.Y. and D.A.; Writing – Original Draft Preparation, G.Y. and D.A.; Writing – Review & Editing, G.Y. and D.A.; Visualization, G.Y. and D.A.; Supervision, D.A.; Project Administration, G.Y. and D.A.

Conflicts of interest

The authors declare no competing interests.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Sakarya University (Document Date-Number: 20/10/2020-E.9543) and written permission was obtained from the institution where the study was conducted.

References

1. Ministry of Health. <https://hsgm.saglik.gov.tr/tr/kanser-nedir-belirtileri>. Accessed November 14, 2020.
2. WHO 2018. https://www.who.int/health-topics/cancer#tab=tab_1. Accessed November 14, 2020.
3. Çalışkan BB. Evaluation of Depression, Quality of Life and Hopelessness Levels of Hematologic Patients. *Journal of Medical Sciences*. 2018;25-40.
4. National Cancer Institute. <https://www.cancer.gov/publications/dictionaries/cancerterms/def/hematologic-cancer>. Accessed December 11, 2020.
5. Turkish Statistical Institute 2018. <https://data.tuik.gov.tr/Bulten/Index?p=Olum-Nedeni-Istatistikleri-2018-30626>. Accessed November 14, 2020.
6. Engin E. Anxiety, Obsessive Compulsive and Related Disorders. In: Foundations of Mental Health and Psychiatric Nursing. Townsend MC (Ed). Akademisyen Medical Bookstore. Ankara. 2016;6:461.
7. Sarıtaş SÇ, Büyükbayram Z. Anxiety levels of patients receiving chemotherapy and their caregivers and affecting factors. *TAF Preventive Medicine Bulletin*. 2016;15(2): 141-150.
8. Çalışkan E, Gürhan N, Tekgündüz AİE. Distress, Anxiety and Depression in Patients Who Have Received Hematologic Cancer Diagnosis. *AOT*. 2017;1-12. doi: 10.5505/aot.2017.70298
9. Karayurt Ö, Ursavaş FE, Çömez S. Endocrine Surgery. In: Surgical Care with Case Studies. Aslan FE (Ed). Akademisyen Medical Bookstore, Ankara, 2016;2:617.
10. Bıçaklı DH, Yılmaz M. Lifestyle Behaviors, Food Consumption Frequencies and Risky Nutritional Habits in Oncology Patients Receiving Chemotherapy. *Journal of Nutrition and Dietetics*. 2018;46(3):230-239.
11. Karakoç MD. The status of oncology patients about using complementary and alternative treatment methods. *Pamukkale Medical Journal*. 2020;13(1):69-80. doi: 10.31362/patd.640488
12. Hindistan S, Çilingir D, Nural N, Gürsoy AA. Applications of Patients With Hematologic Cancers For Experienced Symptoms Due To Chemotherapy. *Gümüşhane University Journal of Health Sciences*. 2012;1(3):153-164.
13. Gök F, Hergül FK. Determination of Level of Anxiety and Depression of Patients Hospitalized in Surgery Clinics. *Istanbul University Institute of Health Sciences Journal of Advanced Research in Health Sciences*. 2020;3(3):195-206.
14. Ulusoy M, Şahin NH, Erkmen H. Turkish Version of the Beck Anxiety Inventory: Psychometric Properties. *Journal of Cognitive Psychotherapy*. 1998;12(2):163-172.
15. Buldan Ö, Kurban NK. Relationship between Nursing Care Perceptions, with Anxiety-Depression Levels of Chronic Disease Cases and Affecting Factors. *Dokuz Eylül University Faculty of Nursing Electronic Journal*. 2018; 11(4):274-282.
16. Özşaker E, Durak H, Canbazogulları Ü. Investigation of the Postoperative Concerns of Day Surgery Patients. *Journal of Contemporary Medicine*. 2019;9(1):100-105. doi:10.16899/gopctd.478417
17. Doğu Ö. Meeting The Needs of Education and Training in Patients with Planned Surgery Preparation Psychological Effects of Individual Patient-Sakarya Sample. *Duzce University Journal of Health Sciences Institute*. 2013;3(3):10-13.
18. Jeong O, Kim HG. Implementation of Enhanced Recovery after Surgery (ERAS) Program in Perioperative Management of Gastric Cancer Surgery: a Nationwide Survey in Korea. *Journal of Gastric Cancer*. 2019;19(1):72-82. doi:10.5230/jgc.2019.19.e3
19. Lehmann M, Monte K, Barach P, Kindler CH. Postoperative Patient Complaints: A Prospective Interview Study of 12,276 Patients. *Journal of Clinical Anesthesia*. 2010;22(1):13-21. doi:10.1016/j.jclinane.2009.02.015
20. Hüppe M, Kemter A, Schmidtke C, Klotz KF. Postoperative Complaints: Gender Differences in Expectations, Prevalence and Appraisal. *Anaesthesist*. 2013;62(7):528-536. doi:10.1007/s00101-013-2182-x
21. Iwanoff C, Giannopoulos M, Salamon C. Follow-up Postoperative Calls to Reduce Common Postoperative Complaints Among Urogynecology Patients. *International Urogynecology Journal*. 2019;30(10):1667-1672. doi: 10.1007/s00192-018-3809-x
22. Özdemir Ü, Taşcı S, Çürük GN, Nemli A, Karaca H. Functional Status of Chemotherapy Receiving Individuals And Caregiver Burden. *Journal of Erciyes University Faculty of Health Sciences*. 2017;4(1):49-61.

23. Seven M, Akyüz A, Sever N, Dinçer Ş. Studying the Physical and Psychological Symptoms of Patients with Cancer. *TAF Preventive Medicine Bulletin*. 2013;12(3):219-224.
24. Pekmezci H, Başaran B. Nutritional Habits of Cancer Patients. *Türkiye Klinikleri Journal of Nursing Sciences*. 2021;13(2):386-395. doi:10.5336/nurses.2020-78631
25. Ustaalioglu BBÖ, Öztürk H, ER H, Peker Ş, Yıldız S, Duman S, Cantürk Ö, Kocatürk K. Depression Analysis in Patients Treated with Chemotherapy: Single Center Experience. *J Kartal TR*. 2014;25(3):203-209. doi:10.5505/jkartaltr.2014.24482
26. Medeni İ, İlhan MN, Medeni V. Depression Prevalence and Related Risk Factors of People 15 Years Old and Over in a District. *GMJ*. 2020;31:630-635.
27. Say A, Çakır D. The Effect of Delayed Medical Care Process on Patients in the COVID-19 Pandemic. *EJONS International Journal on Mathematic, Engineering and Natural Sciences*. 2021;5(17):1-9.
28. Sunu C, Hacibekiroğlu T. Hematology and COVID-19. In: COVID-19 from A to Z. Karabay O, Dheir H, Yaylacı S.(Ed.) Akademisyen Bookstore. Ankara. 2021;1:155-164.
29. Amelia W, Despitasari L, Alisa F, et al. The Relationship between Stress and Sleep Quality in Cancer Patients Undergoing Chemotherapy During the COVID-19 Pandemic at Dr.M.Djamil Hospital, Padang. *Jurnal Keperawatan Muhammadiyah*.2021;6(2):122-130. doi:10.30651/jkm.v6i2.8234
30. Adiputra PAT. Dampak Pandemi COVID-19 pada Pelayanan Pasien Kanker di Rumah Sakit Tersier di Indonesia: Serial Kasus. *DOAJ-JBN*. 2020;4(1):29-33. doi: 10.24843/JBN.2020.v04.is01.p07
31. Sert H. Nursing and COVID-19. In: COVID-19 from A to Z. Karabay O, Dheir H, Yaylacı S.(Ed.) Akademisyen Bookstore. Ankara. 2021;1:395-402.



ORIGINAL PAPER

Stigma and health literacy in individuals with COPD – a cross-sectional research

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ABSTRACT

Introduction and aim. This study was conducted to evaluate the stigma and health literacy levels of individuals with COPD and to determine the relationship between stigma and health literacy.

Material and methods. This study was conducted with 310 individuals with COPD between September 10, 2021 and March 10, 2022. Data were collected using the Patient Information Form, Health Literacy Scale and The Chronic Illness Anticipated Stigma Scale.

Results. The average score of individuals on the Health Literacy Scale is 36.8 ± 12.8 , and the average score on the chronic illness anticipated stigma scale is 30.4 ± 8.5 . Health literacy scores are low in individuals over 65 years of age, female, married, unemployed, and secondhand smoke ($p < 0.05$). Stigma score is high in individuals who are over 65 years old, male, single, and are not working due to illness ($p < 0.05$). There is a significant relationship between the Health Literacy Scale and The Chronic Illness Anticipated Stigma Scale ($p < 0.05$).

Conclusion. It has been determined that age, gender, marital status and employment status affect both stigma and health literacy. It is recommended that the health literacy levels of individuals with COPD be evaluated and supported to increase their health literacy levels.

Keywords. COPD, health literacy, nursing, stigma

Introduction

COPD is a completely irreversible, preventable and treatable disease characterized by airflow limitation in the bronchi.¹ Studies on COPD; It shows that the morbidity, mortality and prevalence of COPD are quite high all over the world.^{1,2} COPD affects nearly 300 million individuals in the world and causes the death of 3.2 million individuals every year. The prevalence of COPD in Turkey is 19.2%. According to studies evaluating the disease burden by the World Health Organization (WHO), COPD ranks 13th among the diseases that most frequently cause morbidity in the world and 11th in our country. In addition, COPD ranks 4th among the diseases that cause mortality most frequently in the world

and 3rd in Turkey.³ Increasing COPD cases cause a global psycho-socio-economic burden.^{2,4}

Due to the low awareness of the disease in individuals with COPD, the severity of the disease increases, the duration of hospitalization is prolonged and the quality of life decreases.^{5,6} Like all individuals with chronic diseases, individuals with COPD need information to be aware of their disease and improve their quality of life. The concept of health literacy is of great importance in ensuring that this information is accurate and effective.⁵⁻⁷ Health literacy is which individuals have the ability to find, understand, and use information and services to inform health-related decisions and actions for themselves and others.⁷⁻¹⁰

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Individuals with COPD experience not only the physiological and psycho-social effects of the disease but also its socio-cultural effects. One of the most important psycho-socio-cultural effects of COPD is stigma.^{5,9,10} The concept of stigma is defined by Goffman as “stigmatizing, discriminating against, or embarrassing a person.”¹⁰ Stigma, which arises especially from prejudices in society, refers to society’s attitude towards a certain person or some patient groups and behaviors that lead to exclusion from society.^{11,12}

In case of illness, low health literacy in individuals and the emergence of stigma cause individuals to experience reluctance, non-compliance and problems in accepting diagnosis, treatment, other supportive services and requesting health care assistance.¹² Evaluating patients in terms of health literacy and stigma perception is important in terms of detecting possible problems in advance and preventing them.^{9,11} The concept of health literacy and stigma is important for nurses who take an active role in patients’ access to health services, protecting and maintaining their health, and planning their education.¹¹

While there are separate studies on health literacy and stigma in individuals with COPD in the national and international literature, no study has been found examining health literacy and stigma together in individuals with COPD.^{13,14}

Aim

The purpose of this study; To evaluate the levels of stigma and health literacy in individuals with COPD and to determine the relationship between stigma and health literacy.

Hypotheses of the research

H₁: What is the health literacy level of individuals with COPD?

H₂: What is the level of stigma in individuals with COPD?

H₃: Is there a relationship between health literacy and stigma in individuals with COPD?

Material and methods

Study design and sample size

The research was conducted as a cross-sectional study to evaluate the stigma and health literacy levels of individuals with COPD and to determine the relationship between stigma and health literacy. The research was conducted between September 2021 and March 2022 at Nevşehir State Hospital Chest Diseases Service and Chest Diseases Polyclinic. The sample of the research; It consisted of individuals diagnosed with COPD who agreed to participate in the study and met the inclusion criteria (n: 310).

Inclusion criteria,^{4,6,11,14,15}

- Being diagnosed with COPD at least 2 months ago,
- Being able to communicate verbally,
- Agreeing to participate in the research.

G Power (v3.1.7) analysis was used to calculate the sample number of the study. In the calculation made based on Türe’s study on ¹⁴ COPD patients, it was aimed to reach 300 patients. During data collection, 316 individuals with COPD were reached. 6 individuals included in the sample were excluded from the study because they did not have time and did not complete the survey questions. According to the Post-Hoc Power analysis result; The total number of patients required is 310, with a 95% confidence interval (1- α) and a 5% margin of error. The power of the test was obtained as 99%.

Exclusion criteria; individuals with a COPD diagnosis of less than 2 months and individuals with COPD exacerbations were not included in the study.

Instrument

Research data were collected using the Patient Information Form, Anticipated Stigma Scale in Chronic Diseases and Health Literacy Scale. Research data was collected using face-to-face interview technique in 15 minutes. The data were collected by the researcher in clinics and outpatient clinics using the question-answer technique.

Patient Introduction Form

Patient introduction form prepared by the researchers by scanning the literature; It consists of a total of 22 questions that include individuals’ socio-demographic (age, gender, marital status, education level, living place, vocation, etc.) and information about their diseases (when COPD was diagnosed, smoking status, knowledge about the disease, etc.).^{3-6,11,14,15}

Health Literacy Scale (HLS-14)

The health literacy scale was developed in Japan in 2010 by Suka et al. (2013) to measure the level of health literacy in adults.¹⁶ The validity and reliability of the scale in our country was conducted by Türkoğlu in 2021.¹⁷ Scale; It has three subscales: Functional Health Literacy (5 items), Interactive Health Literacy (5 items), and Critical Health Literacy (4 items). Each item of the original scale is a 5-point Likert type ranging from “strongly disagree” (1 point) to “strongly agree” (5 points). A total score between “14-70” is received from the scale. An increase in the total score indicates a higher level of health literacy. In the study conducted by Türkoğlu, Cronbach’s alpha value was found to be 0.85.¹⁷ Cronbach’s alpha value in this study is 0.91. Functional Health Literacy Subscale Cronbach’s alpha (0.71), Interactive Health Literacy Subscale Cronbach’s alpha (0.86), Critical Health Literacy Subscale Cronbach’s alpha (0.86).

The Chronic Illness Anticipated Stigma Scale in Chronic Diseases (CIASS)

The scale was developed by Earnshaw et al. in 2012 in order to measure the stigma that individuals with

chronic diseases expect from the people around them.¹⁸ The Turkish validity and reliability of the scale was conducted by Tünerir in 2019.¹⁵ It consists of three subscales to be used to evaluate the stigma expected from family and friends, individuals at work, and healthcare professionals. There are 12 items on the Likert type scale and scores are given between “1-5”.¹⁵ The total score obtained from the scale is between “12-60”. An increase in the total score indicates that the stigma perceived by the individual is high.¹⁵ The Cronbach alpha value of the scale is 0.95, and in this study the Cronbach alpha value is 0.71. Family/Friend Subscale Cronbach's alpha (0.70), Employer/Co-workers Subscale Cronbach's alpha (0.92), Healthcare Workers Subscale Cronbach's alpha (0.85).

Ethical approval

Ethics committee approval was obtained from Amasya University Non-Interventional Ethics Committee (Date: 3.06.2021; Decision No: 91), and institutional permission was obtained from the hospital where the research was conducted. After the individuals were informed about the study and the purpose of the research was explained, the Informed Volunteer Consent Form was signed to conduct the research. Compliance with the World Medical Association Declaration of Helsinki was observed at all stages of the study.

Data analysis

The data used in the research were analyzed using SPSS (Statistical Pack Age for Social Sciences) and Windows 25.0 program. Mean, standard deviation, median, frequency and percentage values were used in the descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov Smirnov test. Kruskal-Wallis and Mann-Whitney U tests were applied to analyze quantitative independent data. Spearman correlation analysis method was applied in the correlation analysis and Cronbach alpha was used in the reliability of the scales. In the study, $p < 0.05$ was considered significant.

Results

The average age of individuals with COPD is 70.5 ± 11 , 58.7% are male, 77.1% are primary school graduates or below, 60% are married, 69% are not working. It was determined that 34.2% were retired, 92.3% lived at home with a large family, and 50.3% used a stove to at heating system home (Table 1).

It was determined that 61% of individuals with COPD did not have COPD in their family, 80.6% did not go to regular health checks for COPD, 42.9% gave up smoking and 29% were exposed to secondhand smoke. 63.5% of the individuals had additional chronic diseases and the most common chronic disease was hypertension with 41.9%, 64.5% were informed by the

doctor and 11.9% were informed by the nurses. It was determined that 69% of the population had knowledge about COPD symptoms, 69% did not know what to do when COPD got worse, 52.6% applied it immediately when they learned new information, and 56.0% were in Stage II according to GOLD's COPD stage (Table 2).

Table 1. Socio-demographic characteristics of individuals with COPD (n=310)

Variables	Average	
	Number	Percent (%)
Age (Mean±SD)	70.5±11	
Gender		
Female	128	41.3
Male	182	58.7
Marital status		
Married	186	60
Single	124	40
Living place		
City	104	33.5
County	95	30.7
Village/Town	111	35.8
Educational level		
≤Primary school	239	77.1
≥Middle school	71	22.9
Working status		
Working	96	31
Not working	214	69
Vocation		
Retired	106	34.2
Farmer	94	30.4
Housewife	57	18.4
Worker	30	9.7
Self-employed	15	4.7
Officer	8	2.6
Living with person/people		
Alone	24	7.7
Large family	296	92.3
Heating system		
Radiator	154	49.7
Stove	156	50.3

According to the HLS-14 sub-dimensions of individuals with COPD; Functional Health Literacy mean score is 13.5 ± 4.6 , Interactive Health Literacy mean score is 12.2 ± 5.1 , Critical Health Literacy mean score is 11.1 ± 4.4 , total Health Literacy mean score is 36.8 ± 12.8 . According to the CIASS sub-dimensions, the mean score of Family/Friends is 14.9 ± 5.3 , the mean score of Employers/Co-workers is 7.8 ± 4.6 , the mean score of healthcare workers is 7.7 ± 3.9 , and the total mean score of the CIASS is 30.4 ± 8.5 (Table 3).

It was determined that the HLS-14 total score was high in individuals aged 65 and under, male, single, employed, and with an education level of secondary school or above ($p < 0.05$). According to the CIASS total score averages of individuals with COPD; It was determined that CIASS was significantly high in individuals over 65 years of age, male, unemployed, single, and educated in secondary school or above ($p < 0.05$, Table 4).

Table 2. Disease-specific characteristics of individuals with COPD (n=310)^a

Variables	Number (n)	Percent%
COPD patient in family		
There is	121	39
None	189	61
Regular health checks for COPD		
Yes	60	19.4
No	250	80.6
Smoking status		
Never smoked	124	40
Gave up smoking	133	42.9
Still smoking	53	17.1
Duration of COPD (years)		
2 months–11 months	60	19.4
1 year–4 years	112	36.4
5 years–9 years	76	24.2
10 years–19 years	44	14.2
20 years and above	18	5.8
Information about secondhand smoke		
Yes	184	59.4
No	126	40.6
Secondhand smoke*		
There is	90	29
None	94	30.3
Chronic disease**		
None	113	36.5
There is	197	63.5
Hypertension	130	41.9
Diabetes mellitus	86	27.7
Heart failure	44	14.2
Asthma	18	5.8
Chronic renal failure	17	5.5
Prostate	11	3.5
Coronary artery disease	5	1.4
Getting information from the doctor about COPD		
Yes	200	64.5
No	110	35.5
Getting information from the nurse about COPD		
Yes	37	11.9
No	273	88.1
Information about COPD		
There is	180	58.1
None	130	41.9
Knowing what to do when COPD gets worse		
Yes	96	31
No	214	69
Application when you learn new information about COPD		
Yes	52.6	
No	47.4	
COPD classification***		
Stage I	15.2	
Stage II	56.1	
Stage III	27.4	
Stage IV	1.3	

^a * – percentages are calculated based on n, ** – multiple answers provided, *** – classification information was taken from the patient file

Table 3. HLS-14 and CIASS average scores of individuals with COPD (n=310)*

Scales	Min–Max	Median	Mean±SD
HLS–14			
Functional Health Literacy	5–25	13	13.5±4.6
Interactive Health Literacy	5–25	13	12.2±5.1
Critical Health Literacy	4–20	12	11.1±4.4
Total	14–70	37	36.8±12.8
CIASS			
Family/Friend	4–20	16.5	14.9±5.3
Employer/Co-workers	4–20	5	7.8±4.6
Healthcare workers	4–20	6	7.7±3.9
Total	12–60	31	30.4±8.5

* HLS-14 – Health Literacy Scale, CIASS – The Chronic Illness Anticipated Stigma Scale

Table 4. HLS-14 and CIASS mean scores of individuals with COPD according to socio-demographic characteristics (n=310)*

	HLS–14			CIASS		
	Mean±SD	Median	Min–Max	Mean±SD	Median	Min–Max
Age						
≤65	42.8±10.3	44	18–70	28.8±8.1	29	12–60
>65	33.8±12.9	33	14–63	32.5±10.1	33	14–60
Test and p value	p<0.001	Z=–5.798		p<0.001	Z=–5.499	
Gender						
Female	32.1±12.2	31	14–70	24.7±6.5	25	12–39
Male	40.2±12.2	41	14–43	34.4±7.4	34	14–60
Test and p value	p<0.001	Z=–5.521		p<0.001	Z=–10.460	
Marital status						
Married	30.9±12.5	29	14–39	28.3±8.8	28	13–56
Single	40.8±11.4	42	14–70	31.8±8.1	32	12–60
Test and p value	p<0.001	Z=–6.668		p<0.001	Z=–3.623	
Educational level						
≤ Primary school	34.3±12.5	34.0	14.0–70.0	29.5±8.7	29.0	12–60
≥ Secondary school	45.3±10.0	49.0	21.0–38.0	33.3±7.2	33.0	14–49
Test and p value	p<0.001	Z=–6.354		p<0.001	Z=–3.735	
Working Status						
Working	40.8±10.6	42.0	14.0–59.0	34.4±8.1	34.0	17–60
Not working	34.4±13.6	33.0	14.0–63.0	27.6±7.6	28.0	12–49
Test and p value	p=0.001	X ² =15,103		p<0.001	X ² =40.201	
Living with person/people						
Alone	34.4±12.7	32.5	15–39	32.0±10.2	33.5	14–56
Large family	37.0±12.8	37.5	14–	30.3±8.4	30	12–60
Test and p value	p=0.352	Z=–0.931		p=0.323	Z=–0.989	
Living place						
City	38.2±12.9	39.5	14–60	30.4±7.9	30.5	13–49
County	37.9±12.7	38	14–63	31.5±8.7	32.0	14–56
Village–Town	34.6±12.6	35	14–59	29.4±8.9	30.0	12–60
Test and p value	p=0.074	X ² =5.211		p=0.208	X ² =3.140	
Heating system						
Radiator	38.6±12.6	40	14–43	30.3±8.1	29.5	13–56
Stove	35.1±12.8	35	14–70	30.5±8.9	31	12–60
Test and p value	p=0.019	Z=–2.338		p=0.849	Z=–0.191	

*K – Kruskal-Wallis, ^m – Mann-Whitney U, HLS-14 – Health Literacy Scale, CIASS – The Chronic Illness Anticipated Stigma Scale

In individuals who have a family history of COPD, who receive information after the diagnosis of COPD and receive this information from the doctor, who know what to do when COPD worsens, who apply it immediately when they read new information about the disease, who go for regular health checks for COPD, and who gave up smoking, the total score of COPD is significantly high ($p < 0.05$). In individuals who are exposed to secondhand smoking, have a chronic disease in addition to COPD, and have a more advanced COPD stage, the HLS-14 total score is significantly lower ($p < 0.05$, Table 5).

Table 5. HLS-14 and CIASS mean scores of individuals with COPD according to disease-specific characteristics (n=310)*

	HLS-14			CIASS		
	Mean±SD	Median	Min–Max	Mean±SD	Median	Min–Max
COPD patient in family						
There is	41.3±12	43	14–70	30.1±8	31	12–49
None	34±12.5	33	14–43	30.6±8.9	31	13–60
Test and p value	p<0.001	Z=-4.983		p=0.718	Z=-0.363	
Smoking status						
Never smoked	32±12.5	30.5	14–59	24.7±6.6	26	12–39
Gave up smoking	41.7±11.7	42.0	15–63	33.2±7.4	33	14–70
Still smoking	35.9±11.8	36.0	14–55	36.7±7.1	37	15–50
Test and p value	p<0.001	χ ² =37.760		p<0.001	χ ² =108.834	
Information about secondhand smoke						
Yes	41.7±11.3	43	14–70	30.1±8.2	30	13–56
No	29.8±11.6	27	14–39	30.8±8.9	31	12–60
Test and p value	p<0.001	Z=-7.995		p=0.579	Z=-0.555	
Secondhand smoke						
Yes	40.1±11.1	41	16–70	27.6±7.6	28	13–44
No	43.1±11.4	45	14–43	32.5±8.2	33	14–56
Test and p value	p=0.043	Z=-2.023		p<0.001	Z=-4.145	
Chronic disease						
None	42.6±9.7	42	20–39	32.5±8.9	32	14–60
There is	33.5±13.2	32	14–70	29.2±8.1	29	12–50
Test and p value	p<0.001	Z=-5.877		p=0.002	Z=-3.15	
COPD stage						
Stage I	43.7±9.8	47	20.0–59	29.5±7.8	31	14–45
Stage II	37.0±12.5	37.5	14–60	30.4±9	29	13–60
Stage III–IV	32.9±13.3	32	14–63	30.9±7.9	32	12–56
Test and p value	p<0.001	χ ² =22.261		p=0.647	χ ² =0.871	
Information about COPD						
There is	40.7±12	42	14–43	31.4±8.4	31	12–60
None	29.7±11	27.5	14–70	28.6±8.4	28	13–49
Test and p value	p<0.001	Z=-7.242		p=0.015	Z=-2.424	
Getting information from the doctor about COPD						
Yes	40.7±12	42	14–43	31.4±8.4	31	12–60
No	29.7±11	27.5	14–70	28.6±8.4	28	13–49
Test and p value	p<0.001	Z=-7.242		p=0.015	Z=-2.424	
Getting information from the doctor about COPD						
Yes	38.7±12.6	40	14–39	30.5±8.3	29	14–56
No	36.6±12.8	36	14–70	30.4±8.6	3	12–60
Test and p value	p=0.336	Z=-0.962		p=0.955	Z=-0.057	

*K – Kruskal-Wallis, ^m – Mann-Whitney U

It was found that the CIASS total score was significantly low in individuals who were exposed to second-hand smoking and had chronic diseases in addition to COPD ($p < 0.05$). It was determined that the total score of the CIASS scale was significantly high in individuals who received information after the diagnosis of COPD, who received information about COPD from the doctor, who knew what to do when the symptoms of COPD worsened, who were knowledgeable about the symptoms of COPD and who still to smoke ($p < 0.05$, Table 6).

Table 6. HLS-14 and CIASS mean scores of individuals with COPD according to disease-specific characteristics (n=310) (Continued)*

	HLS-14			CIASS		
	Mean±SD	Median	Min–Max	Mean±SD	Median	Min–Max
Information About COPD Symptoms						
There is	42.6±10.7	44.5	16–39	31.3±8.2	32	12–56
None	28.9±11.1	27	14–70	29.1±8.8	28.5	13–60
Test and p value	p<0.001	Z=-9.273		p=0.009	Z=-2.631	
Knowing what to do when COPD gets worse						
Yes	43.5±11.2	45.5	16–39	31.8±7.6	32	14–56
No	33.8±12.3	33	14–70	29.7±8.8	29	12–60
Test and p value	p<0.001	Z=-6.218		p=0.023	Z=-2.273	
Application when you learn new information about COPD						
Yes	34.5±12.2	34	14–39	30.3±8.9	31	12–60
No	39.4±13	42	14–70	30.5±8	30	14–56
Test and p value	p=0.001	Z=-3.472		p=0.971	Z=-0.037	
Regular health checks for COPD						
Yes	40.2±11.5	41.5	15–63	30.4±9.2	31	14–56
No	32.2±12.7	30	14–59	31.3±8.7	31	14–60
Test and p value	p<0.001	χ ² =15.650		p=0.782	χ ² =0.492	

*K – Kruskal-Wallis, ^m – Mann-Whitney U, HLS-14 – Health Literacy Scale, CIASS – The Chronic Illness Anticipated Stigma Scale

Table 7. The relationship between HLS-14 and CIASS total scores in individuals with COPD (n=310)*

		HLS-14			
		Functional health	Interactive health	Critical health	Total score
CIASS					
Family/Friend	r	0.121	0.410	-0.315	0.148
	p	0.034	0.000	0.000	0.009
Employer/Co-workers	r	0.047	0.444	-0.261	0.139
	p	0.405	0.000	0.000	0.014
Health workers	r	0.122	0.335	-0.298	0.077
	p	0.032	0.000	0.000	0.175
Total Score	r	0.110	0.446	-0.322	0.142
	p	0.053	0.000	0.000	0.013

* HLS-14 – Health Literacy Scale, CIASS – The Chronic Illness Anticipated Stigma Scale

A significant positive, low-level relationship was observed between the HLS-14 functional health literacy sub-dimension and the CIASS family/friends, healthcare workers sub-dimension scores, and between

the HLS-14 interactive health sub-dimension and the CIASS total family/friends, employers/colleagues and healthcare workers sub-dimension scores ($p < 0.05$). A significant positive, low-level relationship was found between the HLS-14 total score and the CIASS family/friends, employers/colleagues total scores ($p < 0.05$). A significant negative, low-level relationship was detected between the HLS-14 critical health subscale and the CIASS family/friends, employers/colleagues, healthcare professionals total score ($p < 0.05$, Table 7).

Discussion

With aging, physical and psychological changes occur in individuals. Problems such as posture-related changes in elderly individuals, an increase in chronic diseases and the need for more care can cause stigma, which is the situation of different behavior towards the individual by caregiver.¹¹ In the study, the stigma level of individuals with COPD over the age of 65 is higher.

In studies involving different patient groups to evaluate stigma, it has been found that women have a higher level of stigma.^{19,20} In the study, the stigma level of men with COPD was higher. This difference in the results of the study may be associated with the higher number of men in the study. It is thought that the difference will be seen better as studies on stigma in individuals with COPD are carried out.

When the marital status of individuals with COPD was examined in the study. The majority (60%) are married individuals, and the stigma level of single individuals is higher. Similar to previous studies, it has been concluded that single individuals experience more stigma.^{21,22} The reason why stigma is higher in single individuals may be due to the fact that singleness is perceived negatively on a social basis and single individuals are more exposed to negative behavior in the public sphere.

The study found that the health literacy level of men was higher than that of women. In studies examining the relationship between health literacy and gender, it has been concluded that health literacy is higher in men, similar to the study.^{19,20} It is thought that health literacy in men is high due to higher literacy and education levels in men in society.

In the study, singles have higher health literacy. A study found that there was no relationship between marital status and health literacy.²³ The reason why health literacy was found to be high among singles in this study may be related to the fact that singles are younger and have higher education levels.

In COPD, the education level of individuals is important for the prognosis of the disease. Individuals who are informed about the disease participate more effectively in the treatment of the disease and plan the care process better.^{1,6} According to the literature, as the education

level of individuals increases, the level of health literacy increases.^{7,15,23,24} In a study that supports the literature, it was determined that individuals with an education level of secondary school or above have better health literacy.

When studies on health literacy in the literature are examined; It appears that working status affects individuals' health literacy.²³⁻²⁵ In the study, it was determined that the health literacy of individuals who were not employed was lower. Mollakhani's study also stated that the health literacy level of those who are not actively involved in any profession is low.²⁵ The study supports the literature.

In a study by Puente-Maestu, it was found that health literacy was lower in smokers and those exposed to secondhand smoking.²⁶ In the study, the health literacy score is lower in individuals who are knowledgeable about secondhand smoking and who are exposed to and continue to be exposed to secondhand smoking. This may be due to the fact that individuals with COPD do not fully know the harms of smoking and receive inadequate education on this subject.

In the study, it was determined that the health literacy level of individuals decreased as the duration of COPD diagnosis increased. Similar results were obtained in studies examining the health literacy and related factors of individuals with chronic diseases.^{9,27} In line with the literature, this can be interpreted as a decrease in health literacy due to the longer the duration of the disease and the more complicated treatments received. Another reason is that when the disease is first diagnosed, more research is done because there is a curiosity about the disease, but this curiosity decreases as we live with the disease.

In the study, the lowest score in the CIASS is in the healthcare worker's sub-dimension. While this situation may be due to the successful attitude of healthcare professionals, it may also occur because individuals do not seek healthcare services out of fear that they may be stigmatized.

Individuals with COPD need education about the disease in order to continue their daily lives, go to regular health checks and apply their treatments correctly.²⁸ Individuals with COPD and their caregivers must have a certain level of health literacy in order to follow the diagnosis, treatment and progressing processes.^{29,30} It was determined that the health literacy of the individuals participating in the study was low (according to the scale score average). Studies conducted to evaluate health literacy in individuals with COPD have also found that health literacy is low.^{29,30} The study is similar to the literature.

In the study, a positive, low-level significant relationship was found between individuals' stigma level and health literacy. When examined in the literature; While no relationship was found between stigma and health

literacy in the studies conducted by Crowe, Cheng and Mackert, in the study conducted by Corrigan, a positive relationship was determined between stigma and health literacy, similar to the study.³¹⁻³⁴ By increasing the health literacy level of individuals, their awareness will increase and the formation of stigma will be prevented.

Study limitations

The results of this study are limited only to individuals with COPD who applied to the institution where the research was conducted, and cannot be generalized to all individuals with COPD.

Conclusion

As a result of the research, stigma and health literacy scores of individuals with COPD are low, health literacy is low in individuals over 65 years of age, female, married, unemployed, exposed to passive smoking, and whose education level is primary school or below; It was determined that the stigma score was high in individuals who were over 65 years of age, male, single, had at least a secondary school education, and were not working due to illness. In order to increase the health literacy level of individuals with COPD and further reduce the current perception of stigma, providing more information and implementing initiatives by a multidisciplinary (physician-nurse) team, similar studies to evaluate stigma and health literacy in individuals with COPD should be conducted in different regions and outside hospitals. It is recommended to repeat it with larger sample groups, including individuals with COPD.

Declarations

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Author contributions

Conceptualization, N.D.; Methodology, N.D.; Formal Analysis, N.D. and E.A.; Data Curation, N.D. and E.A.; Writing – Original Draft Preparation, E.A.; Writing – Review & Editing, N.D.; Supervision, N.D.

Conflicts of interest

No potential conflict of interest was reported by the authors.

Data availability

The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

Ethics committee approval was obtained from Amasya University Non-Interventional Ethics Committee (Date:

3.06.2021; Decision No: 91), and institutional permission was obtained from the hospital where the research was conducted.

References

1. GOLD 2024. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease. <https://goldcopd.org/2024-gold-report/>. Accessed April 26, 2024.
2. Kocabaş A. Chronic obstructive pulmonary disease epidemiology and risk factors. *TTD Thoracic Surgery Bulletin*. 2010;1(2):105-113.
3. Satman İ, Erkan F. Management of chronic obstructive pulmonary disease in Türkiye: Prevention, Diagnosis and Treatment Standards Guide. Turkish Health Institutes Presidency Turkish Public Health and Chronic Diseases Institute Publication No: 48569, Istanbul, 2021.
4. Singh D, Agusti A, Anzueto A, et al. Global strategy for the diagnosis, management and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. *Eur Respir J*. 2019;53(5):1900164. doi: 10.1183/13993003.00164-2019
5. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global Strategy for the Diagnosis, Management and prevention of chronic obstructive lung disease 2017 report. GOLD Executive Summary. *Eur Respir J*. 2017;49(3):1700214. doi: 10.1183/13993003.00214-2017
6. Kar S, Zengin, N. Examination of health status in patients with COPD according to sociodemographic and disease-related characteristics. *Journal of Health Professional Research*. 2019;1(1):1-7.
7. Bilir N. Health literacy. *Turk J Public Health*. 2014;12(1):61-68. doi: 10.20518/thsd.46492
8. Aydın K. Living conditions and perceptions of health and illness. *Journal of Sociological Research*. 2019;22(1):32-68. doi: 10.18490/sosars.559087
9. Çimen Z, Temel AB. Examining the relationship between health literacy and health perception in elderly individuals with chronic diseases and the factors affecting health literacy. *Ege University Faculty of Nursing Journal*. 2017;33(3):105-125.
10. Goffman E. *Stigma: Notes on The Management of Spoiled Identity*. Englewood Cliffs, NJ: 1963:26-50.
11. Özaslan Çalışkan BÖ, Akca M. The moderating role of personality traits in the relationship between stigma perception and deviant behavior. *International Journal of Academic Value Studies*. 2017;3(13):357-369. doi: 10.23929/javs.437
12. Avcı C, Bulut H, Güçlü Sayar G. Psychiatric diseases and stigma. *Üsküdar University Journal of Social Sciences*. 2016;(2):175-202. doi: 10.32739/uskudarsbd.2.2.4
13. Tel H, Tel H. Sociocultural reflection of chronic obstructive pulmonary disease: Stigma. *Ege University Faculty of Nursing Journal*. 2012;28(3):137-142.
14. Ture DA, Demirci H, Sengoren Dikis O. The relationship between health literacy and disease specific costs

- in subjects with chronic obstructive pulmonary disease (COPD). *Aging Male*. 2020;23(5):396-402. doi: 10.1080/13685538.2018.1501016
15. Tünerir E. Turkish Validity and Reliability Study of the Expected Stigma Scale in Chronic Diseases, <https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp>. Accessed September 15, 2023.
 16. Suka M, Odajima T, Kasai M, et al. The 14-item health literacy scale for Japanese adults (HLS-14). *Environ Health Prev Med*. 2013;18(5):407-415. doi: 10.1007/s12199-013-0340-z
 17. Türkoğlu N, Kılıç D. Adaptation of the health literacy scale into Turkish: validity and reliability study. *Anatolian Journal of Nursing and Health Sciences*. 2021;24(1):25-33. doi: 10.17049/ataunihem.66205
 18. Earnshaw VA, Quinn DM, Kalichman SC, Park CL. Development and psychometric evaluation of the chronic illness anticipated stigma scale. *J Behav Med*. 2013;36(3):270-282. doi: 10.1007/s10865-012-9422-4.
 19. Emekli H, Şakiroğlu M. Stigma experiences and coping methods of women diagnosed with infertility: a review. *World Journal of Human Sciences*. 2022;(2):139-150. doi: 10.55543/human.1070022
 20. Demirel U, Okçin F. Epilepsy and stigma. *Koç University Journal of Education and Research in Nursing*. 2020;17(4):378-382. doi: 10.5222/HEAD.2020.94220
 21. Baltacı M, Arslan S, Nemnezi S, Demirel, Y. Analysis of stigma and discrimination in tuberculosis patients. *Izmir Chest Hospital Journal*. 2021;35(1):11-21. doi:10.5222/IGH.2021.57966
 22. Tezcan F. Celibacy as a stigmatized lifestyle. *Journal of Sociology*. 2021;41-41:81-115.
 23. Lor M, Koleck TA, Bakken S, Yoon S, Dunn Navarra AM. Association between health literacy and medication adherence among hispanics with hypertension. *J Racial Ethn Health Disparities*. 2019;6(3):517-524. doi: 10.1007/s40615-018-00550-z
 24. Furuya Y, Kondo N, Yamagata Z, Hashimoto H. Health literacy, socioeconomic status and self-rated health in Japan. *Health Promot Int*. 2015;30(3):505-513. doi: 10.1093/heapro/dat071
 25. Mollakhalili H, Papi A, Zare-Farashbandi F, Sharifrad G, HasanZadeh A. A survey on health literacy of inpatient's educational hospitals of Isfahan University of Medical Sciences in 2012. *J Educ Health Promot*. 2014;23(3):66. doi: 10.4103/2277-9531.134804
 26. Puente-Maestu L, Calle M, Rodríguez-Hermosa JL, et al. Health literacy and health outcomes in chronic obstructive pulmonary disease. *Respir Med*. 2016;115:78-82. doi: 10.1016/j.rmed.2016.04.016
 27. Çopurlar CK, Kartal M. What is health literacy?, How is it evaluated?, Why is it important? *Turkish Journal of Family Medicine and Primary Care*. 2016;10(1):42-47. doi: 10.5455/tjfm.193796
 28. Tülüce D, Kutlutürkan S, Çetin N, Köktürk N. A pilot study on the effect of patient coaching on dyspnea, cough and sputum symptoms of patients with chronic obstructive pulmonary disease (COPD). *Gümüşhane University Journal of Health Sciences*. 2016;5(2):32-41.
 29. Shnaigat M, Downie S, Hosseinzadeh H. Effectiveness of Health Literacy Interventions on COPD Self-Management Outcomes in Outpatient Settings: A Systematic Review. *COPD*. 2021;18(3):367-373. doi: 10.1080/15412555.2021.1872061
 30. O'Connor R, Muellers K, Arvanitis M, Vicencio DP, Wolf MS, Wisnivesky JP, Federman AD. Effects of health literacy and cognitive abilities on COPD self-management behaviors: A prospective cohort study. *Respir Med*. 2019;160:105630. doi: 10.1016/j.rmed.2019.02.006
 31. Crowe A, Mullen PR, Littlewood K. Self-Stigma, mental health literacy and health outcomes in integrated care. *Journal of Counseling & Development*. 2018;96(3):267-277. <https://doi.org/10.1002/jcad.12201>
 32. Cheng HL, Wang C, McDermott RC, Kridel M, Rislin JL. Self-stigma, mental health literacy and attitudes towards seeking psychological help. *Journal of Counseling & Development*. 2018;96(1):64-74.
 33. Mackert M, Mabry-Flynn A, Donovan EE, Champlin S, Pounders K. Health Literacy and Perceptions of Stigma. *J Health Commun*. 2019;24(11):856-864. doi: 10.1080/10810730.2019.1678705
 34. Corrigan PW, Shah BB, Lara JL, Mitchell KT, Simmes D, Jones KL. Addressing the public health concerns of Fetal Alcohol Spectrum Disorder: Impact of stigma and health literacy. *Drug Alcohol Depend*. 2018;185:266-270. doi: 10.1016/j.drugalcdep.2017.12.027



ORIGINAL PAPER

The impact of an educational game on rational drug use and society's attitudes towards the role of nurses

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ABSTRACT

Introduction and aim. Despite critical role of nurses in managing medication¹, public perspectives of the role nurses play in rational drug use is still unclear. The study aimed to assess the impact of the “HEALTHgain” game, an educational tool, on enhancing individual comprehension of proper medication usage and their perceptions of the significance of the contributions of nurses in society.

Material and methods. This pretest-post-test, randomized control study took place between May and November 2022 in Turkey. Two-hundred and thirty seven individuals aged 18 years and above were recruited.

Results. The “HEALTHgain” game had a noteworthy impact on the knowledge of rational drug usage ($F(1)=45.739$, $p<0.001$) and attitudes of society towards a nurse's role in rational drug use between the baseline and end measurements after 14-day of playing the game ($F(1)=283.434$, $p<0.001$). Moreover, there were a significant improvement in both intervention and control group knowledge level of rational drug use between the initial and final assessments after a two-week period of game play, though it had not been presented in any table ($t=-3.824$, $p<0.001$ for control group; $t=-35.492$, $p<0.001$ for intervention group).

Conclusion. The study recommends that enhancing the game through contributions from various disciplines could elevate the rational use of medical knowledge and positively influence individual attitudes toward the role of nurses.

Keywords. attitude, drug, medicine, nursing practice, public health policy

Introduction

The use of medications in the prevention and treatment of diseases significantly contributes to overall wellbeing and good health.^{1,2} According to estimates, a minimum of 50% of medications are being prescribed and marketed in an improper manner, and a substantial 50% of individuals are not adhering to their prescribed medication regimens. Not following the prescribed dose of medicine not only poses a threat to one's health, but also results in a waste of limited resources.³ The utilization of medications in a rational manner, which entails adherence to medical requirements, accurate dosage, appropriate duration, and minimal financial burden for

individuals, poses a significant hurdle globally, particularly in nations with lower and moderate economic status.^{2,4,5} As a matter of serious concern on a global scale, “irrational drug use” is characterised as several common phrases including polypharmacy, excessive medicine use, and inappropriate self-medication. According to the World Health Organization (WHO), public education about medicines is a necessary intervention to promote rational drug usage.³ This purpose requires effective and cost-effective interventions that can be widely used in primary healthcare settings.

People with limited understanding of sound pharmaceutical practices tend to be more apt to take medi-

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cine without a doctor's prescription and not seek counsel from medical professionals.⁶⁻⁸ A significant number of patients are not following their prescribed medications and treatment plans, leading to a drastic decrease in quality of life and expenditure of financial resources.⁹ Insufficient public awareness and comprehension regarding appropriate pharmaceutical usage can often result in excessive, inadequate, or improper consumption.^{10,11} and expectations for prescription medicines that are not commensurate with their health condition.¹¹ In this context, it is of the utmost importance for health authorities to take action in order to boost public knowledge about rational drug use and implement interventions to modify society's inappropriate behaviors concerning irrational drug use in order to advance public health.^{12,13} Nurses play a critical role, as they often have more frequent contact with individuals than other healthcare professionals. They educate the public and improve adherence to medication regimes, enabling the implementation of appropriate interventions.

Public health interventions such as education, behavior modification, and medication for disease prevention require a multidisciplinary approach.¹⁴ In many stages of medication administration process, especially when administering medications, nurses, pharmacists, and doctors collaborate closely.¹⁵ Given nurses typically being the last to verify that medication is correct before it's given, they have a very special role and responsibility in the administration of medications.¹ Consequently, part of their nursing education should centre on learning from a manual on giving medications and maintaining the safety of patients.¹⁶ Thus, it is important to educate and involve nursing students in managing medication during their education.

A systematic review showed that a few public health interventions utilizing multiple approaches, such as video or written information, as well as face-to-face instruction and interactive educational games, yielded a slight increase in awareness among the public regarding rational use of medication.⁹ Despite nurses' critical role in managing medication through interprofessional cooperation, patient encounters, and respect, public perspectives of the role nurses play in rational drug use is still unclear.¹ Therefore, the intervention tested in this study, created by nursing students under the supervision of a nurse academic, aims to be widely used in primary healthcare settings at a low cost. It also aims to contribute to increasing public awareness regarding the rational use of medicine and the role of nurses in this aspect.

The 'HEALTHgain' game

The 'HEALTHgain' game was used as an intervention in this study. The game was designed by the authors based on the existing scientific literature and guidelines in Turkish.^{3,17-22} The game consists of 47 items, which is

either a 'False' or 'True' statements about rational drug use. One person who is not a player leads the game by reading out the items. Players think about the sentence, decide whether the item is 'False' or 'True', and assign points of 25 (strongly disagree), 50 (somewhat disagree), 100 (somewhat agree), 250 (strongly agree), depending on how certain they are. When the cards have been used up, the game is finished and the person with the highest score wins (Figure 1). The procedure was applied by the second, third, and fourth authors and supervised by the first author.

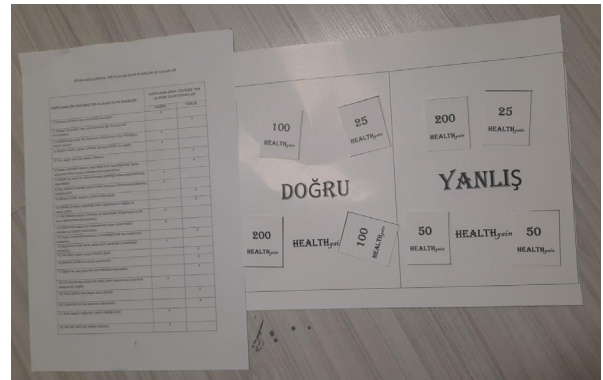


Fig. 1. An example of 'HEALTHgain' game (Doğru=True; Yanlış=False)

Aim

The purpose of this investigation was to evaluate the impact of the "HEALTHgain" game, an educational tool, on enhancing individuals' comprehension of proper medication usage, as well as their perceptions of the significance of nurses' contributions to society.

Hypothesis:

H_1 = 'HEALTHgain' game has a positive effect on knowledge level of rational drug use.

H_2 = 'HEALTHgain' has a positive effect on attitudes of society towards nurses' role in rational drug use.

Material and methods

Participants and study design

This pre-test-post-test, randomized control study analyzed the effects of the 'HEALTHgain' game on knowledge of rational drug use and attitudes of society towards a nurses role in rational drug use. Participants were recruited from a previous study, consisting of 1072 people aged 18 and over, to assess their knowledge level on rational drug use and their attitudes towards a nurses role in rational drug use.²³ The previous study recruited the individuals aged 18 years and old through 18 neighborhood headmanships in the central district, and the data collection process was conducted through these headmanships. Each headmanship was considered as a cluster, and the total number to be reached was collected by proportionally relating it to the population in each headmanship area. We excluded 553 individuals who

did not score 34 or above among participants who did not meet the inclusion criteria (Fig. 2). The inclusion criteria were: i) age of 18 or over; ii) score of 34 or less on the Rational Drug Use Scale, iii) not having graduated from a school related to health science, nor working in this area; iv) being a volunteer for the study.¹⁷ The intervention took place from 1st May 2022 through 20th November 2022 in a province in the Black Sea region of Turkey. All participants provided verbal consent before the beginning of the study. The Bartın University Ethical Committee study approved this study (reference number: 2021-SBB-0238).

Sample size calculation

Sample size was determined through utilization of G*Power 3.1.9.7 software, guided by Jha et al.'s study and utilizing a significance level (α) of 0.05 for Type I error and a power ($1-\alpha$) of 0.80 for Type II error, with an effect size of 0.32. Ultimately, a sample size of 232 participants (split equally between the intervention and control groups at $n=119$ each) was deemed appropriate for this investigation.²⁴

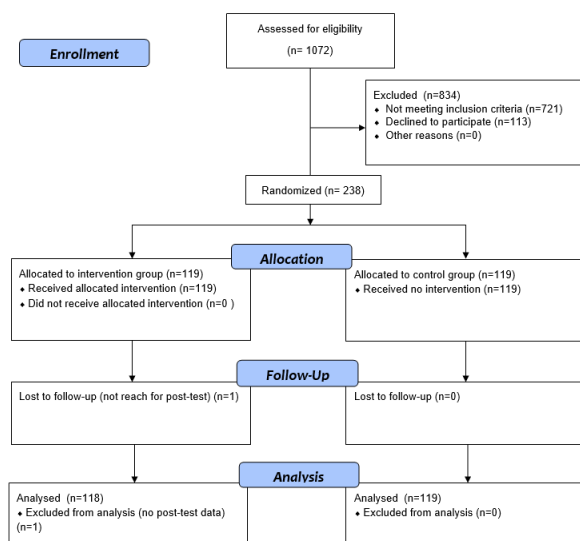


Fig. 2. CONSORT diagram of study procedure

Research protocol

The study comprised of participants who were assigned at random to either an intervention or control group, in a 1:1 proportion, through utilization of a computer-generated algorithm.²⁵ The intervention group comprised of 119 adults aged 18 years and above, while the control group consisted of 119 individuals in the same age range (Fig. 2). Rational Drug Use Scale and Attitudes of the Society Towards Nurses' Role in Rational Drug Use Questionnaire were administered at the initial stage prior to random assignment (pre-intervention) and again at the 14-day mark following the administration of the game (post-intervention). After identifying the potential

participants who scored 34 or less on the Rational Drug Use Scale, we randomly allocated them into intervention and control groups until we reached the required number of participants, 119 for each group. The participants allocated to the intervention group were asked to play the game, provided by the research team for free, at least three times over a 14-day period at home. Following the conclusion of the study, all participants in both the intervention and control groups were conferred the game as a token of appreciation.

Measurement tools

Rational Drug Use Scale

The scale was employed to assess the level of knowledge pertaining to rational drug use.²⁶ The scale consists of 21 items, with 11 of them being marked as 'True' and the remaining 10 being marked as 'False'. Participants mark the items as "(2 point) True", "(0 point) False" or "(1 point) I Don't Know". The total score varies from 0 to 42, and the cut-off point is 34, indicating a lack of knowledge of rational drug use. In the original study, the Cronbach's alpha coefficient for the scale was recorded to be 0.79, and it was calculated as 0.72 in this study.

Attitudes of the Society Towards Nurses' Role in Rational Drug Use Questionnaire

The questionnaire was developed by the authors.²³ The questionnaire comprises 16 questions, with response options on a scale of 'Strongly disagree (1)' to 'Strongly agree (5)'. A higher score on the scale indicates a favorable perception of the role of nurses in promoting rational drug use. The original study reported a Cronbach's alpha coefficient of 0.96 for the questionnaire, a finding likewise replicated and measured at 0.96 in the current study.

Statistical analysis

The data underwent analysis using the Statistical Package for the Social Sciences (SPSS) 25.0 version. Descriptive statistics, including frequency, percentage, mean, and standard deviation, were calculated and reported. Furthermore, the differences between the two study groups at baseline were examined through the utilization of statistical methods such as Student's t test for independent samples and the statistical chi-squared test. Repeated Measure ANOVA was performed, with reading Wilks' Lambda to evaluate the impact of the intervention on dependent variables. A significance level of less than 0.05 for the p value was deemed to be statistically significant. Intergroup effect sizes were calculated using Cohen's d. Value of ≥ 0.8 represents a large-size effect.²⁷

Results

The baseline characteristics of the participants and dependent outcome measures are presented in Table 1. The analysis demonstrated that there were no noteworthy

variations of statistical significance observed between the control group and the intervention group ($p > 0.05$), except for gender ($X^2 = 5.803$, $p = 0.016$) and perception of monthly income ($X^2 = 7.564$, $p = 0.023$).

Table 1. Baseline characteristics of study participants^a

	Total (n=237)	Control group (n=119)	Intervention group (n=118)	X ² /p
Gender				
Female	124	53	71	5.803/0.016
Male	113	66	47	
Age*, mean (±standard deviation)	34.1 (±13.52)	35.31 (±13.33)	32.87 (±13.65)	1.391/0.165
Marital status				
Single	142	70	72	0.119/0.719
Married/having partner	95	49	46	
Educational status				
Secondary school	78	45	33	0.3275/0.194
High school	131	59	72	
Bachelor and above	28	15	13	
Perception of monthly income				
Income=expenditure	107	45	62	7.564/0.023
Income>expenditure	32	22	10	
Income<expenditure	98	52	46	
Do you have any chronic disease?				
Yes	25	10	15	1.166/0.280
No	212	109	103	
Do you use medicine regularly?				
Yes	34	15	19	0.590/0.443
No	203	104	99	
Attitudes of the Society Towards Nurses' Role in Rational Drug Use, Mean (±standard deviation)*				
	3.79 (±0.79)	3.83 (±0.64)	3.75 (±0.91)	0.781/0.436
Rational Drug Use, Mean (±standard deviation)*				
	1.04 (±0.32)	1.02 (±0.35)	1.06 (±0.28)	0.811/0.418

^a* – t-test

Table 2. Effects of 'HEALTHgain' game on rational drug use and attitudes of society towards nurses' role in rational drug use

	Pre-intervention		Post-intervention		F/p	Cohen's d
	Control group	Intervention group	Control group	Intervention group		
Attitudes of the Society Towards Nurses' Role in Rational Drug Use, mean (±standard deviation)	3.83 (±0.64)	3.75 (±0.91)	3.71 (±0.28)	4.45 (±0.53)	45.739/ <0.001	0.882
Knowledge of Rational Drug Use, mean (±standard deviation)	1.02 (±0.35)	1.06 (±0.28)	1.17 (±0.27)	1.99 (±0.36)	283.434 <0.001	2.198

A repeated measures ANOVA was conducted to assess the impact of the 'HEALTHgain' game on both knowledge acquisition regarding rational drug use and societal perceptions of nurses' role in promoting rational drug use. Following the completion of a fourteen-day gaming intervention, a notable differ-

ence was observed in the participants' knowledge level of drug use, as demonstrated by a statistically significant variance between the initial and final assessments ($F(1) = 45.739$, $p < 0.001$). Additionally, it was revealed that there was a statistically significant difference in attitudes of society towards nurses' role in rational drug use between the baseline and end measurements after fourteen days of playing the game ($F(1) = 283.434$, $p < 0.001$) (Table 2, Fig. 3).

The statistical analysis revealed a significant improvement in groups' knowledge level of rational drug use between the initial and final assessments after a two-week period of game play, though it had not been presented in any table ($t = -3.824$, $p < 0.001$ for control group; $t = -35.492$, $p < 0.001$ for intervention group). Moreover, the increase in society attitudes towards nurses' role in rational drug use in the intervention group ($t = -7.033$, $p < 0.001$) was statistically significant, whereas the decrease in the control group was not statistically significant ($t = 1.710$, $p = 0.090$), not presented in any table (Fig. 3).

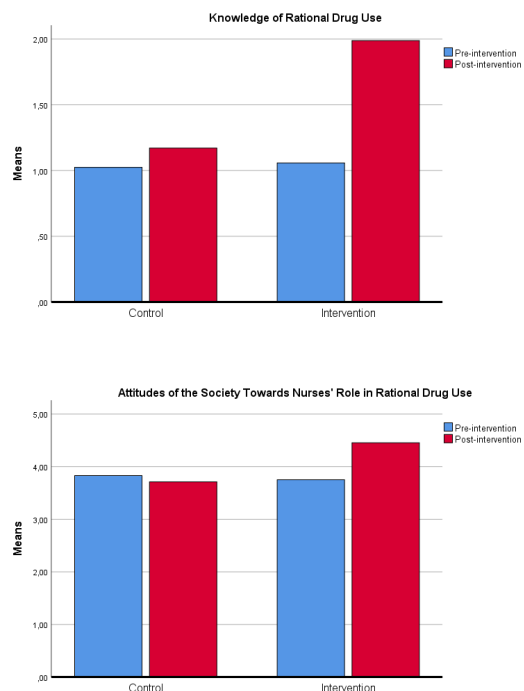


Fig. 3. Between-group and within-group comparison of measurements

Discussion

This study, assessed the impact of an educational game, the 'HEALTHgain' game, on society's knowledge of rational drug use and their attitudes towards nurses' roles in rational drug use. All over the world, people commonly use medications inappropriately and health authorities are making more effort to raise people's awareness of how to use drugs rationally and change their improper behaviors.³ Interventions on rational

drug use in primary care settings are necessary to protect people from adverse events due to medication and promote public health.^{1,3,24}

We found that the educational game tested in this study had a significant impact on people's knowledge levels of rational drug use. It is already known that people with a high level of knowledge are more likely to use medicines appropriately.²⁸ Without adequate awareness of the risks and benefits of taking medications, as well as when and how to use them, it is inevitable that individuals will often not experience the desired therapeutic outcomes.²⁹ A previous study showed that educational interventions had a positive impact on the knowledge levels of individuals with inadequate knowledge when using medicines.³⁰ Promoting rational drug use in the community is among the core component to promote rational use of medicine. Materials to be used for the purpose of public education need to be designed to take into account cultural beliefs and the effectiveness of social factors.²⁹

In recent years, a significant number of educational games have been designed to increase knowledge levels about a particular medical condition. A scoping review revealed the importance of developing health education games are essential for increasing public health knowledge.³¹ In addition to influencing a player's attitudes and values around targeting medical conditions, games can provide them with a rich emotional experience. Games can easily and cheaply create a variety of realistic situations, while removing the undesirable elements of such circumstances, making the learning environment more interesting, attractive, scientific, enjoyable, and effective.³² Therefore, providing free educational games in primary healthcare settings could aid people in comprehending the significance of medicine use rationally and in gaining understanding of the role that nurses play in this regard.

The World Health Organization suggested that the use of medicines should be incorporated into school curricula and adult education programs.²⁹ Moreover, it is highly recommended that rational drug use should be included in both undergraduate Nursing curricula and continuous education programs.³³ Nurses are expected to gain rational drug use competencies, as they are frontline healthcare personnel. Their role is key, given their interactions with individuals in providing care and engaging in broader population.³⁴ Our study findings also showed that 'HEALTHgain' game, a game developed by a nurse educator and four nursing students and tested during this study, had a statistically significant positive impact on public attitudes towards nurses' roles in rational drug use.

Our research team believes that this research is the pioneering investigation on the public's views regarding the involvement of nurses in promoting rational medication use. A qualitative study conducted in 14 Euro-

pean countries from the perspectives of pharmacists, physicians, and nurses reported that assuming the duties and responsibilities associated with administering pharmaceuticals had a beneficial effect on the overall quality of care provided and the outcomes of their patients.³⁵ Nurses guide and educate the public not only in health care settings but in all other areas as well. Public opinion of the nursing profession can influence both individuals and health policies.³⁶ A positive public perception of the health care system is crucial to enhancing the rational use of medicine in public.³⁷ Drugs, as a component of this system, are tied to multiple health variables.³⁸ The health care system is one of the major factors influencing health. Therefore, promoting a positive opinion about nurses in public could help to improve adherence to treatment and increase the benefits derived from treatment.

Study limitations and suggestions for further future research

The study has both strengths and limitations. First, we only stipulated that participants must play the game at least three times over the 14-day period, they have unlimited replays of the game and evaluated its effectiveness at the end of this period. Therefore, there is a lack of follow-up evaluations available to support the long-term efficacy of this intervention. Second, the game was developed by a nurse educator and four nursing students, so we suggest that it could be improved by working with a multidisciplinary team in the future. Third, this study was conducted in one province in Turkey, therefore the findings have limited generalisability. Fourth, participants were recruited from a previous study sample, whose score was 34 or less on the Rational Drug Use Scale.²³ Finally, there were some differences between the participants in the intervention and control groups, such as educational level, monthly income, and chronic diseases, that should be considered when interpreting the study results. Our sample characteristics and size were among the major strengths of this study. It is also recommended to plan further studies to provide evidence on long-term effectiveness of the games.

Conclusion

Individuals frequently misuse prescriptions all across the world, thus health authorities are putting greater effort into teaching individuals how to use medications appropriately and safely. Interventions on rational drug use are required in primary care settings to safeguard patients from medication-related side effects and advance public health. Our study findings revealed that the educational game tested in this study had a greater impact on both the knowledge levels of individuals and positive public attitudes towards a nurse's role in rational drug use. We believe that offering educational games for

free during nursing services in primary healthcare settings could help individuals understand the importance of the rational use of medicine and gain insight into the role of nurses in this aspect. We also considered that improving the game through contributions from a variety of disciplines, designed to take into account cultural beliefs and the effectiveness of social factors, could help to increase its effectiveness in subsequent studies.

Declarations

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Author contributions

Conceptualization, İ.D., Y.Ö., Z.T., S.N.S., and F.Y.; Methodology, İ.D.; Software, Z.T., S.N.S.; Validation, F.Y. and Y.Ö.; Formal Analysis, İ.D.; Investigation, Y.Ö., Z.T., S.N.S., F.Y.; Resources, Y.Ö.; Data Curation, İ.D.; Writing – Original Draft Preparation, Z.T., S.N.S., İ.D.; Writing – Review & Editing, İ.D.; Visualization, İ.D.; Project Administration, Y.Ö.; Funding Acquisition, Y.Ö.

Conflicts of interest

The authors declare that they have no competing interests.

Data availability

All data generated or analysed during this study are included in this published article.

Ethics approval

This study was approved by the Ethics Committee of the Bartın University according to the Declaration of Helsinki, good clinical practice, and applicable laws and regulations (Register no: 2021-SBB-0238).







References

- Intahphuak S, Lorga T, Tipwareerom W. Community Health Nurses' Perspective on the Introduced Rational Drug Use Policy in Primary Care Settings in Thailand: A Descriptive Qualitative Study. *Trop Med Infect Dis.* 2022;7(10):304. doi: 10.3390/tropicalmed7100304
- Sema FD, Asres ED, Wubeshet BD. Evaluation of Rational Use of Medicine Using WHO/INRUD Core Drug Use Indicators at Teda and Azezo Health Centers, Gondar Town, Northwest Ethiopia. *Integr Pharm Res Pract.* 2021;10:51-63. doi: 10.2147/IPRP.S316399
- World Health Organization. Promoting rational use of medicines. <https://www.who.int/activities/promoting-rational-use-of-medicines/>. Accessed March 8, 2024.
- Deniz S. A research on determining attitudes and behavior on rational drug use. *Hacettepe Sağlık İdaresi Dergisi.* 2019;22(3):619-632.
- Melku L, Wubetu M, Dessie B. Irrational drug use and its associated factors at Debre Markos Referral Hospital's outpatient pharmacy in East Gojjam, Northwest Ethiopia. *SAGE Open Med.* 2021; 9:20503121211025146. doi: 10.1177/20503121211025146
- Eteraf-Oskouei T, Mohammadi Y, Najafi M. Evaluating the Causes of Non-Standard Prescription and Drug Use in Iran and Its Improvement Strategies from the Viewpoint of Pharmacy Students of Tabriz University of Medical Sciences. *Depiction of Health.* 2019;10(3):180-188.
- Ercan T, Biçer D. The evaluation of the factors affecting the knowledge levels and behaviors of consumers for rational drug use: Example of Sivas. *Business and Management Studies.* 2019;7(2):998-1021. doi:10.15295/bmij.v7i2.1133
- Deniz S. A research on determining attitudes and behavior on rational drug use. *Hacettepe Sağlık İdaresi Dergisi.* 2019;22(3):619-632.
- Ranjbar M, Aslanpour Z, Kostrzewski A, Cooke A. Public Health Campaigns and Medicine Use Awareness: A Systematic Literature Review. *Health.* 2017;9:1689-1710. doi: 10.4236/health.2017.912124
- Machowska A, Stålsby Lundborg C. Drivers of Irrational Use of Antibiotics in Europe. *Int J Environ Res Public Health.* 2018;16(1):27. doi:10.3390/ijerph16010027.
- Tengilimoğlu D, Tekin PŞ, Zekioğlu A, Kılıç TD. Consumer Awareness, Attitude, and Behavior Related to the Rational Use of Medicines in a Developing Country Context: The Case of Türkiye. *Open Access Macedonian Journal of Medical Sciences.* 2020;8(E):162-171. doi: 10.3889/oamjms.2020.3912
- Yin C, He X, Shen K, Mu X, Tang F. Knowledge and Behavior in Rational Drug Use Among College Students in Zunyi City. *Risk Manag Healthc Policy.* 2022;15:121-131. doi: 10.2147/RMHP.S347822
- Chauhan I, Yasir M, Kumari M, Verma M. The pursuit of rational drug use: Understanding factors and interventions. *Pharmaspire.* 2018;10(2):48-54.
- Smith PG, Morrow RH, Ross DA. Field Trials of Health Interventions: A Toolbox. In: Smith PG, Morrow RH, Ross DA, eds. Types of intervention and their development. 3rd ed. Oxford (UK): OUP Oxford; 2015.
- İlhan SÖ, Yıldız M, Tüzün H, Dikmen AU. Evaluation of irrational drug use of individuals over the age of 18 who applied to a university hospital. *Turkish Journal of Medical Sciences.* 2022;52(2):484-493. doi:10.55730/1300-0144.5337
- Hanson A, Haddad LM. Nursing Rights of Medication Administration. In: Hanson A, Haddad LM, eds. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
- Demirtaş Z, Dağtekin G, Sağlan R, et al. Validity and reliability of rational drug use scale. *ESTÜDAM Halk Sağlığı Dergisi.* 2018;3(3):37-46. doi:10.5336/healthsci.2021-86875
- Bakaruddin S, Mohd Noordin Z, Karuppanan M. Affecting children's knowledge about rational use of me-

- dicines using read-along videos of pictorial storybooks. *Front Pharmacol.* 2022;13:933546. doi:10.3389/fphar.2022.933546
19. Beggi B, Aşık Z. Evaluation of rational drug use in patients applying to family medicine outpatient clinic. *Ankara Medical Journal.* 2019;19(2):251-260. doi:10.17098/amj.582021
20. Macit M, Karaman M, Parlak M. Investigation of individuals' rational drug use knowledge levels. *İstanbul Gelişim Üniversitesi Sosyal Bilimler Dergisi.* 2019;6(2):378-387. doi:10.17336/igusbd.435164
21. Utli H, Turan M. Investigation of attitudes of parents having children aged 0-12 years towards rational drug use. *Ege Üniversitesi Hemşirelik Fakültesi Dergisi.* 2020;36(2):87-95.
22. Republic of Türkiye Ministry of Health. Rational use of medicine. <https://www.titck.gov.tr/faaliyetalanlari/ilac/akilci-ilac-kullanimi>. Accessed March 8, 2024.
23. Dolu İ, Önal, Y, Taşkaya, Z, Savcı, SN, Yılmaz, F. Attitudes of the Society Towards Nurses' Role in Rational Drug Use and Knowledge of Rational Drug Use: A Cross-Sectional Study. 1. Uluslararası 21. Ulusal Hemşirelik Öğrencileri Kongresi; 11-12 of May, 2023; Samsun, Türkiye.
24. Jha N, Shankar PR, Marasini A. Effect of an Educational Intervention on Knowledge and Perception Regarding Rational Medicine Use and Self-medication. *J Nepal Health Res Counc.* 2018;16(3):313-320. doi:10.3126/jnhrc.v16i3.21430
25. Research Randomizer. <https://www.randomizer.org/>. Accessed March 8, 2024.
26. Demirtaş Z, Dağtekin G, Sağlan R, et al. Validity and reliability of rational drug use scale. *ESTÜDAM Halk Sağlığı Dergisi.* 2018;3(3):37-46. doi:10.5336/healthsci.2021-86875
27. Kilic S. Effect size. *Journal of Mood Disorders.* 2014;4(1):44-46. doi: 10.5455/jmood.20140228012836
28. Dawood TO, Hassali MA, Saleem F. Factors affecting knowledge and practice of medicine use among the general public in the State of Penang, Malaysia. *JPHS.* 2017; 8(1):51-57. doi: 10.1111/jphs.12167
29. World Health Organization. Promoting rational use of medicines. <https://apps.who.int/iris/handle/10665/205688>. Accessed March 8, 2024.
30. Guanghui L, Dawood OT, Hassali MA. Development of educational intervention on the responsible use of medicines in public. *J Public Health (Berl).* 2023;31:389-395. doi: 10.1007/s10389-021-01516-y
31. Sharifzadeh N, Kharrazi H, Nazari E, et al. Health Education Serious Games Targeting Health Care Providers, Patients, and Public Health Users: Scoping Review. *JMIR Serious Games.* 2020;8(1):e13459. doi:10.2196/13459
32. Zeng J, Parks S, Shang J. To learn scientifically, effectively, and enjoyably: A review of educational games. *Human Behavior and Emerging Technologies.* 2020;2(2):186-195. doi: 10.1002/hbe2.188
33. Ibrahim DM, Shawki MA, Solayman MH, Sabri NA. Pharmacovigilance education to healthcare professionals: Will it affect their performance in reporting adverse drug reactions? *International Journal of Clinical Practice.* 2021;75(11):e14731. doi:10.1111/ijcp.14731
34. Turner K, Suwannapong K, Putthikhon P, et al. Evaluation of the integrated model of the rational drug use into the Bachelor of Nursing Science program in Thailand: A mixed-methods study. *Belitung Nursing Journal.* 2021;7(6):485-492. doi:10.33546/bnj.1762
35. De Baetselier E, Dilles T, Batalha LM, et al. Perspectives of nurses' role in interprofessional pharmaceutical care across 14 European countries: A qualitative study in pharmacists, physicians and nurses. *PLoS One.* 2021;16(5):e0251982. doi:10.1371/journal.pone.0251982
36. Rodríguez-Pérez M, Mena-Navarro F, Domínguez-Pichardo A, Teresa-Morales C. Current Social Perception of and Value Attached to Nursing Professionals' Competences: An Integrative Review. *Int J Environ Res Public Health.* 2022;19(3):1817. doi:10.3390/ijerph19031817
37. Walicka AM. Public relations in health care system. *Eur J Clin Exp Med.* 2009;2:190-195.
38. Januszewicz P. Drugs as a determinant of public health. *Eur J Clin Exp Med.* 2006;1:79-82.



Assessment of nutritional status in relation to socio-economic status during the COVID-19 pandemic in early childhood in Morocco

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ABSTRACT

Introduction and aim. The objective of this study is to evaluate the nutritional status of children aged 0-24 months, and analyze its association with socioeconomic status during the COVID-19 pandemic in Morocco.

Material and methods. This cross-sectional study was carried out in the outpatient health network between 2021 and 2022, by taking anthropometric measurements of children in accordance with World Health Organization standards and using a questionnaire sent to consenting mothers.

Results. 1012 children were included in this study. The prevalence of overweight was 13.3%, obesity 3.2%, wasting and severe wasting 2.7%. The study revealed that boys had a higher prevalence of overweight compared to girls ($p=0.01$), while girls were more likely to have a normal weight than boys ($p=0.001$). Furthermore, a statistically significant association was observed between nutritional status and age in boys ($p=0.003$); however, malnutrition such as overweight and wasting increased after the age of 12 months in both genders. There was a significant correlation between child nutritional status, gender, and residence, but no significant association was found with parental education or household income.

Conclusion. This study suggests that it is important to develop strategies to improve socio-economic status in the aftermath of the COVID-19 pandemic.

Keywords. COVID-19 pandemic, early childhood, nutritional status, prevalence, socio-economic status

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Introduction

Malnutrition, as defined by the World Food Program (WFP) refers to a condition where an individual's physical function is compromised to the extent that they are unable to sustain proper bodily processes like growth, pregnancy, lactation, physical labor, and the ability to fight off and recuperate from illnesses.¹ The World Health Organization (WHO) also defines malnutrition as the cellular discrepancy between the provision of nutrients and energy and the body's requirement for them to support growth, maintenance, and specific bodily functions.² Inadequate or excessive supply of essential nutrients can lead to the development of pathological conditions, including undernutrition (characterized by wasting, stunting, and being underweight), deficiencies in vitamins or minerals, as well as overweight and obesity.³ The issue of malnutrition poses a substantial risk to the well-being of individuals and has emerged as a pressing public health concern, contributing to approximately 45% of fatalities during childhood.⁴ Malnutrition in infants is a critical factor that can affect a variety of immediate and irreversible long-term developmental outcomes, including growth and cognitive development especially in the first thousand days of life - from conception until two years of age- when growth is rapid, nutrient requirements increase, and dietary diversification takes place.^{3,5} Throughout the initial 1000 days, the nutritional status of children is influenced by a multitude of factors. These factors include genetics, the health and well-being of the mother before and after conception, societal norms within the community, national policies, and the socio-economic status of the household. The household socio-economic status encompasses various elements such as the level of education, employment status, income, geographic location, overcrowding, and gender. The severity of the outcome of early poor nutritional status on a child's current and future well-being is influenced by various factors such as their socio-economic environment, the quality of nutrition they receive later in life, how caregivers respond to their nutritional needs, and the type of childcare services available to them.^{2,5-7} Considerable theoretical and empirical studies have established a strong connection between social determinants and the nutritional well-being of children. These studies suggest that socio-economic factors within communities significantly impact the rates of malnutrition and overall health outcomes, especially among children under the age of five, in numerous developing and underdeveloped nations.⁸⁻¹⁰

The latest worldwide data on malnutrition estimates from the collaboration between United Nations International Children's Emergency Fund (UNICEF), World Health Organization (WHO), and the World Bank Group show that for children under 5 years of age: 21% are stunted, about 7% are wasted and almost 6% are

overweight.¹¹ Moreover, from 2000 to 2017, there was an increase in the prevalence of stunted children under the age of 5 from 50.6 million to 58.7 million, while the number of overweight children in the same age group rose from 6.6 million in 2000 to 9.7 million in 2017.¹² In addition, a study based on data collected in 10 African countries as part of the Demographic and Health Surveys (DHS) program between 2015 and 2019 on malnutrition among under-Five Children revealed that across the 10, the total average prevalence of stunting was 11.6%, the total average for wasting was 1.4% and the overweight total average was 4.9%.¹³

Undernutrition is a pathological nutritional condition that causes morbidity and mortality in children under five. Children afflicted by wasting experience compromised immunity, are vulnerable to enduring developmental impairments, and are at heightened risk of mortality, especially in cases of severe wasting. These children necessitate immediate intervention and support for survival.^{14,15} Likewise, over nutrition during childhood, such as overweight and obesity, represents a crucial predictive determinant of adult obesity, resulting in significant health problems and important comorbidities. Additionally, it is estimated that overweight and obesity currently generate economic and social costs on the order of \$2 trillion worldwide, with an anticipated rise in causal conditions and costs in the years following the pandemic.^{14,16} However, this issue of malnutrition can be addressed by establishing robust programs supported by appropriate investments aimed at strategic interventions focused on child health, including the prevention of malnutrition, particularly during the critical 1000-day period when the risk of malnutrition is highest.^{17,18}

In Morocco, as in most developing countries, malnutrition in children under five remains a public health problem, where the rates are still on the rise. This was confirmed by recent data from the 2018 National Population and Family Health Survey which revealed that the rates of moderate and severe wasting were 2, 6% and 1.1% compared with 2.3% and 1% respectively for 2011, while overweight and obesity rates for the same age group were 10.8% and 2.9% compared with 10.7% and 2.6% respectively in 2011.¹⁹

In the Rabat-Salé-Kénitra region, comprising the Skhirat-Temara prefecture that has the highest projected growth rate between 2014 and 2030 (3%) the prevalence of wasting and overweight was estimated at 3.6% and 10.8% respectively among children under five.²⁰ However, to the best of our knowledge, no research has reported on the nutritional status or risk factors associated with children aged 0-24 months in this prefecture, despite this age group falling within the critical first 1000 days of a child's life, which is widely recognized as a crucial period for nutritional intervention. Moreover, there

is extensive scientific support for the 1000-day window as a strategic timeframe for public health intervention, and giving special consideration to this pediatric population presents a unique opportunity to promote the long-term growth and well-being of children.

Aim

The aim of this study is to assess the nutritional status of infants aged 0-24 months by determining the prevalence of overweight and wasting, two dimensions of malnutrition. In addition, we seek to explore any potential association between socio-economic parameters and nutritional status in this population, particularly during the COVID-19 pandemic, which influenced the environment in which they were born and in their early days of life.

Material and methods

Study settings, design, period and population

This study is a cross-sectional descriptive study that was conducted from May 2021 to January 2022 in urban and rural health centers in the prefecture of Skhirat-Temara in Morocco, where general medicine, nursing, maternal and child health monitoring, chronic disease monitoring, youth and adolescent health monitoring including school health, health information and education services are provided. The study concerned mother and child pairs who came to the health centers to have their children immunized in accordance with the national child immunization program for children.

The research received ethical approval from the Ethics Committee for Biomedical Research of the Faculty of Medicine and Pharmacy at Mohamed V University in Rabat, Morocco (ethical approval no. C68/20 issued on 18 February 2021). Before collecting data, participants were fully informed about the study's purpose, benefits, anonymity and confidentiality guarantees during data handling and publication, as well as their right to withdraw or interrupt the interview at any time. Subsequently, oral and written consent was obtained from all participants.

Inclusion and exclusion criteria

This study included mother-child pairs residing in the Skhirat-Temara prefecture, and whose child's age was between 0 and 24 months.

It was excluded from the study the mother-infant pair whose child was born prematurely, had a history of infection or diarrhea within two weeks of the interview, had a congenital malformation or a metabolic disease influencing growth. The mother-child pair who refused to participate in the study or who had already answered the questionnaire was also excluded.

Sample size determination

To ensure that the study was representative, the popula-

tion size was estimated according to the Lorenz formula developed by Cochran and Ardilly:^{21,22}

$$n = \frac{z^2 \times p \times (1 - p)}{m^2}$$

Where: n = sample size, z = 1.96 for a 95% confidence level, p = 13.2% estimated prevalence of childhood overweight in the region of Rabat-Salé-Kénitra, and m = the tolerated margin of sampling error (set at 5%). The necessary sample size for the results to be significantly representative was estimated at 176 participants.

In the health centers, sampling was exhaustive for all mother-infant pairs who met the inclusion criteria. Our study therefore included 1012 pairs.

Data collection methods

The anthropometric data were obtained by midwives who have been trained, and informed on the objectives of the study, during face-to-face interviews with the mothers, using a structured questionnaire in Moroccan dialect, after having been tested with a dozen women to validate the comprehension of the items.

Mothers were surveyed regarding the child's age and gender, as well as socio-economic factors including the mother's age, marital status, parents' education level (categorized as illiterate, low for primary and college, medium for high school, and high for university), place of residence, parents' occupation, monthly household income defined in reference to the Moroccan guaranteed minimum Inter-professional income (SMIG) set at approximately 2800 Moroccan Dirhams (MAD) or \$282, and medical coverage.

Subsequently, the child's anthropometric measurements were taken according to standard WHO procedures. The variables selected were:

Weight: the child was weighed using the digital baby scale, which has a maximum capacity of 20 kg. The scale was calibrated before each weighing.

Height: this measurement was carried out using a wooden measuring board with a 1.5 m metal strip graduated in millimeters, and a horizontal mobile headrest.

The measurements were taken with the minimum of clothes (nappy and underwear) and without shoes. The material used was the same throughout the survey.

The body mass index (BMI) was calculated according to the formula:

$$BMI = \frac{\text{Weight (kg)}}{\text{Height}^2 (\text{m}^2)}$$

The WHO BMI-for-age (BMI/A) reference curves for girls and boys (0-24 months) were used to calculate BMI/A z-scores, and to classify the child's corpulence into normal weight, overweight, obesity, wasting and severe wasting.

For this study, overweight was defined as a weight-for-height Z-score > 2 standard deviation (SD), obesity as a weight-for-height Z-score > 3SD, wasting as a weight-for-height Z-score < -2SD and severe wasting as a weight-for-height Z-score < -3SD according to WHO recommendations.²³

Table 1. Socio-economic characteristics of the population (n=1012)

Variables	Population, n (%)	95% confidence interval (CI)
Age group of the child		
0–6 months	464 (45.8)	42.9–48.9
7–12 months	302 (29.8)	27–32.5
More than 12 months	246 (24.4)	21.7–27
Gender of the child		
Male	515 (50.9)	47.5–54
Female	497 (49.1)	46–52.5
Age group of mothers		
18–29 year olds	542 (53.6)	50.5–56.4
30–40 year olds	419 (41.4)	38.6–44.4
More than 40 year olds	51 (5)	3.8–6.4
Residence		
Urban	894 (88.3)	86.3–90.2
Rural	118 (11.7)	9.8–13.7
Marital status		
Married	997 (98.5)	97.7–99.2
Not married	15 (1.5)	0.8–2.3
Mother's education level		
Illiterate	167 (16.5)	14.2–19
Low	490 (48.4)	45.3–51.3
Medium	174 (17.2)	15–19.6
High	181 (17.9)	15.7–20.2
Father's education level		
Illiterate	118 (11.7)	9.8–13.7
Low	506 (50)	47–53.2
Medium	222 (21.9)	19.4–24.4
High	166 (16.4)	14.1–18.7
Mother's occupation		
Housewife	844 (83.4)	81–85.6
Civil servant/Employee	134 (13.2)	11.3–15.5
Self-employed	34 (3.4)	2.3–4.5
Father's occupation		
Day laborer	178 (17.6)	15.4–20.1
Civil servant/Employee	553 (54.6)	51.4–57.7
Self-employed	268 (26.5)	23.8–29.2
Unemployed	13 (1.3)	0.7–2.1
Monthly household income		
<\$282	426 (42.1)	38.9–45
\$282–\$504	369 (36.5)	33.4–39.5
>\$504	217 (21.4)	19–24.1

Statistical analysis

The results were analyzed using the Jamovi statistical software, version 2.3.16. Quantitative variables with asymmetric distributions were expressed as median and quartile (age, weight, height and BMI of children), and compared by the Mann-Witney U test. Categorical variables were expressed as numbers and percentages, and then compared by the Chi-square test of independence or Fisher's exact test. Significance was set at a *p* value < 0.05 for all statistical tests.

Results

Socio-economic characteristics of the mother-child population

Our study involved 1012 children. The analysis of socio-economic characteristics (Table 1) revealed a slight preponderance of boys (50.9%) with a male to female sex ratio of 1.04. The age distribution showed that 45.8% of the children were between 0 and 6 months old. More than half of the mothers were between 18 and 29 years old. The majority of the children lived in urban areas with married mothers in 98.5% of cases, housewives in 83.4% of cases and with more than half of the civil servant or employee fathers (54.6%). About two-third of the mothers and fathers were illiterate or had low education level (64.9% and 61.7% respectively). Around 42.1% of the children had parents with a monthly income below the guaranteed minimum wage (SMIG) set at \$282 (Table 1).

Anthropometric data of the child population

Analysis of the children's anthropometric data presented in Table 2 showed a statistically significant difference in medians for weight ($p < 0.001$), height ($p = 0.009$) and BMI ($p < 0.001$) compared to the child's gender.

Table 2. Anthropometric characteristics of the child population*

Variable	Global analysis Me [Q1-Q3] [†]	Population of children n=1012		<i>p</i> [‡]
		Boys (n=515)	Girls (n=497)	
Age (months)	8 [3–12]	8 [3–12]	7 [3–12]	0.422
Weight (kg)	8.27 [6–9.9]	8.58 [6.3–10.3]	7.9 [5.5–9.6]	<0.001
Height (m)	0.68 [0.6–0.7]	0.69 [0.6–0.7]	0.66 [0.5–0.7]	0.009
BMI (kg/m ²)	16.91 [15.5–18.3]	17.31 [15.8–18.6]	16.77 [15.3–17.9]	<0.001

*[†] – values are presented in median and quartile, [‡] – Mann-Whitney U test is used, a *p*-value < 0.05 was statistically significant

Concerning the children's corpulence, the prevalence of overweight was 16.5% (13.3% for overweight and 3.2% for obese). Boys were more overweight than girls with a significant association ($p = 0.01$), and also more obese but without any significant difference ($p = 0.32$). On the other hand, the proportion of normal weight was significantly higher in girls compared to boys (84.9% versus 76.7%; $p = 0.001$). (Table 3).

Table 3. Distribution of the nutritional status among children according to BMI (n=1012)*

Variable	Global analysis	Population of children, n (%)		<i>p</i>
		Girls (n=497)	Boys (n=515)	
Normal weight (%)	817 (80.7)	422 (84.9)	395 (76.7)	0.001
Overweight (%)	135 (13.3)	53 (10.7)	82 (15.9)	0.01
Obesity (%)	32 (3.2)	13 (2.6)	19 (3.7)	0.32
Emaciation & severely emaciation (%)	28 (2.7)	9 (1.8)	19 (3.7)	0.06

* Chi² test was used, a *p*-value < 0.05 was statistically significant

In addition, the distribution of nutritional status by age and sex of the child (Fig. 1) indicated that there is a statistically significant relationship between nutritional status and age in boys ($p=0.003$; Fig. 1a) and the prevalence of overweight increases progressively with age. From the age of 12 months, an increase in the prevalence of wasting reappears for both genders (3.9% for boys and 1.7% for girls) at the detriment of normal weight.

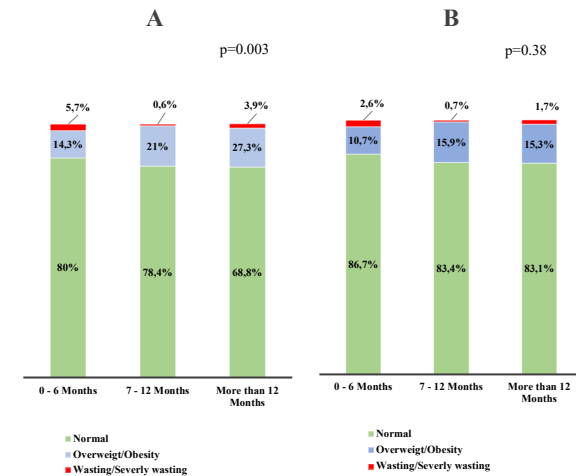


Fig. 1. Distribution of nutritional status by age and sex of the child, A: distribution for boys, B: distribution for girls

The association between the socio-economic characteristics of the population sample and the nutritional status of children

The association analysis between the socio-economic characteristics of the mother-child population and the nutritional status of the children (Table 4) revealed that more than half of overweight and obese children (65.3%) were older than six months, while 67.9% of emaciated or severely emaciated children were in their first six months of life. Indeed, a significant relationship between the child's age and nutritional status was found ($p=0.001$). The prevalence of overweight and obesity was significantly higher in urban children than in rural children (84.3% versus 15.7%; $p=0.03$). Moreover, the prevalence of overweight/obesity and wasting/severely wasting was higher in children whose monthly household income was below the SMIG, with no significant difference. However, our results did not reveal any significant association between children's nutritional status and mother's or father's level of education ($p=0.26$ and $p=0.28$ respectively).

Discussion

The present study was designed to examine the relationship between socioeconomic status and the nutritional status of children up to the age of 24 months. However, due to the lack of sufficient research on the nutritional status of children up to the age of 24 months, the com-

Table 4. Distribution of the nutritional status of children according to socio-economic characteristics (n=1012)

Characteristics	Population of children			p
	Normal n=817	Overweight/ Obesity n=167	Wasting/Severely wasting n=28	
Child age				
0–6 month	387 (47.3)	58 (34.7)	19 (67.9)	0.001 [†]
7–12 month	244 (29.9)	56 (33.5)	2 (7.1)	
More than 12 month	186 (22.8)	53 (31.8)	7 (25)	
Mother's age				
18–29 old year	440 (53.9)	88 (52.7)	14 (50)	0.94 [‡]
30–40 old year	336 (41.1)	71 (42.5)	12 (42.9)	
More than 40 old year	41 (5)	8 (4.8)	2 (7.1)	
Residence				
Urban	725 (88.7)	141 (84.3)	28 (100)	0.03 [‡]
Rural	92 (11.3)	26 (15.7)	0 (0)	
Marital status				
Married	803 (98.3)	167 (100)	27 (96.4)	0.12 [‡]
Not married	14 (1.7)	0 (0)	1 (3.6)	
Mother's level education				
Illiterate	136 (16.6)	25 (15)	6 (21.4)	0.26 [‡]
Low	396 (48.5)	76 (45.5)	18 (64.3)	
Medium	142 (17.4)	31 (18.6)	1 (3.6)	
High	143 (17.5)	35 (21)	3 (10.7)	
Father's level education				
Illiterate	96 (11.7)	16 (9.6)	6 (21.4)	0.28 [‡]
Low	405 (49.6)	84 (50.3)	17 (60.7)	
Medium	183 (22.4)	37 (22.1)	2 (7.2)	
High	133 (16.3)	30 (18)	3 (10.7)	
Mother's occupation				
Housewife	681 (83.3)	136 (81.4)	27 (96.4)	0.25 [‡]
Employee/civil servant	111 (13.6)	22 (13.2)	1 (3.6)	
Self-employment	25 (3.1)	9 (5.4)	0 (0)	
Father's occupation				
Day laborer	144 (17.6)	24 (14.4)	10 (35.7)	0.23 [‡]
Employee/civil servant	449 (55)	92 (55.1)	12 (42.9)	
Self-Employment	212 (25.9)	50 (29.9)	6 (21.4)	
Unemployed	12 (1.5)	1 (0.6)	0 (0)	
Monthly household income				
< \$282	342 (41.9)	67 (39.8)	17 (60.7)	0.09 [†]
\$282–\$504	301 (36.8)	58 (34.7)	10 (35.7)	
>\$504	174 (21.3)	42 (25.1)	1 (3.6)	

* values are presented in frequencies and percentages, [†] – Chi² test, [‡] – Fisher's exact test were used, a p-value<0.05 was statistically significant

parison of the results of this study was extended to the age of 59 months. The results showed that malnutrition is a problem for the sample of children in this study. In fact, the prevalence of overweight, obesity, wasting and severe wasting were 13.3%, 3.2%, and 2.7%, respectively. These results were lower than those of the study conducted by Habibi et al among children under 24 months of age, where the prevalence of overweight, wasting and severe wasting was 22% and 4.7% respectively.²⁴ However, these results were similar to those reported by the Moroccan national nutrition survey of children aged 6-59 months in 2019 for wasting and severe wasting, the prevalence of which was 2.8% and remains well below the global wasting prevalence recorded in

2022 (6.8%) and the 2025 global nutrition target of reducing and maintaining wasting below 5%.^{25,26} In this regard, the Ministry of Health has introduced interventions suggesting a reduction in acute malnutrition by placing nutrition at the heart of the key actions of the 2025 Health Plan, with the institutionalization of a National Nutrition Program (PNN), which sets out new ambitions in terms of prevention, care and nutritional education, to improve the nutritional status of the Moroccan population and contribute to ensuring its physical, mental and psychosocial well-being.²⁷ With regard to overweight and obesity, the current results are higher than those of the same study, in which the prevalence of overweight was 12.7%, indicating the persistence of nutritional problems and the emergence of weight-related disorders. Specifically, overweight and obesity are considered by the World Health Organization to be a risk factor for non-communicable diseases, meaning that greater efforts are needed to get closer to the target of 5.5% overweight prevalence set for 2025.^{12,26} Also, the results of study in Turkey on children under five years indicated a lower prevalence of overweight and obesity (9%).²⁸ Similarly, a study conducted in Vietnam for children under 24 months of age showed that the prevalence of overweight was 10.7%.²⁹ Nevertheless, the results of a study carried out in South Africa indicate a prevalence of overweight and obesity of 17.3%, higher than that reported in this study.³⁰ This variation may be explained by differences in environmental or individual factors of participants in different countries, such as socio-economic status, nature of the diet and perinatal background.³¹ It should also be highlighted that the study was conducted during the COVID-19 pandemic where the majority of children in the study population were born, where rates of job loss and unemployment had increased and sedentary lifestyle linked to confinement was prevalent. This situation could be harmful to the development of healthy behaviors in this pediatric population and consequently contribute to the increased prevalence of childhood wasting and overweight among vulnerable families.³²

There are conflicting reports in the literature regarding the role of gender on malnutrition. In fact, the results of the present study showed that boys are significantly more overweight than girls ($p=0.01$). This result is consistent with that of the previous national survey of 2019, and with other studies conducted with a majority of children ≤ 24 months of age.^{12,33,34} However, the Nigerian study revealed no statistically significant association between nutritional status and gender.³⁵ This would suggest that behavioral and cultural patterns might contribute to this result.

When nutritional status was assessed by age group, it appeared that the prevalence of overweight increased continuously in boys up to the age of 24 months and

in girls up to the age of 12 months, which is consistent with the results of previous surveys. Wasting was more pronounced in the first year of life in both sexes with an increase in boys than girls. This result is inversely related to age and gender in studies where the rate of wasting is higher after 12 months in girls than in boys.^{36,37} In line with these results, this study found a significant relationship between nutritional status and the child's age. Therefore, prevention of malnutrition and monitoring of the nutritional status of children from 0 to 24 months of age are particularly important to ensure optimal growth and to avoid possible adverse effects in adulthood since, this period marks the transition from milk-based to solid and diversified diets may allow malnutrition to set in.^{14,36,38} This last can lead to intellectual and cognitive developmental delays and even long-term disabilities, which might affect productivity and wealth creation. Similarly, it can also lead to chronic non-communicable diseases in adulthood causing a heavy burden on health systems.³⁹

Many authors have documented the impact of socio-economic status on the nutritional status of children from conception as a principal determinant of nutritional success.³⁶ It was generally defined as a combination of economic, social and occupational factors assessed by income or wealth, education and occupation respectively.⁴⁰ In this study, among overweight or obese children, the highest prevalence was observed among urban children, with a statistically significant difference ($p=0.03$; Table 4). This result is also in line with the statements of the High Commission for Planning which reported that overweight affects more urban than rural children (11.7% versus 9.7%), as well as with the results reported in other studies.^{41,42} These results could be explained by the increased availability of commercialized products containing high-energy additives in large cities, and by the replacement of breast milk by artificial milks and sweetened drinks.⁴³ Consequently, these highlighted the need for targeted interventions and policies to address disparities and inequalities in nutritional outcomes between different regions and populations, with the aim of promoting equitable and enhanced health for everyone.⁴⁴

Furthermore, parental education and employment are considered to determine the wellbeing of a family and to influence health behaviors, such as specific eating habits and, knowledge and beliefs about health and nutrition.⁴⁰ According to the results of this study, the majority of children affected by wasting and severe wasting had mothers who were illiterate or had a low level of education. This is consistent with several studies that identify maternal education and maternal weaknesses such as inadequacy, inaccessibility to maternal health services, and precariousness as causal factors of nutritional disparities between regions, as well as one of the most important predictors of healthy growth and protection

against child malnutrition.^{34,45} In other words, considering that mothers with higher levels of education have better health-seeking behavior and are able to access and comply with written medical instructions may explain this result.⁴⁶ This implies giving particular importance to strengthening and expanding the geographical reach of healthcare policies in terms of prevention, early diagnosis of cases, and tailored treatment and follow-up for each nutritional issue. Furthermore, involving mothers through education and raising awareness about childhood malnutrition issues remains a key approach to promoting child health.

For income and wealth, studies have found that children whose families are wealthy are more affected by overweight than children whose families are poor.²⁹ However, the current research revealed that more than one-third of obese and overweight children, as well as 60.7% of wasted and severely wasted children, lived in households with a monthly income less than the minimum wage, while the difference was not statistically significant. This suggests that low economic status may be a risk factor for both overweight and wasting in children, and that malnutrition is prevalent throughout poor families and, low- and middle-income households in developing countries such as Morocco.^{39,40,47,48}

Study limitations

The study is not free of limitations either. The first one is related to the nature of cross-sectional study, which describes relationship, and point estimates of prevalence, without any inference of causality. The second limitation could be associated with the possibility of having committed errors regarding the height measurements of the child in the lying position, which can be considered as a human error. A third limitation is that this study only explored the relationship between socio-economic status and malnutrition, although this may be influenced by other cultural and behavioral parameters of nutrition during the first 1000 days, which could be the subject of future studies.

Conclusion

The current study revealed the malnutrition problem in children up to the age of 24 months, where the prevalence of overweight, obesity, wasting and severe wasting were 13.3%, 3.2% and 2.7% respectively. In addition, the study provided significant results concerning the nutritional status of children and their socio-economic status. These results can be used not only to supplement previous studies carried out in Morocco in order to assess the epidemiological situation in relation to other countries, but also to evaluate and update the actions of the national nutrition program in relation to what remains to be improved.

Declarations

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Author contributions

Conceptualization, F.Z.B and M.O.; Methodology, M.O.; Software, A.E.H; Validation, M.O, R.R. and F.Z.L; Formal Analysis, F.Z.B, R.R; Investigation, F.Z.B; Resources, F.B; Data Curation, S.E; Writing – Original Draft Preparation, F.Z.B, F.B and F.Z.L; Writing – Review & Editing, F.Z.B; Visualization, R.R; Supervision, M.O; Project Administration, M.O.

Conflicts of interest

The others declare that they have no conflicts of interest.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The research received ethical approval from the Ethics Committee for Biomedical Research of the Faculty of Medicine and Pharmacy at Mohamed V University in Rabat, Morocco (ethical approval no. C68/20 issued on 18 February 2021).

References


1. World Food Programme. Food and Nutrition Handbook; World Food Programme: Rome, Italy, 2015.
2. De Onis M, Monteiro C, Akre J, Glugston G. The worldwide magnitude of protein-energy malnutrition: an overview from the WHO Global Database on Child Growth. *Bull World Health Organ.* 1993;71(6):703.
3. Malnutrition. <https://www.who.int/fr/news-room/fact-sheets/detail/malnutrition>. Accessed December 20, 2024.
4. Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet.* 2013;382(9890):427-451. doi: 10.1016/S0140-6736(13)60937-X
5. Black RE, Allen LH, Bhutta ZA, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet.* 2008;371(9608):243-260. doi: 10.1016/S0140-6736(07)61690-0
6. Heidkamp RA, Piwoz E, Gillespie S, et al. Mobilising evidence, data, and resources to achieve global maternal and child undernutrition targets and the Sustainable Development Goals: an agenda for action. *Lancet.* 2021;397(10282):1400-1418. doi: 10.1016/S0140-6736(21)00568-7
7. Victora CG, Adair L, Fall C, et al. Maternal and child undernutrition: consequences for adult health and human

- capital. *Lancet*. 2008;371(9609):340-357. doi: 10.1016/S0140-6736(07)61692-4
8. Beauman C, Cannon G, Elmadfa I, et al. The principles, definition and dimensions of the new nutrition science. *Public Health Nutr*. 2005;8(6a):695-698. doi: 10.1079/phn2005820
 9. Cunningham K, Headey D, Singh A, et al. Maternal and child nutrition in Nepal: examining drivers of progress from the mid-1990s to 2010s. *Glob Food Secur*. 2017;13:30-37.
 10. Maingi Z, Mutuli L, Konyole SO. Linkage between nutritional status of children 6-59 months and some socio-demographic and economic characteristics of mothers in Malava sub-county, Kakamega County. *Afr J Food Agric Nutr Dev*. 2022;22(7):20813-20828.
 11. La Nutrition, Pour Chaque Enfant: Stratégie de l'UNICEF pour la nutrition 2020-2030. [https://www.unicef.org/media/108926/file/ Nutrition Strategy 2020-2030 \(Document\)- French.pdf](https://www.unicef.org/media/108926/file/Nutrition%20Strategy%202020-2030%20(Document)-French.pdf). Accessed October 5, 2022
 12. United Nations Children's Fund, World Health Organization, World Bank Group. *Levels and trends in child malnutrition: Key findings of the 2018 Edition of the Joint Child Malnutrition Estimates*. New York: UNICEF and WHO; 2018
 13. Alaba OA, Chiwire P, Siya A, et al. Socio-Economic Inequalities in the Double Burden of Malnutrition among under-Five Children: Evidence from 10 Selected Sub-Saharan African Countries. *Int J Environ Res Public Health*. 2023;20(8):5489. doi: 10.3390/ijerph20085489
 14. Adebimpe WO. Prevalence and knowledge of risk factors of childhood obesity among school-going children in Osogbo, south-western Nigeria. *Malawi Medical Journal*. 2019;31(1):19-24. doi: 10.4314/mmj.v31i1.4
 15. The world bank and nutrition. <https://www.worldbank.org/en/topic/nutrition/overview>. Accessed April 5, 2024.
 16. United Nations Children's Fund (UNICEF), World Health Organization (WHO), International Bank for Reconstruction and Development/The World Bank. *Levels and trends in child malnutrition: UNICEF / WHO / World Bank Group Joint Child Malnutrition Estimates: Key findings of the 2023 edition*. New York: UNICEF and WHO; 2023.
 17. Thacker N, Namazova-Baranova L, Mestrovic J, et al. Child Malnutrition during the Coronavirus Disease 2019 Pandemic. *J Pediatr*. 2022;244:257-258e2.
 18. Ashworth A. Nutrition, Food Security, and Health, Chapter 46. In: Kliegman RM, Stanton BMD, St. Geme J, Schor NF, editors. *Nelson Textbook of Pediatrics*. 20th ed. Elsevier Health Sciences; 2015.
 19. Enquête Nationale sur la Population et la Santé de Famille (ENPSF)-2018. [https://www.sante.gov.ma/Documents/2020/03/Rapport ENPSF 2018 2ème édition.pdf](https://www.sante.gov.ma/Documents/2020/03/Rapport%20ENPSF%202018%202%C3%A8me%20%C3%A9dition.pdf). Accessed October 6, 2023
 20. Projections de la population: région de Rabat- Salé-Kénitra 2014-2030. [https://www.hcp.ma/region rabat/docs/ProjectionsPopulation/ProjectionsPopulationRegion2014_2030.pdf](https://www.hcp.ma/region%20rabat/docs/ProjectionsPopulation/ProjectionsPopulationRegion2014_2030.pdf). Accessed September 28, 2023.
 21. Cochran WG. *Sampling techniques*. 3rd ed. New York: NY, USA; 1977.
 22. Ardilly P. *Survey Sampling Techniques*. 2nd ed. France: Edition Technip; 2006.
 23. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development. World Health Organization; 2006. <https://www.who.int/publications/i/item/924154693X>. Accessed December 28, 2022
 24. Habibi M, Laamiri FZ, Aguenau H, et al. Evaluation of the infant and young child feeding index among Moroccan children. *Journal of Medical and Surgical Research*. 2017;3:297-312.
 25. Cibles mondiales de nutrition 2025 : note d'orientation sur l'émaciation [Global nutrition targets 2025: wasting policy brief]. <https://apps.who.int/iris/rest/bitstreams/1085909/retrieve>. Accessed October 4, 2022.
 26. Enquête nationale sur la nutrition (EN2019-2020). [https://www.sante.gov.ma/Documents/2022/07/rapport ENN2019-2020 ajout preface \(1\).pdf](https://www.sante.gov.ma/Documents/2022/07/rapport%20ENN2019-2020%20ajout%20preface%20(1).pdf). Accessed October 6, 2022.
 27. Programme national de nutrition. [https://www.sante.gov.ma/Documents/2019/06/Programme National de Nutrition.pdf](https://www.sante.gov.ma/Documents/2019/06/Programme%20National%20de%20Nutrition.pdf). Accessed April 6, 2024.
 28. Ardic C, Usta O, Omar E, et al. Caesarean delivery increases the risk of overweight or obesity in 2-year-old children. *Journal of Obstetrics and Gynaecology*. 2021;41(3):374-379. doi: 10.1080/01443615.2020.1803236
 29. Giao H, Le An P, Truong Vien N, et al. Stunting and Overweight among 12-24-Month-Old Children Receiving Vaccination in Ho Chi Minh City, Vietnam. *BioMed Research International*. 2019;2019:1-7. doi: 10.1155/2019/1547626
 30. Senekal M, Nel JH, Malczyk S, et al. Provincial Dietary Intake Study (PDIS): Prevalence and Sociodemographic Determinants of the Double Burden of Malnutrition in A Representative Sample of 1 to Under 10-Year-Old Children from Two Urbanized and Economically Active Provinces in South Africa. *Int J Environ Res Public Health*. 2019;16(18):3334. doi: 10.3390/ijerph16183334
 31. Salinier-Rolland C, Simeoni U. From the child's conception until the age of 2, the first 1,000 days of life are a key period in terms of prevention. *Contraste*. 2017;46(2):13-38. doi: 10.3917/cont.046.0013
 32. Ribeiro KD da S, Garcia LRS, Dametto JF dos S, et al. COVID-19 and Nutrition: The Need for Initiatives to Promote Healthy Eating and Prevent Obesity in Childhood. *Childhood Obesity*. 2020;16(4):235-357. doi: 10.1089/chi.2020.0121
 33. Sserwanja Q, Mutisya LM, Olal E, et al. Factors associated with childhood overweight and obesity in Uganda: a national survey. *BMC Public Health*. 2021;21(1):1494. doi: 10.1186/s12889-021-11567-1
 34. Chehab RF, Nasreddine L, Forman MR. Determinants of nutritional status during the first 1000 days of life in Lebanon: Sex of the child matters. *Paediatr Perinat Epidemiol*. 2021;35(4):501-510. doi: 10.1111/ppe.12747

35. Jude CK, Chukwunedum AU, Egbuna KO. Under-five malnutrition in a South-Eastern Nigeria metropolitan city. *African Health Sciences*. 2019;19(4):3078-3084. doi: 10.4314/ahs.v19i4.29
36. Chowdhury TR, Chakrabarty S, Rakib M, et al. Factors associated with stunting and wasting in children under 2 years in Bangladesh. *Heliyon*. 2020;6(9):e04849. doi: 10.1016/j.heliyon.2020.e04849
37. Aguree S, Soyiri IN, Ziem JB. Maternal educational attainment is associated with child nutrition status, in northern Ghana. *Acta Sci Nutr Heal*. 2020;4:1-8.
38. Niama AC, Nkodia AJ, Ndziessi G, et al. Prévalence de la Malnutrition des Enfants de 0-24 Mois au Centre de Santé Intégré de Moukondo de Brazzaville, 2017. *Health Sciences And Disease*. 2021;(22)4. doi: 10.5281/hsd.v22i4.2630.
39. La Situation des enfants dans le monde 2019: Enfants, nourriture et nutrition - Bien grandir dans un monde en mutation. United Nations; 2020. 257 p. <https://www.unicef.org/fr/rapports/situation-enfants-dans-le-monde-2019>. Accessed October 6, 2022.
40. Pathak S. The association between socioeconomic status and linear growth in Nepalese children under 2 years of age [Master's Thesis]. The University of Bergen; 2021.
41. Les Indicateurs sociaux du Maroc. https://www.hcp.ma/downloads/Indicateurs-sociaux_t22430.html. Accessed October 4, 2023.
42. Khan Mds, Halder HR, Rashid M, et al. Impact of socioeconomic and demographic factors for underweight and overweight children in Bangladesh: A polytomous logistic regression model. *Clinical Epidemiology and Global Health*. 2020;8(4):1348-1355. doi: 10.1016/j.cegh.2020.05.010
43. Reed BA, Habicht JP, Niameogo C. The Effects of Maternal Education on Child Nutritional Status Depend on Socio-Environmental Conditions. *Int J Epidemiol*. 1996;25(3):585-592. doi: 10.1093/ije/25.3.585
44. Jain A, Agnihotri SB. Assessing inequalities and regional disparities in child nutrition outcomes in India using MANUSH—a more sensitive yardstick. *Int J Equity Health*. 2020;19(1):138. doi: 10.1186/s12939-020-01249-6.
45. Chauhan BG, Chauhan S, Chaurasia H. Decomposing the gap in child malnutrition between poor and non-poor in Sierra Leone. *J Public Health*. 2019;27(1):119-127. doi: 10.1007/s10389-018-0924-6
46. Jude CK, Chukwunedum AU, Egbuna KO. Under-five malnutrition in a South-Eastern Nigeria metropolitan city. *African Health Sciences*. 2019;19(4):3078-3084. doi: 10.4314/ahs.v19i4.29
47. Management of obesity in children and adolescents. National Health Accreditation and Evaluation Agency (ANAES). <http://affairesjuridiques.aphp.fr/textes/prise-en-charge-de-lobesite-de-lenfant-et-de-ladolescent-recommandation-anaes-septembre-2003/telecharger/599426>. Accessed October 4, 2022.
48. Bouglé D, Vérine-Robine C, Duhamel JF. Childhood obesity: contributing factors, management. *Nutrition Clinique et Métabolisme*. 2001;15(3):202-211. doi: 10.1016/S0985-0562(01)00069-3



Minimally invasive percutaneous technique for harvesting iliac crest graft using a tap and drill sleeve

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ABSTRACT

Introduction and aim. Orthopedic surgeries often require acquiring cancellous bone grafts, commonly sourced from the iliac crest. Traditional harvesting methods pose risks of donor site morbidity, prompting interest in minimally invasive techniques. This study introduces and evaluates the efficacy and safety of a percutaneous technique using a tap and drill sleeve for iliac crest bone graft harvesting. This study aims to assess outcomes and complications associated with a minimally invasive percutaneous technique for iliac crest bone graft harvesting through a retrospective analysis of twenty patients undergoing upper limb reconstructive surgery.

Material and methods. A retrospective analysis was conducted on twenty patients who underwent upper limb reconstructive surgery between January and March 2023. The technique involved making a bone deep stab incision, precisely positioning a drill and tap sleeve, utilizing controlled tapping techniques, and extracting the graft. Post-operative assessments included evaluating pain levels, ambulation, and patient satisfaction.

Results. The minimally invasive percutaneous technique demonstrated favorable outcomes, with reduced donor site morbidity observed. Within 24 hours post-operatively, 70% of patients reported low visual analogue scale scores, and 80% regained normal walking ability. No instances of post-operative paresthesia were reported.

Conclusion. The examined minimally invasive percutaneous technique for iliac crest bone graft harvesting showed reliability and safety, particularly in low resource settings. Utilizing basic orthopedic tools such as tap and drill sleeves offers accessibility and affordability. This approach could effectively mitigate donor site morbidity in orthopedic reconstructive treatments.

Keywords. bone grafting, donor site morbidity, iliac crest, minimally invasive technique, percutaneous, tap and drill sleeve

Introduction

Bone grafting procedures are routine in orthopedic surgeries, often requiring the acquisition of cancellous bone grafts. An autograft is usually preferred because it possesses osteogenic, osteoconductive, and osteoinductive properties. Additionally, its usage helps prevent graft rejection and the transmission of viral infections.¹ The iliac crest is often the preferred source of autoge-

nous bone grafts due to its abundance.² However, traditional harvesting techniques pose significant risks of donor site morbidity, including pain, neurovascular injury, and prolonged recovery.³ In response, researchers have increasingly shown interest in developing minimally invasive methods to address these concerns. The classic approach to iliac crest bone harvesting involves a larger incision and the use of specialized tools such as

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Steinmann pin, chisels and osteotomes, which may not be readily available in all surgical settings.⁴ In contrast, minimally invasive techniques utilize basic orthopedic tools, such as a drill fitted with a tap sleeve, to achieve graft extraction with reduced tissue trauma and shorter recovery times.

This paper aims to introduce a minimally invasive percutaneous technique for harvesting iliac crest bone grafts, utilizing a tap and drill sleeve, and compare its efficacy and safety with traditional harvesting methods. By conducting a retrospective analysis of twenty patients undergoing upper limb reconstructive surgery. We seek to evaluate the outcomes and complications at the donor site associated with this novel approach. By emphasizing affordability, accessibility, and reduced morbidity particularly in scenarios where access to specialized instruments is limited. We aim to contribute to the ongoing optimization of orthopedic reconstructive treatments.

Aim

A retrospective study of twenty patients undergoing reconstructive surgery on the upper limbs demonstrates favorable outcomes with reduced donor site morbidity. The presented method entails thorough preparation of the iliac crest, a bone deep stab incision, and graft extraction utilizing a drill equipped with a tap sleeve. The study uncovers the potential benefits of this minimally invasive approach in mitigating typical concerns associated with iliac crest bone graft harvesting.

Material and methods

A retrospective examination analyzed 20 patients (15 males and 5 females) who underwent bone grafts for various upper limb reconstructive procedures between Jan 2023 and Mar 2023. Each patient provided written informed consent for publication. When assessing bone graft volume requirements, the surgeon considered factors such as bone loss, degree of comminution, and post-fixation fracture gap. Grafting the transplant according to each patient's specific requirements ensured optimal outcomes. Patients positioned supine or lateral depending on the location of the fracture. Sterility maintained by cleaning the anterior iliac crest with a povidone-iodine solution and covering the donor site.

Results

The process of initiating the minimally invasive bone graft harvesting technique involved creating a bone deep stab incision, approximately 2 cm in length, directly above the widest area of the iliac crest (Fig.1).

To safeguard the integrity of the lateral femoral cutaneous nerve, this incision was carefully placed away from the anterior superior iliac spine (ASIS) using a sur-

gical blade No. 11. By palpating the surfaces of the iliac crest, precise positioning of a 3.5mm drill and tap sleeve with base teeth at the midpoint of the crest was achieved. This ensured accurate placement for subsequent steps in the procedure. To optimize alignment between the drill sleeve edge and the core bone, employ meticulous rotational adjustments and controlled tapping techniques. This ensures direct contact between the drill sleeve and the core bone (Fig. 2).



Fig. 1. Bone-deep stab incision positioned above the widest point of the iliac crest



Fig. 2. Palpation-guided drill placement with meticulous adjustments for optimal alignment with core bone

Employing gentle hammering followed by screwing to initiate the fracture of the core. Subsequently, the sleeve was adjusted through either hammering or screwing into the crest, tailored according to the size of the defect and the specific needs of the patient.

Rotating the sleeve in a 360-degree arc facilitated the entrapment of the core graft within the sleeve, after which we expelled it along with the core bone. Additional crestal perforations were made as necessary to enable the acquisition of multiple corticocancellous bone pegs. The core cancellous bone is pushed out from the sleeve along with the core bone. Average extracted core bone size is approximately 1.5 cm (Fig. 3).

The wound closure entailed using a full thickness 1-0 nylon suture, supplemented with absorbent dressing (Fig. 4).

In terms of bone grafts, 40% of patients received grafts from their left crests, whereas 60% received grafts from their right. Stable fixation required bone grafting for four ankle fractures, two humerus fractures, one lateral condyle fracture, and thirteen forearm fractures. Post-operatively, visual analogue scale scores over 24 hours indicated that 70% of individuals reported a score of 0, while 15% reported a score of 1, 10% reported a score of 2, and 5% reported a score of 4. No post-operative reports of paresthesia were recorded. Within 24 hours, 80% of patients with upper limb fractures regained normal walking ability, while the remaining 20% required assistance for up to 72 hours. Moreover, all patients were satisfied with the aesthetic outcome of the procedure.

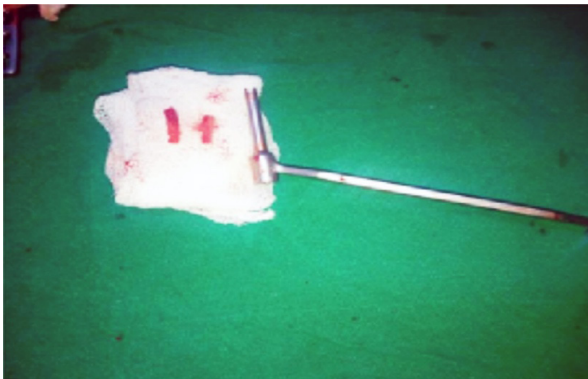


Fig. 3. A cylindrical shaped cancellous bone graft delivered by tap sleeve

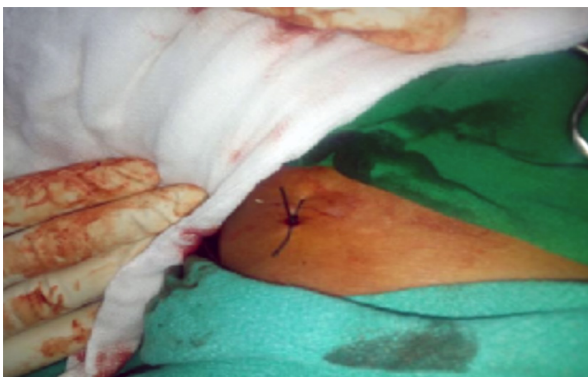


Fig. 4. Wound closure performed with a full-thickness 1-0 nylon suture, complemented by absorbent dressing

Discussion

Bone grafting is one of the most common procedures performed in orthopedic surgery. Bone graft harvesting from iliac donor sites can cause complications, such as pain, neurovascular injury, and avulsion fractures.⁵ Minimally invasive techniques, such as the custom bone graft harvester, allow harvesting of autologous bone from the iliac crest, potentially reducing morbidity in fusion procedures.⁶ Drill tap sleeve techniques result in fewer complications, reduce hospitalization durations,

and earlier ambulation compared to traditional open harvesting methods. It also linked with less postoperative pain, local tenderness, discomfort on walking, and sensory disturbances.⁷ Various sophisticated bone harvesting instruments available on the market are quite expensive. Accessing such tools might not always be possible, especially in a remote location having basic amenities.

The percutaneous method entails making a bone deep stab incision, approximately 2 cm in length, over the widest portion of the iliac crest, which is smaller compared to the traditional classic technique involving a larger incision providing direct access to the iliac crest, with the incision size typically varying but generally being larger than the percutaneous approach.⁸ Current technique utilizes a 3.5mm tap sleeve with a drill for graft harvesting, relying on basic orthopedic operating room tools, whereas the classic harvesting technique typically employs specialized tools like Steinmann pin, chisels and osteotomes to create a larger bone graft.⁹ Iliac crest is cleansed with a povidone-iodine solution, and the donor site is covered during the procedure, while the other technique may require preparation of a larger area and more extensive cleaning owing to the larger incision.¹⁰ Our method aims to mitigate donor site morbidity, such as discomfort, hematoma, infection, nerve damage, and iliac crest fractures, contrasting with the traditional technique, which is linked to greater donor site morbidity due to the larger incision and more invasive instruments used. The study highlights fluctuating levels of postoperative pain, with many patients achieving low VAS scores within 24 hours and regaining normal walking ability within the same timeframe. This contrasts with potential variations in postoperative pain, increased discomfort, and a prolonged recovery period in the classic technique.

Conclusion

The findings of this study suggest that the examined approach can harvest bone grafts reliably and safely, especially in low demand scenarios. Drill tap sleeves emerge as an essential tool for our method particularly in settings with limited access to complex instruments, such as peripheral environments with only basic amenities. Additionally, their widespread availability entails no extra expenses. We propose that embracing a minimally invasive approach to graft harvesting could reduce donor site morbidity. Our institution has extensively employed the technique outlined in this study confirming its efficacy and practicality over an extended period.

Declarations

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Author contributions

Conceptualization, R.K., A.M., N.S., A.S., R.R. and A.B.; Methodology, R.K., A.M., N.S., A.S., R.R. and A.B.; Investigation, R.K., A.M., N.S., A.S., R.R. and A.B.; Resources, R.K., A.M., N.S., A.S., R.R. and A.B.; Writing – Original Draft Preparation, R.K., A.M., N.S., A.S., R.R. and A.B.; Writing – Review & Editing, R.K., A.M., N.S., A.S., R.R. and A.B.; Project Administration, R.K., A.M., N.S., A.S., R.R. and A.B.

Conflicts of interest

The authors declare that there are no conflicts of interest associated with this work.

Data availability

Not applicable.

Ethics approval

Written informed consent for publication was obtained from the patient. We complied with the policy of the journal on ethical consent.



Reference

1. Roberts TT, Rosenbaum AJ. Bone grafts, bone substitutes and orthobiologics: the bridge between basic science and clinical advancements in fracture healing. *Organogenesis*. 2012;8(4):114-124. doi:10.4161/org.23306
2. Campana V, Milano G, Pagano E, et al. Bone substitutes in orthopedic surgery: from basic science to clinical practice. *J Mater Sci Mater Med*. 2014;25(10):2445-2461. doi:10.1007/s10856-014-5240-2
3. Myeroff C, Archdeacon M. Autogenous bone graft: donor sites and techniques. *J Bone Joint Surg Am*. 2011;93(23):2227-2236. doi:10.2106/JBJS.J.01513
4. Pokharel RK, Paudel S, Lakhey RB. Iliac crest bone graft harvesting: modified technique for reduction of complications. *JNMA J Nepal Med Assoc*. 2022;60(247):325-328. doi:10.31729/jnma.7086
5. Ebraheim N, Elgafy H, Xu R. Bone-graft harvesting from iliac and fibular donor sites: techniques and complications. *J Am Acad Orthop Surg*. 2001;9(3):210-218. doi:10.5435/00124635-200105000-00007
6. Saha A, Shah S, Waknis P, Bhujbal P, Aher S, Vaswani V. Comparison of minimally invasive versus conventional open harvesting technique for iliac bone graft in secondary alveolar bone grafting in cleft palate patients: a systematic review. *J Korean Assoc Oral Maxillofac Surg*. 2019;45(5):241-253. doi:10.5125/jkaoms.2019.45.5.241
7. McLain RF, Techy F. Trepine technique for iliac crest bone graft harvest: long-term results. *Spine*. 2021;46(1):41-47. doi:10.1097/BRS.0000000000003702
8. Arora S, Sankaran A, Dhal A. Minimally-invasive bone graft harvesting technique without sophisticated instruments. *The American Journal of Orthopedics*. 2014;43(1):45-46.
9. Missiuna PC, Gandhi HS, Farrokhyar F, Harnett BE, Dore EM, Roberts B. Anatomically safe and minimally invasive transcristal technique for procurement of autogenous cancellous bone graft from the mid-iliac crest. *Can J Surg*. 2011;54(5):327-332. doi:10.1503/cjs.028010
10. Sezavar M, Mesgarzadeh V, Shafayifard S, Soleimanpour MR. Management of bone grafting complications in advanced implant surgery. In: Bagheri SC, ed. *A Textbook of Advanced Oral and Maxillofacial Surgery Volume 2*. IntechOpen; 2015. doi:10.5772/59834



REVIEW PAPER

Vitamin D – a key player in diabetes management – a review

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ABSTRACT

Introduction and aim. Diabetes mellitus is a major health concern around the world and requires new management strategies. Several investigations have shown the connection between a lack of vitamin D and diabetes and its complexities. The objective of this review was to investigate the impact of vitamin D on maintaining glucose levels.

Material and methods. The material and methods section of this review involved conducting a literature review. This process included searching databases such as PubMed Crossref, Google Scholar, Scopus, Web of Science, Embase, and the Cochrane Library for studies examining the relationship between vitamin D levels and complications of diabetes. These databases were selected to ensure a comprehensive exploration of the existing literature to provide a comprehensive analysis of the relationship between vitamin D status and diabetic complications.

Analysis of the literature. Vitamin D plays an important role in preventing macrovascular and microvascular complications such as diabetic retinopathy, diabetic neuropathy, diabetic kidney disease, and diabetic foot ulcer in people with diabetes mellitus. Correcting vitamin D deficiency through optimal dosages of vitamin D supplements is an effective way to address the management and prevention of macrovascular and microvascular complications in diabetic individuals. This review emphasizes the critical importance of vitamin D supplementation for individuals with diabetes mellitus as it significantly maintains optimal blood glucose levels and reduces diabetes-associated risks.

Conclusion. Vitamin D is vital for managing and preventing diabetes complications. It stabilizes blood glucose levels and reduces risks of complications like retinopathy, neuropathy, kidney disease, and foot ulcers. Including it in diabetes management is crucial for better health outcomes.

Keywords. diabetes mellitus, diabetic complications, vitamin D deficiency

Introduction

Diabetes mellitus is a chronic metabolic condition in which blood glucose levels increase due to an absolute or relative impaired ability to produce insulin and may be associated with peripheral resistance to the action of insulin.¹ Due to the increasing incidence of diabetes mellitus, it is a major health concern worldwide.² Vitamin D is vital in bone health, immune function, and calcium regulation.³ In addition to this function, most related studies have shown promising results for

the correlation between Vitamin D and diabetes mellitus.⁴ For example, a cross-sectional study by Vijay et al. found that individuals with diabetes mellitus had significantly lower levels of vitamin D compared to those without the condition.⁵ Another study conducted by Wu et al. explores factors such as age, ethnicity, lifestyle habits, genetics, and seasonal variation i.e. vitamin D deficiency mostly occurs during winter which is also linked to the progression of type 2 diabetes mellitus (T2DM).⁶ A meta-analysis conducted by Hu et al.

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demonstrated that vitamin D supplementation was associated with improved glycemic control.⁷ Therefore, due to the increasing prevalence of diabetic complications, it is important to determine the role of vitamin D in the prevention and management of diabetic complications in diabetic individuals.⁸ However, the association between vitamin D levels and diabetes mellitus complications in diabetic individuals is still under investigation.

Aim

This review aimed to investigate the impact of vitamin D on maintaining glucose levels and preventing complications in individuals with diabetes mellitus.

Material and methods

The material and methods section of this review involved conducting a literature review. This process included searching databases such as PubMed Crossref, Google Scholar, Scopus, Web of Science, Embase, and the Cochrane Library for studies examining the relationship between vitamin D levels and complications of diabetes. These databases were selected to ensure a comprehensive exploration of the existing literature to provide a comprehensive analysis of the relationship between vitamin D status and diabetic complications.

Analysis of the literature

Vitamin D and its importance

Vitamin D is a fat-soluble vitamin that is also called calciferol and has two primary forms that are D2 and D3.^{8–10} Both vitamin D2 and D3 are biologically inactive forms that are activated by two enzymatic reactions in the liver and kidney.^{9,10} Vitamin D2 (ergocalciferol) cannot be produced within the human body so it can be generated from either plants or supplements. Vitamin D2 and D3 both help in calcium and phosphorus absorption.^{8,10} Vitamin D3 (cholecalciferol) synthesis occurs in the skin through the action of ultraviolet B (UVB) radiation.^{9–12} Vitamin D3 can be obtained from dietary sources such as fatty fish, eggs, and dairy. Calcidiol, also known as 25(OH)D, is a form of vitamin D used to assess vitamin D levels.¹² It acts as an intermediary before being converted to calcitriol.^{8,9,11} Calcitriol (1,25(OH)₂) is the active form of vitamin D.^{9–11}

A deficiency in vitamin D is a serious concern that can be worsened by factors such as limited sunlight exposure, lower dietary intake, malabsorption, and chronic disease related to the liver or kidney.^{10–12} It is necessary to recognize the consequences of low vitamin D levels for public health to increase awareness and implement strategies, especially in areas with limited sunlight and different lifestyles.¹³

This study aims to provide novel insights into the association between vitamin D deficiency and diabetes

mellitus and explore potential mechanisms and therapeutic implications.

The relationship between vitamin D and diabetes

Pancreatic beta cells are responsible for insulin production and also express vitamin D receptors.¹⁴ Therefore, various studies have been conducted to investigate the relationship between vitamin D deficiency and diabetes which is a favorable area of research. Low levels of vitamin D are associated with insulin-related issues such as insulin resistance and impaired insulin secretion which are important factors in diabetes.¹⁴ Additionally, vitamin D protects against autoimmune mechanisms that lead to diabetes.^{3,15} In contrast, some studies conducted by Szymczak-Pajor et al., Xiao et al., and Zhao et al. suggest that vitamin D supplementation could be beneficial for preventing and managing diabetes and diabetes-associated complications.^{14,16}

Vitamin D insufficiency is linked to diabetes complications such as diabetic foot ulcers, diabetic retinopathy, diabetic neuropathy, and diabetic kidney disease.^{16,17} However, well-designed clinical trials with detailed studies are needed to determine the underlying mechanism involved.

HbA1c and vitamin D

Hemoglobin A1c (HbA1c) is used for diagnostic purposes to determine whether a patient has diabetes mellitus if the blood sugar levels are abnormally elevated over the previous 2 to 3 months.¹⁸ Monitoring HbA1c levels is essential in reducing the risk of complications associated with diabetes for guiding the treatment and management of the condition.¹⁸ Recent studies have shown that high-dose vitamin D supplements can help reduce HbA1c levels and improve blood glucose levels by enhancing beta cell function and insulin sensitivity and reducing inflammation.^{14,19} Obesity is linked to vitamin D deficiency and insulin resistance.²⁰ In addition to insulin sensitivity and anti-inflammatory properties, it's worth noting that there is substantial evidence to the contrary regarding the assertion that vitamin D helps in muscular function, as suggested by studies such as Bislev et al.²¹ Specifically, vitamin D strengthens skeletal muscles that enhance glucose utilization by promoting insulin sensitivity and facilitating glucose transport into muscle cells. That leads to efficient glucose utilization and stable HbA1c results.^{21–23} However, further research is needed to determine the optimal dosage and duration of vitamin D for effectively managing HbA1c levels in diabetic individuals.

Diabetic peripheral neuropathy and vitamin D

Diabetic peripheral neuropathy (DPN) is a condition that causes nerve damage and affects both sensory and motor functions. DPN presents with symptoms such as tingling, numbness, and weakness in the extremities.²⁴

Numerous studies have demonstrated a correlation between inadequate levels of vitamin D and neuropathic symptoms in patients with diabetes mellitus. These findings suggest that vitamin D deficiency may worsen DPN by increasing oxidative stress and inflammation, which can exacerbate nerve damage.²⁵ Vitamin D protects nerves by reducing oxidative stress, facilitating nerve tissue repair, and maintaining calcium balance.^{25,26} Additionally, it promotes the immune system by reducing inflammation through the reduction of oxidative stress and helps in managing DPN.²⁶ Nerve growth factor (NGF) is necessary for nerve tissue regeneration and deficiency in vitamin D is associated with decreased NGF levels.²⁷ Studies conducted by Putz et al., Habib et al. and Ou et al. have conducted studies exploring the relationship between vitamin D and diabetic neuropathy, highlighting its potential therapeutic implications.^{25,28} Therefore, several studies suggest that restoring vitamin D levels or promoting NGF expression may improve nerve impairment and can be used for the therapeutic management of DPN.^{26,28}

Thus, vitamin D can play a protective role in DPN by reducing oxidative stress, facilitating nerve tissue repair, and maintaining calcium balance which will be a useful resource for managing and preventing DPN.

Diabetic nephropathy or diabetic kidney disease and vitamin D

Diabetic nephropathy is also known as diabetic kidney, and this is a condition in which deterioration of kidney function results from an increased excretion of urine albumin or a decreased glomerular filtration rate (GFR).²⁹ Several studies suggest that a low level of vitamin D can cause the overexpression of renin.³⁰ This overexpression can ultimately lead to the activation of the renin-angiotensin-aldosterone system (RAAS), which contributes to kidney damage.³⁰ Another possible way that a low level of vitamin D can cause diabetic kidney disease (DKD) is by progressing to kidney damage via renal fibrosis and impairing podocyte function, which leads to glomerular damage and proteinuria.^{31,32} Studies conducted by Zhang ZH et al. (2020) on animals have shown that vitamin D deficiency increases the levels of fibrogenic factors and collagen deposition, which promotes renal fibrosis.³² Therefore, managing vitamin D deficiency is essential in treating diabetic kidney disease.

Diabetic foot ulcer and vitamin D

The practical guidelines formulated by the International Working Group on the Diabetic Foot (IWGDF) defined diabetic foot ulcer (DFU) as symptoms secondary to current or previous diabetes, including skin chapping, ulceration, infection, or destruction of foot tissue.³³

Vitamin D helps in wound healing through its anti-inflammatory effects.^{16,34,35} Vitamin D receptor (VDR)

expression in wound margin tissues (T-VDR) is directly proportional to the level of vitamin D.³⁶ Decreased expression of T-VDR due to low levels of vitamin D in diabetic individuals is also a risk factor for the onset of DFU.³⁶ Vitamin D plays a crucial role in tissue restoration as well as the stimulation of antimicrobial peptides (AMPs) like cathelicidin and β defensin 2. This has been supported by the study conducted by Lowry MB et al. on a mouse model that demonstrated the effect of vitamin D on the expression of the human cathelicidin antimicrobial peptide gene expression.³⁷ Cathelicidin and β defensin 2 also participate in the wound healing process.³⁷ Thus, supplementation with vitamin D can increase the secretion of antimicrobial peptides making the affected foot healing process faster.^{37,38}

Furthermore, insufficient vitamin D levels hinder the angiogenesis process resulting in a lack of nutrients and oxygen supplied to the injury site. This leads to increased inflammation and oxidative stress, which hinder the tissue repair process and worsen the condition.³⁸ Therefore, addressing low vitamin D levels is necessary for the effective management of DFU in promoting wound healing and tissue repair which offers innovative approaches for managing DFU.

Diabetic retinopathy and vitamin D

Diabetic retinopathy (DR) is one of the common causes of vision loss among diabetic individuals.³⁹ Vitamin D plays a crucial role in regulating angiogenesis, which is the process of forming new blood vessels. In DR, abnormal neovascularization in the retinal tissue impairs vision.⁴⁰ In an animal model study done by Li et al., where vitamin D has been shown to reduce vascular endothelial growth factor (anti-VEGF) which decreases retinal vascular permeability and retinal capillary cell apoptosis.^{40,41} Additionally, in vitro model studies conducted by Lazzara et al., have also shown that the thioredoxin-interacting protein/ Nod-like receptor protein 3 (TXNIP/ NLRP3) pathway was activated due to increased reactive oxygen species (ROS) production induced by high glucose.^{40,42} Studies conducted by Li et al., Lazzara et al., and Tecilazich et al. have shown vitamin D can cause inhibition of the TXNIP/NLRP3 pathway and act as an anti-VEGF agent, which may serve as an effective marker of the progression, prevention, and treatment of DR.⁴⁰⁻⁴² Additionally, low vitamin D levels intensify inflammation and oxidative stress, leading to further retinal damage.^{42,43} Lower vitamin D levels correlate with higher DR incidence and severity among type 2 diabetes patients.^{44,45} Furthermore, the exact optimal vitamin D dosage for preventing DR by which vitamin D regulates angiogenesis and inhibits retinal damage in diabetic retinopathy, provides valuable insights for preventive and therapeutic interventions.^{41,45}

Conclusion

This literature review explores the associations between vitamin D and diabetes mellitus, emphasizing the potential of taking vitamin D supplementation to maintain optimal blood glucose levels, which can prevent and manage microvascular diabetic complications. However, further research is needed to determine the optimal dosage of vitamin D supplementation for effective prevention and management of diabetes-associated risks in individuals with diabetes mellitus. This study has the potential to highlight the crucial role of vitamin D in managing diabetes, which could significantly improve the quality of life for the millions of people affected by this condition.

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Conflicts of interest

All authors declare that they have no conflicts of interest.

Data availability

Data sharing not applicable – no new data generated.

References





- American diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2009;32(1):62-67. doi: 10.2337/dc09-S062
- Khan MAB, Hashim MJ, King JK, et al. Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends. *JEGH*. 2019;10(1):107. doi: 10.2991/jegh.k.191028.001
- Charoenngam N, Holick MF. Charoenngam N, Holick MF. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients*. 2020;12(7):2097. doi: 10.3390/nu12072097
- Bouillon R, Marcocci C, Carmeliet G, et al. Skeletal and Extraskelatal Actions of Vitamin D: Current Evidence and Outstanding Questions. *Endocrine Reviews*. 2018;40(4):1109-1151. doi: 10.1210/er.2018-00126
- Vijay GS, Ghonge S VSPD. Vijay GS, Ghonge S, Vajjala SM, Palal D. Prevalence of Vitamin D Deficiency in Type 2 Diabetes Mellitus Patients: A Cross-Sectional Study. *Cureus*. 2023;15(5):38952. doi: 10.7759/cureus.38952
- Wu Y DTYTZW. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. *Int J Med Sci*. 2014; 11(11):1185-1200. doi: 10.7150/ijms.10001
- Hu Z CJSXWLWA. Hu Z, Chen J, Sun X, Wang L, Wang A. Efficacy of vitamin D supplementation on glycemic control in type 2 diabetes patients: A meta-analysis of interventional studies. *Medicine (Baltimore)*. 2019;98(14):14970. doi: 10.1097/MD.00000000000014970
- Amrein K, Scherkl M, Hoffmann M, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr*. 2020;74(11):1498-1513. doi: 10.1038/S41430-020-0558-Y
- Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium, Ross AC, Taylor CL, Yaktine AL, Del Valle HB, eds. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington (DC): National Academies Press (US); 2011.
- Bikle DD. Bikle DD. Vitamin D: Production, Metabolism and Mechanisms of Action. In: Feingold KR, Anawalt B, Blackman MR, et al., eds. *Endotext*. South Dartmouth (MA): MD-Text.com, Inc.; December 31, 2021. Published online 2021.
- Dominguez LJ, Farruggia M, Veronese N, et al. Vitamin D Sources, Metabolism, and Deficiency: Available Compounds and Guidelines for Its Treatment. *Metabolites*. 2021;11(4):255. doi: 10.3390/metabo11040255
- Mostafa WZ, Hegazy RA. Mostafa WZ, Hegazy RA. Vitamin D and the skin: Focus on a complex relationship: A review. *J Adv Res*. 2013;6(6):793-804. doi: 10.1016/j.jare.2014.01.011
- Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr*. 2008;87(4):1080-1086. doi: 10.1093/ajcn/87.4.1080S
- Szymczak-Pajor I, Śliwińska A. Szymczak-Pajor I, Śliwińska A. Analysis of Association between Vitamin D Deficiency and Insulin Resistance. *Nutrients*. 2019;11(4):794. doi: 10.3390/nu11040794
- Aranow C. Aranow C. Vitamin D and the Immune System. *Journal of Investigative Medicine*. 2011;59(6):881-886. doi: 10.2310/jim.0b013e31821b8755
- Xiao Y, Wei L, Xiong X, et al. Association Between Vitamin D Status and Diabetic Complications in Patients With Type 2 Diabetes Mellitus: A Cross-Sectional Study in Hunan China. *Front Endocrinol*. 2020;11:564738. doi: 10.3389/fendo.2020.564738
- Zhao WJ, Xia XY, Yin J. Relationship of serum vitamin D levels with diabetic microvascular complications in patients with type 2 diabetes mellitus. *Chin Med J (Engl)*. 2021;134(7):814-820. doi: 10.1097/CM9.0000000000001364
- Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. *Biomark Insights*. 2016;11:95-104. doi: 10.4137/Bmi.s38440
- Cojic M, Kocic R, Klisic A, Kocic G. The Effects of Vitamin D Supplementation on Metabolic and Oxidative Stress Markers in Patients With Type 2 Diabetes: A 6-Month Follow Up Randomized Controlled Study. *Front Endocrinol (Lausanne)*. 2021;12:610893. doi: 10.3389/fendo.2021.610893

20. Contreras-Bolívar V, García-Fontana B, García-Fontana C, Muñoz-Torres M. Mechanisms Involved in the Relationship between Vitamin D and Insulin Resistance: Impact on Clinical Practice. *Nutrients*. 2021;13(10):3491. doi: 10.3390/nu13103491
21. Bislev LS, Grove-Laugesen D, Rejnmark L. Vitamin D and Muscle Health: A Systematic Review and Meta-analysis of Randomized Placebo-Controlled Trials. *J Bone Miner Res*. 2021;36(9):1651-1660. doi:10.1002/jbmr.4412
22. Dzik KP, Kaczor JJ. Mechanisms of vitamin D on skeletal muscle function: oxidative stress, energy metabolism and anabolic state. *Eur J Appl Physiol*. 2019;119(4):825-839. doi: 10.1007/s00421-019-04104-x
23. Girgis CM, Clifton-Bligh RJ, Hamrick MW, Holick MF, Gunton JE. The roles of vitamin D in skeletal muscle: form, function, and metabolism. *Endocr Rev*. 2013;34(1):33-83. doi: 10.1210/er.2012-1012
24. Feldman EL, Callaghan BC, Pop-Busui R et al. Diabetic neuropathy. *Nat Rev Dis Primers*. 2019;5(1):42. doi: 10.1038/s41572-019-0097-9
25. Putz Z, Tordai D, Hajdú N, et al. Vitamin D in the Prevention and Treatment of Diabetic Neuropathy. *Clin Ther*. 2022;44(5):813-823. doi: 10.1016/j.clinthera.2022.03.012
26. Zakhary CM, Rushdi H, Hamdan JA, et al. Protective Role of Vitamin D Therapy in Diabetes Mellitus Type II. *Cureus*. 2021;13(8):17317. doi: 10.7759/cureus.17317
27. Habib AM, Nagi K, Thillaiappan NB, Sukumaran V, Akhtar S. Vitamin D and Its Potential Interplay With Pain Signaling Pathways. *Front Immunol*. 2020;11:820. doi: 10.3389/fimmu.2020.00820
28. Ou Y, Liang Z, Yang Y, Zhou YK. Association of diabetic peripheral neuropathy with vitamin D levels depends on vitamin D status. *Med Sci Monit*. 2021;27:931244. doi: 10.12659/MSM.931244
29. Hussain S, Chand Jamali M, Habib A, Hussain MS, Akhtar M, Najmi AK. Diabetic kidney disease: An overview of prevalence, risk factors, and biomarkers. *Clin Epidemiol Glob Health*. 2021;9:2-6. doi: 10.1016/j.cegh.2020.05.016
30. Usluogullari CA, Balkan F, Caner S, et al. The relationship between microvascular complications and vitamin D deficiency in type 2 diabetes mellitus. *BMC Endocr Disord*. 2015;15(1):29. doi: 10.1186/s12902-015-0029-y
31. Zhang Y, Jin D, Kang X, et al. Signaling Pathways Involved in Diabetic Renal Fibrosis. *Front Cell Dev Biol*. 2021; 9:696542. doi: 10.3389/fcell.2021.696542
32. Zhang ZH, Luo B, Xu S, et al. Long-term vitamin D deficiency promotes renal fibrosis and functional impairment in middle-aged male mice. *Br J Nutr*. 2020;125(8):841-850. doi: 10.1017/s0007114520003232
33. Wang X, Yuan CX, Xu B, et al. Diabetic foot ulcers: Classification, risk factors and management. *World J Diabetes*. 2022;13(12):1049-1065. doi: 10.4239/wjd.v13.i12.1049
34. Wang F, Zhou L, Zhu D, Yang C. A Retrospective Analysis of the Relationship Between 25-OH-Vitamin D and Diabetic Foot Ulcer. *Diabetes, Metabolic Syndrome and Obesity*. 2022;15:1347-1355. doi: 10.2147/DMSO.S358170
35. Razzaghi R, Pourbagheri H, Momen-Heravi M, et al. The effects of vitamin D supplementation on wound healing and metabolic status in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial. *J Diabetes Complications*. 2017;31(4):766-772. doi: 10.1016/J.JDIACOMP.2016.06.017
36. Tang Y, Huang Y, Luo L, et al. Level of 25-hydroxyvitamin D and vitamin D receptor in diabetic foot ulcer and factor associated with diabetic foot ulcers. *Diabetol Metab Syndr*. 2023;15(1):30. doi: 10.1186/s13098-023-01002-3
37. Lowry MB, Guo C, Zhang Y, et al. A mouse model for vitamin D-induced human cathelicidin antimicrobial peptide gene expression. *J Steroid Biochem Mol Biol*. 2020;198. doi:10.1016/j.jsmb.2019.105552
38. Dai J, Jiang C, Chen H, Chai Y. Vitamin D and diabetic foot ulcer: a systematic review and meta-analysis. *Nutr Diabetes*. 2019;9(1):8. doi:10.1038/s41387-019-0078-9
39. Lee R WT, Sabanayagam C. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Eye and Vis*. 2015;2(1):17. doi: 10.1186/s40662-015-0026-2
40. Lu L, Lu Q, Chen W, et al. Vitamin D3 Protects against Diabetic Retinopathy by Inhibiting High-Glucose-Induced Activation of the ROS/TXNIP/NLRP3 Inflammasome Pathway. *Journal of Diabetes Research*. 2018;2018:1-11. doi: 10.1155/2018/8193523
41. Lazzara F, Longo AM, Giurdanella G et al. Lazzara F, Longo AM, Giurdanella G, et al. Vitamin D3 preserves blood retinal barrier integrity in an in vitro model of diabetic retinopathy. *Front Pharmacol*. 2022;13. doi: 10.3389/fphar.2022.971164
42. Tecilazich F, Formenti AM, Giustina A. Tecilazich F, Formenti AM, Giustina A. Role of vitamin D in diabetic retinopathy: Pathophysiological and clinical aspects. *Rev Endocr Metab Disord*. 2020;22(4):715-727. doi: 10.1007/s11154-020-09575-4
43. Fernandez-Robredo P, González-Zamora J, Recalde S, et al. Vitamin d protects against oxidative stress and inflammation in human retinal cells. *Antioxidants*. 2020;9(9):1-18. doi: 10.3390/antiox9090838
44. Luo BA, Gao F, Qin LL. Luo BA, Gao F, Qin LL. The Association between Vitamin D Deficiency and Diabetic Retinopathy in Type 2 Diabetes: A Meta-Analysis of Observational Studies. *Nutrients*. 2017;9(3):307. doi: 10.3390/nu9030307
45. Gverović Antunica A, Znaor L, et al. Vitamin D and Diabetic Retinopathy. *IJMS*. 2023;24(15):12014. doi: 10.3390/ijms241512014



REVIEW PAPER

Selected treatment methods for colloid milium – a literature review

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ABSTRACT

Introduction and aim. Colloid milium is a rare degenerative skin condition of unknown origin. Typically, it affects sun-exposed areas of the skin. Nevertheless, non-sun-exposed areas may also be affected. Clinically it presents with yellow or red papules, filled with gelatinous masses. There are four subtypes of colloid milium, each with its distinct characteristics: adult, juvenile, nodular, and pigmented. Although diagnosis is primarily clinical, skin biopsy and various staining techniques are required to exclude similar diseases. There is no single effective treatment for colloid milium. Most methods involve the use of lasers, dermabrasion, and oral medications. Yet, the final results differ.

Since this topic has not been addressed very frequently in recent literature, the purpose of this review is to present the currently available treatment methods for colloid milium.

Material and methods. A literature review was performed to identify the most efficient treatment approaches for colloid milium, focusing on their effectiveness in eliminating nodules and preventing recurrence.

Analysis of the literature. Due to its rarity and consequent lack of extensive scientific research, the number of available therapy options for colloid milium is limited. Commonly used treatment methods include lasers, oral medications, dermabrasion, and photodynamic therapy. Microablative fractionated CO₂ laser treatment resulted in complete ablation of the lesions with no recurrence. Non-ablative fractional resurfacing after multiple therapies led to the total elimination of the lesions, with no signs of reappearance during follow-up. Dermabrasion required a lengthy healing process. During follow-up no new papules were detected. After multiple sessions of treatment with MAL-PDT, the skin was devoid of nodules and recurrence was prevented. Following full recovery, treatment with the long-pulsed ER:YAG laser revealed the skin without any textural changes, scars, or pigmentation. During follow-up, no new papules were reported. Oral medication provided insignificant results. The majority of patients undergoing these procedures did not need preparation or analgesia. However, non-ablative fractional resurfacing required topical analgesia with 30% lidocaine gel, long pulsed Er:YAG laser treatment demanded intravenous sedation, and dermabrasion involved axillary block analgesia. None of the procedures provoked adverse effects.

Conclusion. Skin lesions caused by colloid milium may provoke esthetic concerns, prompting patients to remove them. However, available treatments methods are limited and yield varying outcomes. Among the prominent procedures are microablative fractionated CO₂ laser, non-ablative fractional resurfacing, long pulsed ER:YAG laser, and treatment with MAL-PDT, which led to complete ablation, required minimal convalescence time, and provided long-lasting remission. Dermabrasion displayed partial results, with no observed relapse of colloid milium during follow-up. Oral treatment presented the least significant results. Further research is necessary in order to develop new treatment methods for colloid milium that are safe, effective, and affordable.

Keywords. adult colloid milium, colloid milium, colloid milium treatment, juvenile colloid milium, juvenile colloid milium treatment

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Introduction

Colloid milium (CM), alternatively referred to as colloid degeneration of the skin or dermal hyalinosis, is a rare degenerative dermatological condition with an unknown origin.^{1,2} It is characterized by the deposition of colloid in the cutis, particularly in sun-exposed areas such as the face, neck, cheeks, dorsum of hands, forearms, back, nose, and ear.^{1,3,4} However, colloid milium may also affect the non-sun-exposed areas, such as the oral cavity, the inner part of the tragus, the eyelid margins, trunk and penis.⁵⁻¹⁰ Microscopic examination reveals homogenous and amorphous eosinophilic masses in the dermis.¹¹⁻¹³ Clinically, it presents with 0.5–5 mm amber, flesh-colored, or yellow papules and pseudo vesicles, from which a mucoid or gelatinous fluid can be expressed with gentle pressure or puncture.^{2,4,12,14,15} Any injury to the skin lesions may lead to the development of purpura.^{10,16} There are typically four subtypes of CM, each with distinct etiologies and origins: adult colloid milium (ACM), juvenile colloid milium (JCM), nodular, and pigmented.^{17,18} The ACM occurs between the ages of 30 and 50. It affects more males than females, with a ratio of 4:1, and is thought to be caused by the destruction of the elastic fibers.^{1,2} The JCM is associated with the degeneration of UV-transformed keratinocytes, which results in formation of deposits in the dermis and epidermis.^{4,19} The literature suggests that a juvenile subtype might be inherited (familial JCM) in an autosomal recessive or dominant pattern, and can present before puberty.²⁰⁻²² Chemicals and toxins such as petroleum and hydroquinone may contribute to the pigmented subtype of CM.^{23,24} The nodular subtype can be observed in older patients.¹⁸ Some authors recognize an additional subtype - acral keratosis with eosinophilic dermal deposits (AKEDD), which is extremely rare.¹³ In reports by Abalos-Babaran et al. from 2019 and Azzazi et al. from 2023, there is a correlation between CM and vitamin C deficiency, trichinosis, and beta-thalassemia. However, this connection remains controversial.^{25,26} Colloid milium may be confused with amyloidosis, sarcoidosis, Favre-Racouchot disease, trichoepitheliomas, syringomas, sebaceous hyperplasias, common milium, molluscum contagiosum, steatocystoma multiplex, papular mucinosis, lipid proteinosis, senile sebaceous hyperplasia, and retention cyst. Therefore, the key to diagnose dermal hyalinosis is to perform a full-thickness skin biopsy.^{11,15,17} Staining with crystal violet, hematoxylin and eosin (H&E), periodic acid-Schiff (PAS), and Congo red is crucial to make colloid masses visible.^{10,27} Figure 1 illustrates colloid depositions alongside solar elastosis within the cutis.²⁷ While, a patient's history is helpful in making a diagnosis.²⁸ Since adult colloid milium is infrequent, there is currently no effective treatment for it.^{9,29} Systemic ascorbic acid or exfoliative products have proven ineffective. Even topical retinoids

in combination resulted in insignificant cosmetic outcome.^{4,10} Case reports present various approaches to management of CM.²⁹ These methods incorporate the use of topical retinoids, creams containing urea, cryotherapy, chemical peels, oral medications, microablative fractionated CO₂ laser, non-ablative fractional resurfacing, dermabrasion, long-pulse Er: YAS laser treatment, and methyl aminolevulinate photodynamic therapy.^{29,30-32}

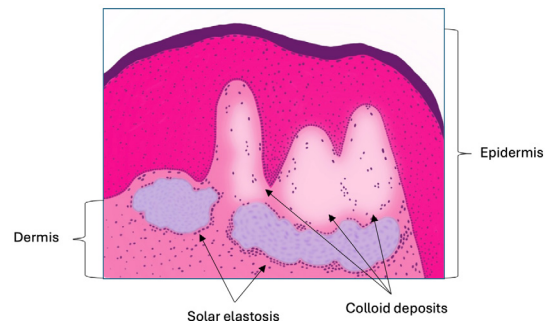


Fig. 1. Visualization of colloid milium within the skin tissue²⁷

Aim

The objective of this literature review is to present and evaluate the efficacy of contemporary treatment methods for colloid milium.

Material and methods

This review was conducted using electronic databases, including PubMed, Medline, Elsevier, and Google Scholar, to search for articles presenting treatment methods for colloid milium. We utilized the following keywords: “Colloid milium”, “Adult colloid milium”, “Juvenile colloid milium”, “Colloid milium treatment”, “Juvenile colloid milium treatment”. Articles were selected based on their relevance to the subject. The inclusion criteria consisted of literature reviews, case reports, and histochemical studies written in English. We excluded abstracts, duplicates, and irrelevant articles.

The initial exploration, applying the described keywords and criteria, yielded a total of 115 publications. Subsequently, duplicates and irrelevant publications were removed. Fig.2 demonstrates the inclusion and exclusion criteria used in this process. Afterward, 52 identified manuscripts underwent a thorough examination, resulting in the selection of 36 articles (31 case reports (9 depicting treatment methods, 22 with none or insufficient treatment description, yet displaying significant diagnostic value), 4 review articles, and 1 histochemical study) to be included in this literature review. The array of available therapy options for colloid milium is constrained by its rarity and the consequent lack of extensive scientific research. The described treatment approaches were chosen based on their accessibility as well

as their efficacy in both eliminating existing lesions and preventing recurrence.

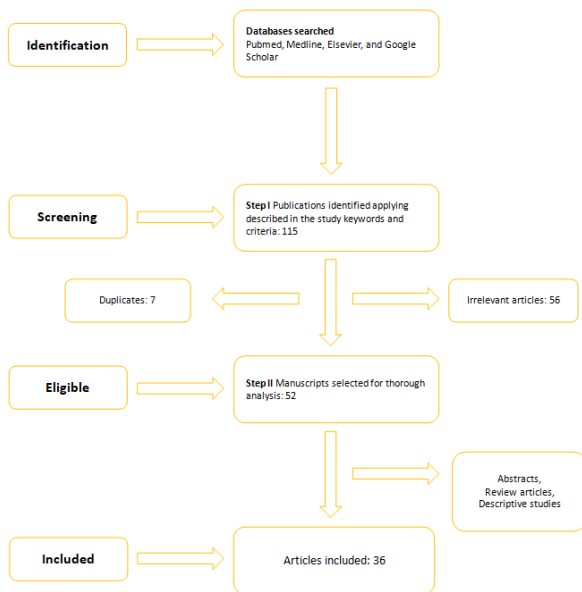


Fig. 2. A flow chart illustrating the process of literature research

Analysis of the literature

Based on the literature, in this review we are going to focus on the selected methods for treating colloid milium, including microablative fractionated CO₂ laser, non-ablative fractional resurfacing, long pulsed Er:YAG laser, oral treatment, dermabrasion, and photodynamic treatment with methylaminolevulinic acid (MAL-PDT). Table 1 illustrates the summary of presented treatment methods.^{5,25,29,31-36}

Microablative fractionated CO₂ laser

In a 2013 case report by Li et al. a 33-year-old male patient, presented with yellow papules measuring 1–5 mm in size on the forehead, jowl, nose, and lips. The patient experienced pruritus and discharge upon pressing the lesions. Histopathological examination revealed the presence of gelatinoids and horizontal fissuring enclosed by the solar elastosis. Cells with a hyaline composition within horizontal clefts and a wavy appearance distinguished it from amyloidosis. Following the diagnosis of CM, he received treatment with a microablative fractionated CO₂ laser (Lumens Ltd, Santa Clara, CA, USA) emitting at a wavelength of 10600 nm. The utilized parameters were: shape 3 (square), size 4, density 7, energy 125 mJ and frequency 200 Hz with pulse delay of 0.3 seconds. Along with laser treatment a test patch was performed on the patient's forehead. The whole procedure involved eight ablations until residual fluid emerged and was removed. The lesions were then cleared with gauze. After 4 days, the patient's forehead appeared smooth and devoid of lesions, with no

additional papules observed on the skin. During the 3-month follow-up, no new lesions were reported on the treated area, and no side effects were detected. Good cosmetic results were achieved.³²

In a 2019 case report by Abalos-Babaran et al. a 65 year old female patient, suffering from chronic kidney disease, presented with a 6 month history of yellow papules on her eyelids, periorificial area, concha of both ears, and in the oral cavity. Following punch biopsies of the lesions and revealing in the histopathologic examination depositions of amorphous, pale, homogeneous eosinophilic material; atrophic epidermis with a thin grenz zone; along with elastosis in the dermis and inflammatory infiltrate enclosing the eosinophilic deposits, the female was diagnosed with CM. Initially, the patient was prescribed a tretinoin cream with a concentration of 0.025% to be applied on her entire face at night. During the daytime, she was instructed to use sun protection with SPF 30. Subsequently, the patient underwent lesion ablation on her face using a microablative fractionated CO₂ laser, with a wavelength of 10600 nm. Two modes of this laser were employed: fractional active mode, size square, delivering energy of 300mJ, with a depth level of 5um for the periorbital area, which is layered with thinner skin and thus prone to purpura, and surgical mode for the perinasal and perioral areas. The results were assessed after two weeks. The periorbital area exhibited slight thinning of the plaques with complete re-epithelialization. A significant improvement was observed in the perinasal and perioral areas, where the skin lesions were completely ablated.²⁵

Non-ablative fractional resurfacing

In a 2007 case report by Marra et al. a 54-year-old male patient presented with yellow plaques and pseudovesicles on his cheek. Histopathology displayed eosinophilic hyalinized depositions in the papillary dermis, with positive Congo red staining. He was diagnosed with CM and underwent a series of fractional resurfacing treatments using a commercially available non-ablative 1550 nm diode-pumped erbium fiber laser (Fraxel, Reliant Technologies, Palo Alto, Calif). The device operates via photothermolysis, generating an array of extremely thin microscopic dermal zones, reaching depths ranging from 400 to 700 um and having a diameter of 100 um. This process induces a column of thermal damage, leading to collagen denaturation within the treated area. Before treatment, a tracking dye was applied, followed by a 30% lidocaine gel, which was left in place for about an hour. In total, 5 sessions were performed, with intervals of 2 to 3 weeks between each session. The laser parameters: fluence 20mJ, 125 microthermal zones per square centimeter, with 10 to 12 passes applied, delivering 1.6 to 2.1 kJ energy per session. Overall, the patient responded well to the therapy. However, there were no

remarkable changes after the first and second sessions. The changes began to occur after the third treatment. After the last (fifth) procedure, the patient's skin surface improved significantly, leaving it completely clear.³³

In a 2014 case report by Zeng et al. a 58-year-old female patient presented with asymptomatic yellow plaques on her face. Histopathological findings presented deposits of amorphous and fissured material in the sub-epidermis, as well as epidermal thinning. Congo red staining was negative. The patient was diagnosed with ACM and underwent treatment with a non-ablative 1550 nm wavelength erbium-glass fractional laser system (Sellas, Dinona Inc. Seoul, South Korea). The machine was set to a density of 100 MTZ/cm² along with a fluence of 80 mJ/cm². The affected area was covered with 4 to 5 passes during each session. A total of 5 sessions were performed to achieve the final results. The improvement in the skin condition was significant. After 6 months, there was no recurrence.²⁹

Long Pulsed Er:YAG Laser

In a 2002 case report by Ammirati et al. a resurfacing long-pulsed Er:YAG laser (CO₂) with a wavelength of 2940 nm that has a higher affinity to water than the CO₂ laser, is absorbed readily by collagen, and creates zones of thermal damage ranging from 40 to 60 µm, was used on a 41 year old male patient who presented with extensive 1–5 mm yellow papules on his forehead, nose, cheek, temples, chin, and lower lip. Histological examination revealed hyalinized depositions inside the papillary dermis and solar elastosis, leading to CM diagnosis. Before the procedure, a test area on the left temple was treated. Thereafter, the treatment area was locally anesthetized with 1% lidocaine plus epinephrine 1:100,000. The laser parameters used were: a dozen passes at 8.5 J/cm² with 4 msec pulse duration and a 5 mm spot size. These parameters resulted in the ablation of up to 80% of the affected skin areas. The procedure concluded with covering the treated area with Second Skin (Spenco Medical Co. Waco, TX) for 48 hours. Subsequently, the skin was washed three times a day with acetic acid compress (concentration 0.25%) followed by application of Aquaphor healing ointment (Beiersdorf, Wilton, CT). A patch test conducted earlier resulted in completely epithelialized skin after 10 days. No signs of scars, textural changes or pigmentation were seen. At the 6 month follow-up, there was no recurrence. Thus, the patient opted for another full face resurfacing, this time under deep intravenous sedation. Preparation for the operation involved the use of tretinoin cream with a concentration of 0.5% for 6 weeks. Additionally, on the day of surgery, he commenced oral dicloxacillin 250 mg twice a day for 7 days, valacyclovir 500 mg twice a day for 20 days, and prednisone 60 mg, tapering to 20 mg over 4 days. The same laser was utilized, with different param-

eters – a CO₂ laser at 9.8 J/cm² with a 5 mm spot and 10 msec pulse duration to increase the homeostasis. Initially, the entire facial skin was resurfaced with 50% overlapping passes. Then, the CO₂ laser was focused on the most affected areas, which led to ablation of 80% of the lesions with at least 10 passes. Moderate bleeding from deeper wounds was observed and managed by applying a gauze soaked in a combination of 1% lidocaine plus epinephrine 1:100,000 and aluminum chloride solution. Post operative wound care included applying Silon TSR (BioMed Sciences, Bethlehem, PA) for 3 days, followed by a compress of 0.25% acetic acid with Aquaphor healing ointment three times a day. Overall, the patient's recovery was smooth and uneventful. Complete epithelialization of the skin was achieved within 14 days. The patient was instructed to use sun protection regularly. At the 7 months follow-up examination, there were no signs of scarring, textural changes, or reappearance of CM. Moreover, a patch test performed on the left temple 13 months after the procedure showed no signs of hypopigmentation or recurrence.³⁴

Oral treatment

Instances of colloid milium in the oral cavity are very rare. There are only a few documented reports describing this condition. In a 2008 case report by Ojha et al. an 83-year-old male patient presented with 1-2 mm nodules in the oral cavity and concomitant papules on the left side of his face. The lesions manifested as nodule-shaped formations located submucosally, affecting his lower lip and the borders of the tongue. The lesions were tender to touch, giving him a painful sensation. Histopathological examination displayed amorphous eosinophilic deposits. Congo red staining was negative. PAS staining for eosinophilic material was positive. Following the diagnosis of CM, the man was prescribed a topical ointment for use within the oral cavity. The cream contained fluocinonide (Lindex) in a concentration of 0.05% with Orabase. Surgical procedures were also considered. However, the patient did not attend the next appointment. Consequently, the efficacy of this oral treatment remains unknown.⁵

In a 2019 case report by Voicu et al. a 10 year old boy presented with multiple 2-5 mm skin lesions on his nose, cheeks and upper lip. Histopathology revealed papillary findings with amorphous eosinophilic masses, along with thinning of the epidermis, and dilated capillary vessels. Congo red staining was negative. PAS staining was positive. The patient was diagnosed with JCM and treated with oral medications. He was recommended to apply sunscreen and take 250 mg of vitamin C daily. Upon reevaluation during the subsequent visit, there was slight improvement noted in his skin condition. Still, the changes were not significant. No new papules were observed during the follow-up examination.³¹

Table 1. Summary of described treatment methods^{*,5,25,29,31-36}

Paper	Age/Gender	Location of lesions	Family history	Clinical presentation	Histological aspects	Size (cm)	Treatment method	Use of anesthesia	Time until effects appear	Outcome
Li et al.	33/M	Forehead, nose, lips, jowl	Negative	Yellow spots, pruritus, and discharge after pressing the lesions	Hyaline masses, upper dermis and dermal papilla layer composed of gelatinous fissure and solar elastosis	1–5 mm	Microablative fractionated CO ₂ laser	N/A	4 days	Complete ablation of lesions, no recurrence during a 3 month follow-up
Babaran et al.	65/F	Eyelids, periorbital area, concha of both ears, oral cavity	N/A	Multiple yellow papules and plaques, hemorrhage on the left periorbital plaque	In H&E staining, deposits of amorphous, homogenous, pale eosinophilic material, atrophic epidermis with a thin grenz zone, elastosis in the dermis and inflammatory infiltrate around the eosinophilic deposits	N/A	Microablative fractionated CO ₂ laser	N/A	2 weeks	Subtle thinning of the plaques with re-epithelialization on the periorbital area. In the perinasal and perioral areas complete ablation of lesions
Marra et al.	54/M	Cheeks	Negative	Large yellow plaques, pseudovesicular lesions	Biopsy exposed eosinophilic hyalinized deposits inside the papillary dermis, staining with Congo red was positive	N/A	Non-ablative fractional resurfacing	30% lidocaine gel	After the third session.	Completing 5 therapies left skin with no visible lesions
Zeng et al.	58/F	Face	Negative	Yellow colored papules	Thinning of the epidermis, amorphous and fissured material in sub-epidermis, staining with Congo red was negative	N/A	Non-ablative fractional resurfacing	No needed	After 5 treatments	6 months after the last procedure, the face was lesions-free without any new changes
Ammirati et al.	41/M	Forehead, temples, nose, lower lip, cheeks, chin	Negative	Solid amber colored papules	Punch biopsy exhibited hyalinized masses within the papillary dermis, near the deposits, the solar elastosis was found	1–5 mm	Long Pulsed Er:YAG Laser	Local utilization of 1% lidocaine and epinephrine. Subsequently a deep intravenous sedation was performed	6 months after the first procedure	After the full recovery the skin was free of textural changes, without any scars and dyspigmentation, no new papules were reported
Ojha et al.	83/M	Face, oral cavity within the submucosa	Negative	Few lesions on the face, white to yellow nodules on the lower lip and tongue	Amorphous and eosinophilic masses, Congo red staining was negative, PAS staining for eosinophilic material was positive	1–2 mm	Oral treatment	No needed	The patient did not show up at the follow-up	The patient did not show up at the follow-up
Voicu et al.	10/M	Nose, upper lip, cheek	Negative	Pellucid papules	Papillary findings filled with eosinophilic and amorphous cells-free masses, dilated capillary vessels were observed. Congo red staining was negative, staining with PAS was positive	2–5 mm	Oral treatment	No needed	1 month	Minor skin changes at the next visit, no sign of new lesions reported
Apfelberg et al.	47/M	Face, neck, hands	Positive	Translucent papules followed by pseudovesicles	Assemble of eosinophilic deposits, staining with PAS was positive	1–3 mm	Dermabrasion	Axillary block anesthesia	After 12 months	No relapse of colloid milium
Gomes et al.	55/M 47/M	Temples, nose, cheeks	Positive	Firm lesions characterized by yellow or translucent structure	Homogeneous findings, slightly eosinophilic	N/A	Treatment with MAL-PDT	No needed	First patient after 2 sessions, second patient after 3 extra sessions	Skin was free of lesions. No new papules developed after 1 year

*F – female, M – male, N/A – not available

Dermabrasion

In a 1978 case report by Apfelberg et al. a 47-year-old male patient presented with 1-3mm translucent papules and pseudovesicles on his face, neck and hands. Biopsies displayed eosinophilic deposits. PAS staining was positive. A rotary-powered Stryker unit with a diamond burr was used on the patient's hand under axillary block anesthesia and induced ischemia by a tourniquet. The healing process took about 14 days. After 12 months, no new skin lesions were detected.³⁵

Treatment with MAL-PDT

In a 2012 case report by Gomes et al. a 55-year-old male and his 47 year old brother presented with similar asymptomatic yellow papules on their faces. Histological examination exhibited slightly eosinophilic homogeneous masses corresponding to CM in both cases, observed in the papillary dermis. Several treatment methods were performed on both patients to address the papules on the nose, temples and cheekbones. The initial approach involved cryotherapy and photoprotective creams, but yielded unsatisfactory results. The next step included the utilization of topical photodynamic therapy (PDT). Prior to the PDT procedure, patients underwent a superficial curettage. Subsequently, a cream containing 160 mg/g of MAL (Metvix®, Galderma, Portugal) was applied to the skin and covered with an adhesive occlusive bandage for three hours. Following this, red light illumination was administered with an Aktelite® CL 128 lamp (PhotoCure ASA, Oslo, Norway). The lamp emits light with an average wavelength of 635 nm and delivers light at a dosage of light of 37 J/cm². Two PDT treatments, administered 7 days apart, led to the complete resolution of the lesions. During irradiation, the patients experienced a mild burning sensation. However, this did not necessitate the cessation of the procedure. No adverse effects, such as swelling or blistering, were observed. At a follow-up visit after one year, no relapse was reported.³⁶

Conclusion

Colloid milium is an infrequent skin condition with unknown origin. Typically, patients who develop CM have a history of prolonged exposure to sunlight, such as working outdoors on a farm or as a driver. Those exposed to chemical compounds like petroleum or hydroquinone may also develop colloid milium. While most cases of CM involve adult patients, there is some evidence of its occurrence among juveniles as well. The JCM is claimed to be inherited. The majority of skin lesions appear in sun-exposed skin areas. However, the oral cavity or tragus may also be affected. Colloid milium is not a fatal disease, but it can lead to esthetic and cosmetic concerns, prompting individuals to eliminate the papules. Treatment options for this condition are based on a few

case reports and systematic reviews. Therefore, there is no simple solution to eliminate the CM. Most databases include laser treatments, oral medications, or dermabrasion. The highest efficacy in removing lesions and preventing recurrence over time was achieved with the use of microablative fractionated CO₂ laser, non-ablative fractional resurfacing, dermabrasion, and treatment with MAL-PDT. Patients experienced remarkable outcomes, resulting in smooth skin with no visible or new lesions, and requiring a short time of convalescence. Post-treatment skincare was easy to abide or even unnecessary, and no adverse effects were reported. Satisfactory results were also obtained with the use of a long-pulsed Er:YAG laser. Nevertheless, it's worth noting that in this particular case report by Ammirati et al. the patient underwent intravenous sedation, which could pose a contraindication for certain patients.³⁴ The least effective treatment was found to be oral medication. Although it is an accessible and cost-effective solution, a case report by Voicu et al. demonstrated that its effects are minimal and might not be satisfactory.³¹ Some patients were advised to use sunscreen to minimize the influence of UV light on the skin and the development of skin lesions. However, there isn't much data on this information and further research must be conducted. The main disadvantage of the most effective solutions, such as laser treatments, dermabrasion, and MAL PDT, is their high cost. Therefore, they are less accessible to a vast majority of people. Consequently, there is a necessity to develop treatment methods for colloid milium that are not only effective and safe but also affordable.

Declaration

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Author contributions

Conceptualization, Ł.C. and M.P.; Methodology, M.P.; Software, A.K.; Validation, Ł.C., M.P. and J.F.; Formal Analysis, A.K.; Investigation, Ł.C., M.P., A.K. and J.F.; Resources, M.P., A.K. and J.F.; Data Curation, Ł.C.; Writing – Original Draft Preparation, Ł.C., M.P. and J.F.; Writing – Review & Editing, Ł.C., M.P., A.K. and J.F.; Supervision, Ł.C.; Project Administration, Ł.C., M.P., A.K. and J.F.

Conflict of interest

The authors declare no conflicts of interest.

Data availability

Not applicable.

References

1. Siadat AH, Mokhtari F. Colloid milium. *Adv Biomed Res.* 2013;2:28. doi:10.4103/2277-9175.107996

2. Shenoy T, Harber I, Cruse A, Brodell R. Adult colloid milium is clinically distinguishable from its histopathologic mimic cutaneous amyloidosis. *Dermatol Online J*. 2021;27(7):3. doi:10.5070/D327754362
3. Zamora A, Simon M, Sánchez AT, Olivera RM. Adult colloid milium. An underdiagnosed and difficult to treat entity. *Revista Médica Del Hospital General De México*. 2016;79(1):21-25. doi: 10.1016/j.hgmx.2015.10.002
4. Azimi SZ, Zargari O, Rudolph RI. Nodular colloid milium mimicking keloid. *J Cosmet Dermatol*. 2017;16(4):45-47. doi: 10.1111/jocd.12325
5. Ojha J, Bhattacharyya I, Islam N, Wong F, Cohen DM. Colloid milium of the oral cavity: a rare presentation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105(4):34-38. doi: 10.1016/j.tripleo.2007.11.032
6. Lim C, Li M. Colloid milium arising on a non-sun-exposed area in an adult. *Australas J Dermatol*. 2006;47(2):137-138. doi: 10.1111/j.1440-0960.2006.00245.x
7. Muzaffar W, Dar NR, Malik AM. Colloid milium of the upper eyelid margins. *Ophthalmology*. 2002;109(10):1944-1946. doi: 10.1016/s0161-6420(02)01180-6
8. Safneck JR, Quinonez G, Wiens J. Adult colloid milium of the eyelid. *Am J Ophthalmol*. 1997;123(3):402-403. doi: 10.1016/s0002-9394(14)70140-0
9. Dávila-Rodríguez JJ, Aguilar-Benavides K, García L. Colloid milium, an expression of excessive sun exposure in Ecuadorian patients. *Int J Dermatol*. 2019;58(4):80-82. doi: 10.1111/ijd.14384
10. Oskay T, Erdem C, Anadolu R, Peksan Y, Özsoy N, Gül N. Juvenile colloid milium associated with conjunctival and gingival involvement. *J Am Acad Dermatol*. 2003;49(6):1185-1188. doi: 10.1016/s0190-9622(03)00457-2
11. Figini M, De Francesco V, Finato N, Errichetti E. Dermoscopy in adult colloid milium. *J Dermatol*. 2020;47(4):127-128. doi: 10.1111/1346-8138.15232
12. Osorio-Aragón I, Salazar Del Valle JJS, Valle GIQ, Arenas R, Vega-Memije ME. Acral Lesions With a Nodular Appearance: A Case Report Illustrating a Complex Differential Diagnosis. *Actas Dermosifiliogr*. 2023;114(5):452-455. doi: 10.1016/j.ad.2021.08.018
13. Boyd AS, Cleary LC. Acral Keratosis with Eosinophilic Dermal Deposits: A Rare Subtype of Colloid Milium. *J Cutan Pathol*. 2022;49(6):557-559. doi: 10.1111/cup.14198
14. Graham JH, Marques AS. Colloid milium: a histochemical study. *J Invest Dermatol*. 1967;49(5):497-507. doi: 10.1038/jid.1967.170
15. Kırtak N, İnalöz HS, Karakök M, Özgöztaş O. A case of adult colloid milium with chronic sun exposure. *Int J Dermatol*. 2002;41(12):936-938. doi: 10.1046/j.1365-4362.2002.01664_2.x
16. Lewis AT, Le EH, Quan LT, Krishnan B, Schulmeier J, Hsu S. Unilateral colloid milium of the arm. *J Am Acad Dermatol*. 2002;46(2):5-7. doi: 10.1067/mjd.2002.104965
17. Piccolo V, Russo T, Ossola M, Ferrara G, Ronchi A, Argenziano G. Colloid milium: the expanding spectrum of orange color at dermoscopy. *Int J Dermatol*. 2018;57(8):46-48. doi: 10.1111/ijd.14062
18. Krishnaram A, Geetha TS, Sriram CK, Shibani MI, Priya SS. Pinch Purpura in Adult Colloid Milium-A Case Report. *Indian Dermatol Online J*. 2023;14(4):521. doi: 10.4103/idoj.idoj_466_22
19. Martorell A, Balmer N, Sanmartin O, Botella-Estrada R, Requena C, Guillen-Barona C. Familial juvenile colloid milium: Report of a well documented case. *J Am Acad Dermatol*. 2011;64(1):203-206. doi: 10.1016/j.jaad.2009.06.051
20. Ekmekci T, Köşlü A, Sakiz D. Juvenile colloid milium: a case report. *JEur Acad Dermatol Venereol*. 2005;19(3):355-356. doi: 10.1111/j.1468-3083.2005.01110.x
21. Giordano G, Ricci R, Froio E, Izzi G, Barone A, Boccaletti V. A case of colloid milium in patient with beta thalassaemia major. *J Cutan Pathol*. 2008;35(6):566-569. doi: 10.1111/j.1600-0560.2007.00834.x
22. Alshami M. Unusual Manifestations of Familial Juvenile Colloid Milium in Two Siblings. *Pediatr Dermatol*. 2016;33(3):201-203. doi: 10.1111/pde.12854
23. Gudiño SA, López AJF, Orozco MS, Martínez AYP, Padilla MR. Severe colloid milium presenting as papillomatosis cutis associated with vitiligo. *Int J Dermatol*. 2017;56(8):878-880. doi: 10.1111/ijd.13681
24. Gönül M, Cakmak SK, Kılıç A, Gül Ü, Heper AO. Pigmented coalescing papules on the dorsa of the hands: Pigmented colloid milium associated with exogenous ochronosis. *J Dermatol*. 2006;33(4):287-290. doi: 10.1111/j.1346-8138.2006.00069.x
25. Abalos-Babaran S, Cubillan ELA. A Case of Mucocutaneous Colloid Milium in an Adult Filipino Female with Chronic Kidney Disease. *Acta Med Philipp*. 2019;53(4):374-378. doi: 10.47895/amp.v53i4.25
26. Azzazi Y, Khedr H, Abdel-Halim MRE. Pigmented colloid milium in a beta-thalassemia major patient: a case report. *Int J Dermatol*. 2023;62(12):626-628. doi: 10.1111/ijd.16819
27. Touart DM, Sau P. Cutaneous deposition diseases. Part I. *J Am Acad Dermatol*. 1998;39(2):149-171. doi: 10.1016/s0190-9622(98)70069-6
28. Mehregan D, Hooten J. Adult colloid milium: a case report and literature review. *Int J Dermatol*. 2011;50(12):1531-1534. doi: 10.1111/j.1365-4632.2010.04737.x
29. Zeng Y, Nguyen GH, Fang K, Jin H. A split-face treatment of adult colloid milium using a non-ablative, 1550-nm, erbium-glass fractional laser. *J Eur Acad Dermatol Venereol*. 2016;30(3):490-491. doi: 10.1111/jdv.12874
30. Tierney E, Kouba DJ, Hanke CW. Review of fractional photothermolysis. *DermatolSurg*. 2009;35(10):1445-1461. doi: 10.1111/j.1524-4725.2009.01258.x
31. Voicu C, Lisievici C, Coman C, Tebeică T. Juvenile Colloid Milium: Case Report and Literature Review. *Maedica*. 2019;14(2):173-178. doi: 10.26574/maedica.2019.14.2.173
32. Li Y, Ying L, Wu Y, et al. Infrared-induced adult colloid milium treated with fractionated CO2 laser. *Dermatol Ther*. 2014;27(2):68-70. doi: 10.1111/dth.12056

33. Marra DE, Pourrabbani S, Fincher EF, Moy RL. Fractional Photothermolysis for the Treatment of Adult Colloid Milium. *Arch Dermatol*. 2007;143(5):572-574. doi: 10.1001/archderm.143.5.572
34. Ammirati CT, Giancola JM, Hruza GJ. Adult-Onset Facial Colloid Milium Successfully Treated with the Long-Pulsed Er:YAG Laser. *Dermatol Surg*. 2002;28(3):215-219. doi: 10.1046/j.1524-4725.2002.01133.x
35. Apfelberg DB, Druker D, Spence B, Maser MR, Lash H. Treatment of colloid milium of the hand by dermabrasion. *J Hand Surg Am*. 1978;3(1):98-100. doi: 10.1016/s0363-5023(78)80124-5
36. Gomes JÁP, Ventura F, Da Luz Duarte M, Brito C. Colloid milium successfully treated with MAL-PDT. *Int J Dermatol*. 2012;52(6):767-769. doi: 10.1111/j.1365-4632.2011.04980.x



REVIEW PAPER

Acne vulgaris during pregnancy – management ensuring both maternal and fetal safety

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ABSTRACT

Introduction and aim. Acne vulgaris represents a condition commonly encountered by women during pregnancy. However, its treatment becomes particularly demanding when occurring during gestation. The aim of this review is to present multiple strategies for management of acne in pregnant women, prioritizing both maternal and fetal safety.

Material and methods. Review and analysis of the scientific literature available in November and December 2023.

Analysis of literature. The study describes commonly used topical treatments and oral medications emphasizing difficulty and responsibility of assessing the safety of drug use during pregnancy. Apart from that, the importance of skin care is stressed with a focus on usage appropriate to the condition and pregnancy-safe cosmetics. The influence of diet and physical activity on acne development is also underlined, as well as the significant association between acne and mental health.

Conclusion. Dealing with acne during pregnancy might be difficult; however, there are effective and safe acne treatments suitable for pregnant women, along with various supportive approaches. Considering above, the authors highlight a holistic nature of acne management that includes not just medication but also procedural interventions, skin care practices, diet, physical activity, and psychological support.

Keywords. acne vulgaris, dermatology, pregnancy

Introduction

Acne vulgaris is a chronic inflammatory skin condition frequently encountered by women during pregnancy. It is estimated that up to 42% of gravidas suffer from acne and the vast majority of them had the condition pre-existing before pregnancy.^{1,2} The clinical manifestation of the disease includes different types of skin lesions. These can be classified into primary non-inflammatory lesions (microcomedones, closed comedones, open

comedones), secondary inflammatory lesions (papules, pustules, nodules, cysts, abscesses), as well as post-inflammatory lesions and scars. The severity of acne may differ, starting as isolated scattered comedones and very few papules and pustules up to more intense inflammatory changes with the presence of nodules or cysts.³

During pregnancy, acne tends to be inflammatory and spreads to the trunk region,⁴ however its severe form is typically rare during this period.⁵ Interestingly, throughout gestation, the intensity of acne can either

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escalate, alleviate, or remain unchanged, but the exact mechanisms by which pregnancy modifies its course in individual cases remain unclear.⁶ Nevertheless, it is noted that due to heightened maternal androgen levels affecting sebum production acne tends to aggravate in the third trimester.⁷ Besides hormonal changes, immunologic and metabolic factors associated with pregnancy may also contribute to the development of acne during this period.⁷⁻⁹

Even though sometimes trivialized as a purely cosmetic issue, acne exerts a substantial impact on the well-being and social interactions of individuals.⁶ Moreover, combination of physiologic changes in female's bodies and rather difficult to predict character of the acne during pregnancy may be especially aggravating.⁹ Unfortunately, while there is a broad range of pharmacological possibilities for treating acne vulgaris, the options become more limited when dealing with this condition during pregnancy, primarily due to the potential risks to the developing fetus.⁶ Therefore treatment of acne in this situation can be challenging and the absence of sufficient clinical studies on the safety and effectiveness of common acne medications during gestation also complicates the decision-making process.⁴

Aim

Management of acne vulgaris should focus on mitigating and resolving skin lesions, preventing their consequences like scarring and discoloration, and concurrently enhancing the patient's quality of life.³ In this review, we discuss various approaches to the management of acne in pregnant women, ensuring both maternal and fetal safety. However, our publication emphasizes that the therapeutic approach should extend beyond pharmacological interventions, incorporating dermatological procedures, appropriate daily skincare routines, dietary considerations, physical activity, and essential psychological support. In other words – we underscore the holistic nature of acne management during pregnancy, recognizing the importance of a comprehensive approach that surpasses conventional pharmaceutical treatments.

Material and methods

Review and analysis of the scientific literature available in November and December 2023. The articles were searched on Google Scholar and PubMed using combined keywords (in both Polish and English languages): acne, acne vulgaris, pregnancy, treatment, management, safety, dermatology, procedural interventions, skin care, cosmetics, diet, physical activity, psychological support. Google search engine was also utilized, along with Polish-language scientific textbooks related to the topic of the study. No specific inclusion and exclusion criteria were defined. The writing of this manuscript involved

the use of ChatGPT as a tool for assistance in translation, paraphrasing and linguistic proofreading the text.

Analysis of the literature

Topical treatments

Topical agents often mentioned in the context of treating acne vulgaris in pregnant women include:^{4,9,10}

- benzoyl peroxide,
- azelaic acid,
- salicylic acid,
- antibiotics.

Benzoyl peroxide demonstrates antibacterial effects against *Cutibacterium acnes*, a bacterium strongly linked to acne, as well as sebostatic and keratolytic properties. Its optimal effectiveness is observed when used in combination with other acne therapies.¹¹ Benzoyl peroxide is typically applied once a day in various forms, such as gel or cream, with concentration available from 2.5% up to 10%.¹² However, research suggests that its higher concentrations are not significantly more effective than 2.5%.^{12,13} Furthermore, 2.5% is generally better tolerated and may reduce the likelihood of skin irritation.¹² Approximately 5% of benzoic acid undergoes systemic absorption, but it is rapidly excreted unchanged in the urine.^{14,15} Consequently, the associated risk of causing congenital malformations is very low, making it considered safe for use on limited skin areas by pregnant women (despite being previously perceived as potentially dangerous).^{16,17}

Topical application of 20% cream or 15% gel forms of azelaic acid is another well-established therapeutic approach for acne vulgaris.¹⁸ Azelaic acid exhibits antibacterial, anti-inflammatory, and keratolytic properties, hence the precise mechanism by which this substance treats acne is likely complex.¹⁹ Similarly to benzoyl peroxide, approximately only 4% of azelaic acid applied to the skin is being systemically absorbed.^{9,20} In the context of our publication's topic, there are limited studies on the use of azelaic acid in pregnant individuals; however, the available ones have not reported any adverse effects on fetal development. Consequently, azelaic acid is generally regarded as safe for topical use throughout all trimesters of pregnancy.⁴ Nevertheless, some authors recommend applying this substance only on small skin areas and advise against its use in the first trimester.^{14,21}

Another popular acid – salicylic acid – is not as effective against acne as the substances mentioned before.²² In any case, its reasonable usage (over small skin areas, not for prolonged time or under occlusive dressings) is generally considered safe throughout all stages of pregnancy, as its minimal systemic absorption is acknowledged.⁴

Topical acne treatment for pregnant patients can also encompass the use of antibiotics, especially eryth-

romycin and clindamycin, which are characterized by anti-inflammatory, strong antibacterial, and mild comedolytic properties. Primarily applied in the form of solutions, topical antibiotics rarely cause irritations and are well-tolerated.^{23,24} When applied topically to the skin, erythromycin and clindamycin result in minimal systemic absorption, making them safe for use during all trimesters of pregnancy.⁴ Unfortunately, the use of local antibiotics in acne treatment can lead to the development of bacterial drug resistance, which is a notable drawback of this approach.²⁴ To mitigate that risk, it is advisable to combine all topical antibiotics with an additional antimicrobial agent, such as benzoyl peroxide.^{24,25}

Topical retinoids also have a central role in acne vulgaris therapy, but the use of retinoic acid and its derivatives is generally contraindicated for pregnant women due to the potential risks to the developing fetus. Retinoids, such as isotretinoin, have been associated with congenital malformations, making it advisable to avoid their use during pregnancy. This applies to both topical and oral treatments.^{12,14} Nevertheless, it is worth noting that in regards to the safety of using topical retinoids in pregnant women, there have been contradictory reports. While some studies suggest limited use may be safe, most experts advise caution and avoiding topical retinoids during pregnancy due to potential risks.⁴ Table 1 provides information regarding the properties of acne topical treatments and their safety during pregnancy.

Table 1. Acne treatment during pregnancy – topical treatments^{4,11,14,16,19,21-24}

Topical treatment	Properties	Safety during pregnancy
Benzoyl peroxide	– antibacterial – sebostatic – keratolytic	Safe for use by pregnant women on limited skin areas
Azelaic acid	– antibacterial – anti-inflammatory – keratolytic	Generally considered safe for use throughout all trimesters of pregnancy Some authors advise against its use in the first trimester
Salicylic acid	– keratolytic	Generally considered safe for use throughout all trimesters of pregnancy
Antibiotics (erythromycin and clindamycin)	– antibacterial – anti-inflammatory – comedolytic	Safe for use during all trimesters of pregnancy
Retinoids (isotretinoin)	– keratolytic – anti-inflammatory	Not recommended during pregnancy

Oral medications

Oral isotretinoin is regarded as the foremost efficacious anti-acne medication, recommended for severe acne and, in less severe cases, when other methods prove ineffective. Additionally, it is prescribed in situations of significant psychological distress triggered by the condition.²⁶ Nevertheless, as mentioned earlier, it is contraindicated for pregnant women. Studies have shown that isotretinoin, a known teratogen, increases the risk of miscarriage and exhibits harmful effects on the fetus.

Prenatal exposure to isotretinoin may result in central nervous system abnormalities, facial dysmorphism, cleft palate, external ear malformations, parathyroid and thymus gland abnormalities.¹⁴

In contrast to retinoids, some of the many oral antibiotics used for treating acne vulgaris are suitable for pregnant individuals, among which penicillin agents, cephalosporins and macrolide agents are especially suggested by experts.^{6,16} Throughout all stages of pregnancy, penicillin and cephalexin are deemed safe for use. On the other hand, research findings on amoxicillin are inconclusive. Amoxicillin, while generally considered safe, has been associated with a potential risk of cleft lip and cleft palate when used in the first trimester.^{4,6,27,28} Considering this, it is advisable to limit the use of amoxicillin to the others trimesters.⁴ The administration of oral erythromycin, a representative of macrolide agents, is perceived to be safe for treating moderate to severe inflammatory acne at any trimester of pregnancy when used for a limited period of time (a few weeks).^{9,29} Caution is advised in prolonged treatment decisions, as its extended use beyond six weeks has not been studied.⁹ For patients who do not respond to or cannot tolerate erythromycin, azithromycin serves as an alternative macrolide, albeit with less safety data available.⁴ Once macrolides and penicillins/cephalosporins are deemed to be ineffective, clindamycin can be prescribed as a next option for oral antibiotic therapy against acne as it too has been found safe in pregnant individuals. On the other hand, several other oral antibiotics commonly administered for the treatment of *acne vulgaris* are basically advised against during pregnancy, and their use, if any, is allowed only in very special circumstances. For instance, experts recommend avoiding tetracyclines after the 15th week of pregnancy due to the potential risks of teeth discoloration and bone growth inhibition, yet consideration of their use may be warranted during the first trimester.¹⁶ It is crucial to note that prescribing oral antibiotics during pregnancy should be reserved for situations with a clear and justified need. Moreover, to address the increasing prevalence of bacterial resistance, it is generally recommended to combine such therapy with topical benzoyl peroxide and minimize the duration of oral antibiotic usage as much as possible.⁹

For pregnant patients experiencing a severe form of antibiotic-resistant acne, considering a short regimen of low-dose prednisone may be also appropriate. Although, based on available research, oral prednisone is deemed safe only in the second and third trimesters, with a recommended dosage of < 20 mg/day and a maximum treatment duration of 1 month.⁹

In the context of hormonal acne another beneficial drug worth mentioning is spironolactone, an anti-androgenic agent with inhibitory effects on 5-alpha reductase.¹⁶ However, akin to retinoids, the use of this

medication is not recommended during pregnancy (due to the potential risk of hypospadias and the feminization of male fetuses).^{16,30}

Table 2 summarizes the oral medications used in the treatment of acne vulgaris, along with indications of their safety during pregnancy.

Table 2. Acne treatment during pregnancy – oral medications^{4,9,14,16}

Oral medications	Safety during pregnancy
Isotretinoin	Contraindicated in pregnancy
Penicillin	Safe in all pregnancy stages
Cephalosporins	Safe in all pregnancy stages
Macrolide agents (erythromycin, azithromycin*)	Safe in all pregnancy stages when used for a limited period of time (a few weeks)
Amoxicillin	Safe in the second and third trimester
Clindamycin	Safe in all pregnancy stages
Tetracyclines	Consideration of their use may be warranted only in first trimester
Low-dose prednisone (<20 mg/day)	Safe only in the second and third trimesters, maximum 1-month treatment duration
Spirinolactone	Contraindicated in pregnancy

*azithromycin – less safety data available than in erythromycin

For medical professionals assessing the safety of drug use during pregnancy is a highly responsible and sometimes incredibly challenging task. In everyday medical practice assistance in this matter can come from several systems that rate the teratogenicity of medications, as well as up-to-date scientific reports. In the past, the most recognized and widely used classification was that of the Food and Drug Administration (FDA) on which reliance is now not recommended as it is deemed out of date. As its successor, the FDA has issued Pregnancy and Lactation Labeling Rule (PLLR). PLLR, instead of giving alphabetical classification (A, B, C, D and X) provided by its predecessor, went into the direction of allowing specialists for easier decision making based on current data analysis, through establishment of a set of rules and guidelines according to which safety of a product should be explained.³¹

Procedural interventions

Light and laser therapies, such as photodynamic therapy (PDT), narrowband-ultraviolet B phototherapy (NBUVB), neodymium-doped yttrium aluminum garnet laser (Nd:YAG laser) and pulsed-dye laser, constitute alternative options for acne treatment, even in pregnant patients without known teratogenic effects. It must be noted, though, that when using this type of treatment during pregnancy, there are also some important considerations.⁴ The safety of using PDT with photosensitizing agents, such as aminolevulinic acid (ALA), during pregnancy is uncertain; therefore it is advisable to avoid

combining PDT with ALA in pregnant individuals.^{4,16,32} Moreover high cumulative doses of NBUVB may decrease folic acid levels, posing concerns for proper fetal development; thus ensuring the right supplementation is recommended.⁴

In the management of acne vulgaris during pregnancy chemical glycolic acid peels may be also considered. According to studies, such intervention can effectively address both inflammatory and comedonal acne, as well as postinflammatory lesions. Additionally glycolic acid peels enhance the cutaneous absorption of other topical agents.^{9,33} Notably, no published reports indicate its negative outcomes during pregnancy.⁹

Skin care

In addition to acne treatment, proper skin care is essential for maintaining healthy skin, and pregnancy is one of the more demanding periods in this regard.³⁴ Ensuring adequate skin care is important not only during the active period of acne, but also when the condition is mostly clear and well-managed.³⁵ Selecting appropriate products is crucial. Sebum regulation, antibacterial and anti-inflammatory actions as well as moisturizing should be the focus of acne-prone skin care. Well-chosen cosmetics should purify the skin, reduce the pathological bacterial flora residing on it, alleviate inflammation and improve the overall appearance of the skin.³⁶ However, reading and understanding the chemical composition of products is vital, as certain substances are not recommended during pregnancy.³⁴ Many dangerous chemical compounds can cross the epidermal barrier, getting further into the dermis and finally into the systemic blood circulation.³⁷ In general, during pregnancy it is not recommended to use cosmetics with: retinoids, high concentrations of fruit acids, hydroquinone, caffeine, trichloroacetic acid, essential oils, triclosan, fluoride, ammonia or synthetic detergents.^{34,38} Hypoallergenic and alcohol-free cosmetics are preferred.³⁸ For facial cleansing, it is advisable to choose a non-soap cleanser with a pH close to 5.5.³⁹ It is strongly discouraged to use products that act aggressively on the skin and can lead to its further irritation. Moreover, acne-prone skin typically does not require additional oiling; instead, it benefits more from effective moisturization.³⁶ Another important aspect is proper photoprotection, as sun exposure may trigger or exacerbate acne, and contribute to the formation of comedones.³⁹

Diet

Recent studies concluded a connection between the diet and the intensity of acne, even though the debate about the actual correlation has been ongoing for years.²³ Adherence to a certain diet is associated with lipid metabolism, carbohydrate metabolism, and hormonal balance, as well as with the regulation of the gut microbiome and

the presence of inflammation. Some studies suggest a higher prevalence of acne among individuals who follow the so-called Western diet, which is characterized by a high intake of carbohydrates with a high glycemic index, dairy products, nuts, and chocolate, while being low in polyunsaturated fatty acids.⁴⁰ Following a high-glycemic diet requires increased insulin production to maintain normal glucose levels, and frequently results in insulin resistance, which could modify sebum production, consequently contributing to the development of acne.^{40,41} On the other hand, protective effects against acne are also attributed to unsaturated fatty acids, fruits, and vegetables.²³ Another intriguing aspect of the diet-acne nexus is the role of increased milk intake in the development of new acne lesions. The results of past studies have repeatedly been controversial, but a meta-analysis by M. Aghsi and al. found a positive correlation between the intake of dairy products, including total milk, whole milk, low-fat milk, and skim milk, and the acne occurrence.⁴² Additionally, it is worth noting that people with acne have been found to have lower concentrations of certain elements and vitamins, presumably whose deficiency may affect the skin condition. Among the vitamins that affect the condition of the skin are vitamin A, D and E.⁴⁰ However, special care should be taken, remembering that excess vitamin A in pregnant women can cause teratogenic effects.⁴³ An essential element in the context of acne is zinc, which possesses antibacterial, anti-inflammatory and anti-seborrheic effects. The recommended dietary zinc intake for pregnant individuals is set at 11 milligrams per day.⁹

Physical activity

Attitudes toward physical activity in pregnant women have evolved over the years. According to research, engaging in moderate physical activity during an uncomplicated pregnancy offers various benefits for maternal health.⁴⁴ Among these advantages is enhanced blood circulation and skin oxygenation, which in turn improves the condition and appearance of the skin. Nonetheless, during intense workouts a significant amount of sweat and sebum is secreted, which combine with impurities on the skin. This condition can cause clogged pores, consequently promoting inflammatory processes. Therefore, it is important to remove makeup before engaging in physical activity and adhere to proper hygiene practices.⁴⁵

Psychological support

In the clinical management of acne in pregnant patients, it is crucial for healthcare providers to consider the psychosocial impacts of the condition.⁶ The literature indicates a higher incidence of depression and suicidal ideation among individuals receiving acne treatment.⁴⁶ Furthermore, patients often face additional social challenges, which may include difficulties with social interaction

and public engagements, concerns about sexual attractiveness, strained relationships with family and friends, experiences of negative judgment and stigmatization, elevated stress levels, and fears regarding scarring or the chronicity of the disease. Stress plays a significant role in the context of acne, demonstrating a mutual pathophysiological link to its susceptibility and severity. This means that not only can stress increase the risk and worsen the manifestation of acne, but the presence of acne can also lead to heightened stress levels in individuals. Furthermore, stress-related behaviors, such as “skin scratching,” can lead to additional adverse acne outcomes including inflammation, scarring, discoloration, and exacerbation of concerns regarding one’s appearance.³⁹ It is also worth noting that pregnancy itself is a period of the so-called “psychological crisis”, with the most critical phases being the first and third trimesters.⁴⁷ In light of the psychological challenges during pregnancy, especially in relation to acne, it is essential to offer a holistic model of maternal care that incorporates both dermatological treatment and psychological support. To address these psychological needs, various support groups for acne sufferers are available, providing a community for sharing experiences, access to educational resources, and support through telephone helplines.

In light of the aforementioned, it is worth considering a comprehensive approach to managing acne vulgaris during pregnancy, which, in addition to pharmacological treatment, includes the use of procedural interventions, an appropriate skin care and diet, physical activity, as well as psychological support (Fig. 1).

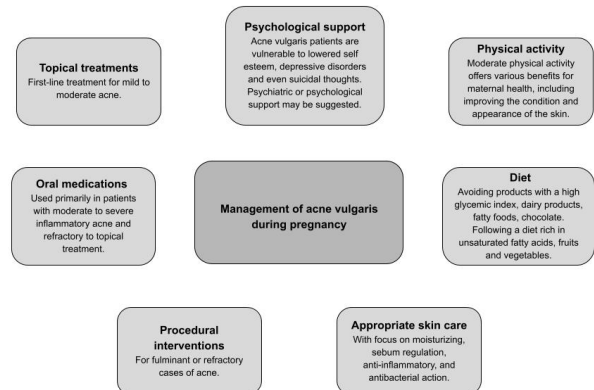


Fig. 1. Acne vulgaris during pregnancy comprehensive approach^{4,9,23,26}

Conclusion

Management of acne vulgaris in pregnant women can be challenging, but when effectively conducted, it not only eliminates the physical symptoms of the disease on the skin, but may also contribute to improving the mental well-being of patients and their ability to function in daily life. Naturally, many issues in that matter are still uncertain, and there are bound to be many

new research results that may clear up doubts. Medicine is a dynamically changing science, so it makes sense to revisit the same issues repeatedly and update the state of knowledge based on the most recent research. Nevertheless, when it comes to managing acne during gestation, the prevailing consensus across various studies underscores the paramount importance of prioritizing safety for both the mother and the developing fetus, and it is crucial to always bear this in mind.

Declarations

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Author contributions

Conceptualization, D.M., M.B. and J.K.; Resources, J.K., D.M., M.B. and U.G.; Writing – Original Draft Preparation, J.K., D.M. and M.B.; Writing – Review & Editing, J.K., D.M., M.B., U.G., A.U., A.R.C. and F.C.; Visualization, J.K., D.M. and A.U.; Supervision, J.K.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

Not applicable.




References

- Dréno B, Blouin E, Moysé D, Bodokh I, Chantal Knol A, Khammari A. Acne in Pregnant Women: A French Survey. *Acta Derm Venereol.* 2013;94(1):82-83. doi: 10.2340/00015555-1594
- Bechstein SK, Ochsendorf F. Acne and rosacea in pregnancy. *Hautarzt.* 2017;68(2):111-119. doi: 10.1007/s00105-016-3918-8
- Bergler-Czop B, Trądzik. In: *Contemporary dermatology.* 1st ed. Rudnicka L, Olszewska M, Rakowska A, Sar-Pomian M. Warszawa: PZWL Wydawnictwo Lekarskie; 2022;2:22-25.
- Ly S, Kamal K, Manjaly P, Barbieri JS, Mostaghimi A. Treatment of Acne Vulgaris During Pregnancy and Lactation: A Narrative Review. *Dermatol Ther (Heidelb).* 2023;13(1):115-130. doi: 10.1007/s13555-022-00854-3
- Kutlu Ö, Karadağ AS, Ünal E, et al. Acne in pregnancy: A prospectivemulticenter, cross-sectionalstudy of 295 patients in Turkey. *Int J Dermatol.* 2020;59:1098-1105. doi: 10.1111/ijd.14999
- Awan SZ, Lu J. Management of severe acne during pregnancy: A case report and review of the literature. *Int J Womens Dermatol.* 2017;3(3):145-150. doi: 10.1016/j.ijwd.2017.06.001
- Bedi A, Khatu SS, Poulkar CB, Palaskar N, Chaudhari ND, Patokar AS. The Spectrum of Mucocutaneous Manifestation during Pregnancy: An Observational Study of 170 Pregnant Women Visiting a Tertiary Care Hospital. *Medical Journal of Dr. D.Y. Patil Vidyapeeth.* 2023;16(4):521-527. doi: 10.4103/2589-8302.335113
- Yang CC, Huang YT, Yu CH, Wu MC, Hsu CC, Chen W. Inflammatory facial acne during uncomplicated pregnancy and post-partum in adult women: a preliminary hospital-based prospective observational study of 35 cases from Taiwan. *J Eur Acad Dermatol Venereol.* 2016;30(10):1787-1789. doi: 10.1111/jdv.13667
- Chien AL, Qi J, Rainer B, Sachs DL, Helfrich YR. Treatment of acne in pregnancy. *J Am Board Fam Med.* 2016; 29:254-262.
- Tan I, Cohen BA. Managing Acne Vulgaris During Pregnancy and Lactation. *Dermatology Times.* 2023;44(7).
- Matin T, Goodman MB. Benzoyl Peroxide. National Library of Medicine. <https://www.ncbi.nlm.nih.gov/books/NBK537220/>. Updated October 10, 2022. Accessed November 29, 2023.
- Graber E. Acne vulgaris: Overview of management. UpToDate. <https://www.uptodate.com/contents/acne-vulgaris-overview-of-management/>. Updated February 23, 2023. Accessed November 29, 2023.
- Mills OH Jr, Kligman AM, Pochi P, Comite H. Comparing 2.5%, 5%, and 10% benzoyl peroxide on inflammatory acne vulgaris. *Int J Dermatol.* 1986;25(10):664-667. doi: 10.1111/j.1365-4362.1986.tb04534.x
- Tuszyński PK. Acne treatment during pregnancy. In: *Drugs and pregnancy. Safe pharmacotherapy and supplementation of pregnant women.* 2nd ed. Kraków: Wydawnictwo Farmaceutyczne; 2023:382-388.
- Putra IB, Jusuf NK, Dewi NK. Skin Changes and Safety Profile of Topical Products During Pregnancy. *J Clin Aesthet Dermatol.* 2022;15(2):49-57.
- Pugashetti R, Shinkai K. Treatment of acne vulgaris in pregnant patients. *Dermatol Ther.* 2013;26(4):302-311. doi: 10.1111/dth.12077
- Murase JE, Heller MM, Butler DC. Safety of dermatologic medications in pregnancy and lactation: Part I. Pregnancy. *J Am Acad Dermatol.* 2014;70(3):401-414. doi: 10.1016/j.jaad.2013.09.010
- Reszke R, Szepietowski J. Azelaic acid in dermatological treatment – current state of knowledge. *Przegl Dermatol.* 2016;103:337-343. doi: 10.5114/dr.2016.61785
- Măgerușan ȘE, Hancu G, Rusu A. A Comprehensive Bibliographic Review Concerning the Efficacy of Organic Acids for Chemical Peels Treating Acne Vulgaris. *Molecules.* 2023;28(20):7219. doi: 10.3390/molecules28207219
- Wolverton SE. *Comprehensive Dermatologic Drug Therapy.* 3rd Edition, Philadelphia: Saunders Elsevier; 2012.
- Kirtschig G, Schaefer C. Dermatological medications and local therapeutics. In: *Drugs during pregnancy and lactation.* 3rd ed. Schaefer C, Peters P, Miller RK. Oxford: Elsevier limited; 2015:467-492.
- Plewig G. Diseases of skin appendages. In: *Dermatology.* 3rd ed. Braun-Falco. Lublin: Wydawnictwo Czelej sp. z o.o.; 2017:1017-1041.

23. Bechtold A, Zalewska -Janowska A. Diseases of the sebaceous and sweat glands. In: *Dermatology in the primary health care doctor's office*. 1st ed. Zalewska-Janowska A, Błaszczuk H. Warszawa: PZWL Wydawnictwo Lekarskie; 2021:191-215.
24. Wolska H. Seborrheic diseases. In: *Dermatology in practice*. 2nd ed. Błaszczuk-Kostanecka M, Wolska H. Warszawa: PZWL Wydawnictwo Lekarskie; 2017:147-158.
25. Lookingbill DP, Chalker DK, Lindholm JS, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double-blind investigations. *J Am Acad Dermatol*. 1997;37(4):590-595. doi: 10.1016/s0190-9622(97)70177-4
26. Acne and related disorders. In: *Dermatology*. 2nd ed. Rycroft RJG, Robertson SJ, Wakelin SH. Boca Raton: CRC Press Taylor & Francis Group; 2010:76-81.
27. Daniel S, Doron M, Fishman B, Koren G, Lunenfeld E, Levy A. The safety of amoxicillin and clavulanic acid use during the first trimester of pregnancy. *Br J Clin Pharmacol*. 2019;85(12):2856-2863. doi: 10.1111/bcp.14118
28. Lin KJ, Mitchell AA, Yau WP, Louik C, Hernández-Díaz S. Maternal exposure to amoxicillin and the risk of oral clefts. *Epidemiology*. 2012;23(5):699-705. doi: 10.1097/EDE.0b013e318258cb05
29. Romøren M, Lindbæk M, Nordeng H. Pregnancy outcome after gestational exposure to erythromycin - a population-based register study from Norway. *Br J Clin Pharmacol*. 2012;74(6):1053-1062. doi: 10.1111/j.1365-2125.2012.04286.x
30. Kong YL, Tey HL. Treatment of acne vulgaris during pregnancy and lactation. *Drugs*. 2013;73(8):779-787. doi: 10.1007/s40265-013-0060-0
31. Woron J. Drug therapy during pregnancy. In: *Pregnancy and chronic diseases*. 1st ed. Olesińska M, Teliga-Czajkowska J. Warszawa: PZWL Wydawnictwo Lekarskie; 2023:741-750.
32. Yang YG, Zou XB, Zhao H, Zhang YJ, Li HJ. Photodynamic therapy of condyloma acuminata in pregnant women. *Chin Med J (Engl)*. 2012;125(16):2925-2928.
33. Taub AF. Procedural treatments for acne vulgaris. *Dermatol Surg*. 2007;33(9):1005-1026. doi: 10.1111/j.1524-4725.2007.33215.x
34. Waleśkiewicz-Ogórek K. Skin care during pregnancy. Forum of Obstetrics and Gynecology. <https://www.forumginekologii.pl/artykul/pielegnacja-skory-w-ciazy/>. Published June 29, 2018. Accessed December 5, 2023.
35. Del Rosso JQ. The role of skin care as an integral component in the management of acne vulgaris: part 1: the importance of cleanser and moisturizer ingredients, design, and product selection. *J Clin Aesthet Dermatol*. 2013;6(12):19-27.
36. Deda A. Acne vulgaris. In: *Basics of therapeutic cosmetology*. 1st ed. Wcisło-Dziadecka D. Warszawa: PZWL Wydawnictwo Lekarskie; 2022:1-38.
37. Li H, Zheng J, Wang H et al. Maternal cosmetics use during pregnancy and risks of adverse outcomes: a prospective cohort study. *Sci Rep*. 2019;9:8030. doi 10.1038/s41598-019-44546-z
38. Dulaska A, Kubiak B, Droszdol-Cop A, Dudek M, Pawlica PJ. Care and cosmetic treatments during pregnancy. Forum of Obstetrics and Gynecology. <https://www.forumginekologii.pl/artykul/zabiegi-pielegnacyjne-i-kosmetyczne-w-czasie-ciazy/>. Published September 1, 2020. Accessed December 6, 2023.
39. Dreno B, Bagatin E, Blume-Peytavi U, Rocha M, Gollnick H. Female type of adult acne: Physiological and psychological considerations and management. *Journal of the German Society of Dermatology*. 2018;16(10):1177-1301. doi: 10.1111/ddg.13664
40. Kowalska H, Sysa-Jędrzejowska A, Woźniacka A. Role of diet in the etiopathogenesis of acne. *Dermatology Review*. 2018;105:51-62. doi: 10.5114/dr.2018.74166
41. Pappas A. The relationship of diet and acne: A review. *Dermatoendocrinol*. 2009;1(5):262-267. doi: 10.4161/derm.1.5.10192
42. Aghasi M, Golzarand M, Shab-Bidar S, Aminianfar A, Omidian M, Taheri F. Dairy intake and acne development: A meta-analysis of observational studies. *Clin Nutr*. 2019;38(3):1067-1075. doi: 10.1016/j.clnu.2018.04.015
43. Bastos Maia S, Rolland Souza AS, Costa Caminha MF, et al. Vitamin A and Pregnancy: A Narrative Review. *Nutrients*. 2019;11(3):681. doi: 10.3390/nu11030681
44. Downs DS, Chasan-Taber L, Evenson KR, Leiferman J, Yeo S. Physical activity and pregnancy: past and present evidence and future recommendations. *Res Q Exerc Sport*. 2012;83(4):485-502. doi: 10.1080/02701367.2012.10599138
45. Karwańska A, Kulbat A, Świercz K, et al. The impact of physical activity, diet and stress on acne vulgaris. Pathogenesis and therapeutic procedures. *J Educ Health Sport*. 2023;13(3):18-23.
46. Picardi A, Mazzotti E, Pasquini P. Prevalence and correlates of suicidal ideation among patients with skin disease. *J Am Acad Dermatol*. 2006;54(3):420-426. doi: 10.1016/j.jaad.2005.11.1103
47. Makara-Studzińska M, Wdowiak A, Plewik I, Kryś KM. Sexuality of pregnant women. *Seksuologia Polska*. 2011; 9(2):85-90.



Improving diabetes mellitus care in Nigeria – health promotion and education perspectives

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ABSTRACT

Introduction and aim. In this review, we suggest ways to improve diabetes mellitus (DM) care in Nigeria from a Health Promotion and Education (HPE) perspective by addressing the gap in DM care through the adoption of strategies from the Ottawa Charter and National Health Promotion Policy (NHPP) guidelines.

Material and methods. This review conducted a comprehensive literature search on Africa Journal Online, PubMed, Google Scholar, and Science Direct, from 1986 to 2023, using relevant keywords.

Analysis of the literature. The adoption of the Ottawa charter and NHPP remains a key strategy in addressing the gap in DM care in Nigeria. This could be achieved by the adoption of population-focused multi-sectoral interventions encompassing legislation, regulation, and fiscal measures, creating sustaining and expanding health-promoting environments to reduce modifiable risk factors, and reorienting the primary health care services to aid the diagnosis, treatment and rehabilitation of DM patients.

Conclusion. This review concluded that the government and other critical stakeholders should adopt the HPE strategies that covers increased financing, strict legislation on DM modifiable risk factors, reorientation of the primary healthcare system, and capacity building for HPE practitioners into DM care in Nigeria as a strategy to improving DM care and prevention in Nigeria.

Keywords. community participation, diabetes mellitus care, HPE, Nigeria, primary health care

Introduction

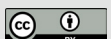
Nigeria, which has a total surface area of about 923,768 square kilometers and an estimated population of over 200 million, is the most populous country in Africa. Thirty-six states make up the country's six geopolitical zones, with the federal capital territory acting as the administrative capital.¹ Nigeria with his large population size and land mass, coupled with migration, industrialization, and globalization have resulted in disease burden of both communicable and non-communicable

diseases. Communicable diseases prevalent in Nigeria are the HIV/AIDS epidemic, Lassa fever, cholera etc. Non-communicable diseases (NCDs), which include chronic renal disease, diabetes mellitus (DM), cancer, and cardiovascular diseases, have become more common in recent times. The average life expectancy has decreased due to the weight of the disease burden, with males surviving an average of 53.7 years and women living an average of 55.4 years.² Figure 1 illustrates the death rates associated with non-communicable diseases,

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which comprise of chronic respiratory disorders 2%, diabetes 1%, malignancies 4%, and cardiovascular diseases 11%.³ However, the review focuses on DM because of its prevalence among all strata of the population and it imposes a degree of morbidity when poorly managed which affects almost all organs of the body.

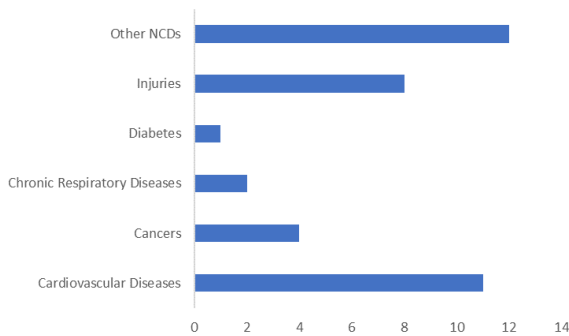


Fig. 1. Mortality due to NCDs diseases in Nigeria³

Diabetes mellitus (DM) is a long-term metabolic illness characterized by high blood glucose levels which when poorly managed could lead to serious damage to the heart, blood vessels, eyes, kidneys and nerves.⁴ The three major types of DM include type 1 DM, type 2 DM and gestational DM. Of the three types, type 2 DM, which is adult onset, is the most common and it occurs when the body becomes resistant to insulin or doesn't make enough insulin.^{4,5} Type 1 DM is a long-term disease in which the pancreas generates little or no insulin on its own; while gestational DM is associated with pregnant women.^{4,5}

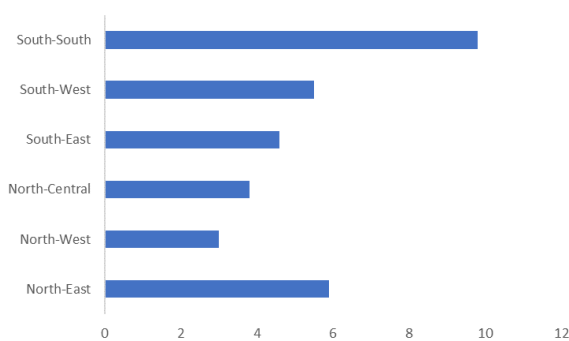


Fig. 2. Pooled prevalence of DM in Nigeria⁷

In Nigeria, the last time a national study estimating the prevalence of DM was carried out was over 30 years ago. The 1992 Nigerian National NCD survey, estimated the prevalence of DM to be 2.2%.⁶ According to the International Diabetes Federation atlas, the number of people aged 20-79 years living with DM is 3.6 million.⁵ Owing to paucity of data there is currently no national prevalence of DM in the 36 states of the nation, except pooled prevalence of DM (Fig. 2) and other prevalence

studies published in various local and international journals.⁸⁻¹⁵

The rising prevalence of DM has been associated with the increase of cardiovascular diseases, end-stage kidney disease, erectile dysfunction, stroke and lower extremity amputation.^{14,16-19} In addition, DM constitute a third of all hospital admissions in Nigeria non-surgical wards and patients with DM has the longest hospital stay and highest medical bills.²⁰⁻²³

In terms of health care organization, in Nigeria there is poor screening activities taking place at the community level as most cases of DM are either diagnosed with classic symptoms or complications or during routine public health screening, pre-medical screening programs, pre-employment medical checks and for investigations such as stroke, hypertension, infertility, HIV/AIDS and tuberculosis.^{16,20} In addition, most DM care takes place at the secondary level of care and fewer more complicated cases at the tertiary level of care with little or no form of care at the primary care level in most states of the federation.^{20,24}

Furthermore, DM care in Nigeria has been suboptimal in all ramifications. This was buttressed by the former Nigeria Minister of State for Health Mr. Eku-mankama Joseph Nkama on 14th November, 2022 during the commemoration of the World Diabetes Day who stated “the risk of having DM has been rising because the vast majority of Nigerians with the condition are unaware of it or only have a basic understanding of it.” He bemoaned the lack of understanding about DM prevention, testing, and treatment that has contributed to the disease's rising prevalence. Furthermore, Mr. Nkama said the management of the disease in the nation has been impacted by the lack of sufficient education for Type 2 diabetes prevention, education for those living with all types of diabetes, and access to cost-effective medication, particularly insulin. Additionally, he emphasized that while diabetes can be effectively prevented or controlled by encouraging healthy lifestyle choices, educating medical professionals, and improving the quality of care's capacity for diagnosis, treatment, and support, the disease is still a major public health concern” (WHO, 2023).²⁵

Similarly, a World Health Organization report also documented the prevalence of DM to be 4.3% (males 4.4% and females 4.3%).²⁷ The report brought to light the deficiencies in the national response to DM in terms of policy guidelines and monitoring. These included the operational policy plan aimed at reducing overweight and obesity, the diabetes registry, and the national risk factor survey, which measured blood glucose levels in relation to the accessibility of medications, fundamental technologies, and public health procedures. The study demonstrated the overall lack of insulin availability in primary healthcare institutions, as well as the absence

of treatments including retinal photocoagulation, renal replacement therapy through dialysis, and renal replacement therapy through transplantation. Furthermore, primary health care facilities lack fundamental technology such as the Doppler foot vascular status, dilated fundus examination, HbA1c test, and foot vibration sensing by turning fork.²⁷

Consequently, due to the reported constraints in the management, prevention and control of DM in Nigeria which include lack of political will to implement adopted national healthcare policies, poor levels of coordination and integration within the multi-sectoral health care and related agencies, poor and inadequate funding and cultural inhibitions and attachments among others.²⁸ It has been recommended that Nigeria should adopt a holistic approach in curtailing the DM scourge. The adopted approach should align with the Nigerian Multi-Sectoral Action Plan 2019–2025, Ottawa Charter and the Nigerian Health Promotion Policy (NHPP). The inclusion of the Ottawa Charter and the NHPP is important because it provides a Health Promotion and Education (HPE) road map for addressing the burden of both communicable and non-communicable diseases in Nigeria.

The process of empowering people to take more responsibility over their health and its determinants in order to improve their health is known as HPE.²⁹ On November 21, 1986, the first worldwide conference on HPE took place in Ottawa, Canada. The main reasons for this meeting were the increasing global expectations for a new public health movement and the significance of HPE in accomplishing the movement’s goals. The charter centered on three basic prerequisites of advocate, enable and mediate. The conference also outlined HPE actions to include build healthy public policy, create supportive environments, strengthen community actions, develop personal skills and reorient health services (Fig. 3). The Ottawa Charter made it necessary to create a national health promotion policy for Nigeria that is tailored to the country’s unique needs while taking into account its social, cultural, and economic structures. The Nigerian Health Promotion Policy (NHPP) was first developed in year 2006. The need for NHPP became necessary because of the prevailing communicable diseases and demographic and epidemiological transition, rapid urbanization and changing lifestyles which have been correlated with the advent of NCDs. The NHPP contains guidelines to assist in creating affirmative outcomes through enablement for positive health action and enhanced community involvement. The NHPP had to be revised, though, due to a number of issues that were found to be preventing its implementation, including systemic issues, inadequate infrastructure at all three levels of government, the appropriation of health promotion responsibilities by other sectors

and programs, and a lack of political will on the part of leaders to give health promotion a higher priority. The revised NHPP was drafted to deliver health care that is preventive, promotive, protective, restorative and rehabilitative to every citizen of the country. The review will highlight the importance of the Ottawa Charter and NHPP in providing advocacy efforts in addressing the establishment of policy, providing enabling environment for DM care which include provision of integrated DM care at the primary care level in Nigeria, increase in community participation in DM care, awareness about DM, strengthening of the health system, mobilization of increased political will and the need for the national DM survey.³⁰

The NHPP consists of guiding principles and values with major stakeholders in the implementation of NHPP. Also, the NHPP consists of a broad goal and four specific objectives with action points (Fig. 3).

Aim

The aim of the review was to suggest ways to improve DM care in Nigeria from HPE perspective by addressing the gap in DM care through the adoption of strategies from the Ottawa Charter and NHPP guidelines.

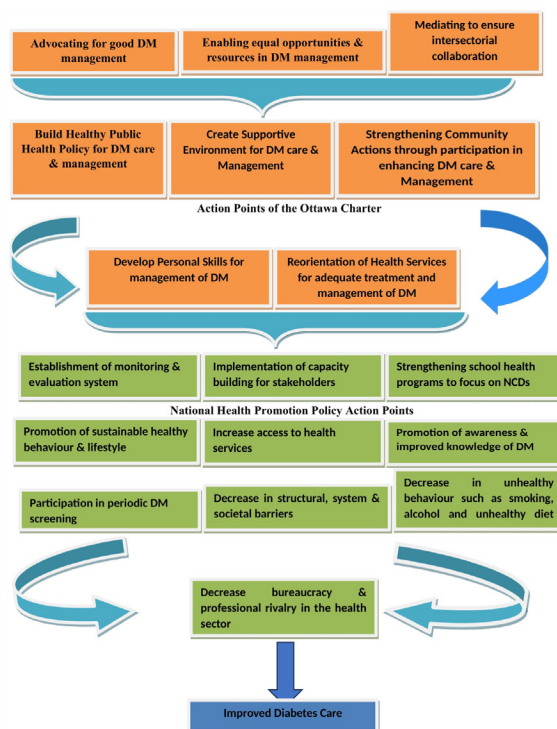


Fig. 3. Highlights of the constructs from the Ottawa Charter and NHPP to improve diabetes care in Nigeria

Material and methods

A collation of published articles on DM care as it relates to the domains or action points of the Ottawa charter and NHPP over the period of establishment of the charter to 2023 was retrieved between April and September,

2023 to develop an all-inclusive distribution of articles in the review. The authors searched online bibliographic archives such as google scholar, African Journal Online, PubMed and Science Direct. Using MesH headings, the terms “diabetes mellitus”, “diabetes care in Nigeria”, “Ottawa Charter”, “NHPP”, “HPE” activities as well as variations thereof were searched for. The results of the literature search were screened for their compliance to the eligibility criteria, which include original studies, reviews, reports and intervention studies reporting findings on DM care related to the domains or action points of the Ottawa charter and NHPP. Data extraction from the eligible articles were carried out independently by two authors (AG and OOA) in line with the objective of the study which include DM care in Nigeria, Ottawa Charter, NHPP and ways of investing and improving HPE activities as it relates to DM care in Nigeria.

Analysis of the literature

Domains of the Ottawa Charter

Build healthy public policy

In order to effectively manage and prevent NCDs, the United Nations High-Level Meeting on NCDs highlighted the necessity of population-focused, multisectoral interventions encompassing legislation, regulation, and fiscal measures.^{31,32} By enacting public policies that prioritize the identification and elimination of health barriers, this action point seeks to make the “healthier choice the easy choice.” These regulations give people and the community a way to choose the healthier choice, lowering their chance of contracting diseases like DM.

The responsibility of addressing the social determinants of DM and health lies mainly with the non-health sector and so it will require collaborative efforts with policy makers in other sectors such as finance, judiciary, political, agriculture, and environment etc. to be able to address the issue of DM and its consequences.^{32,33} In order to promote better DM care in Nigeria, it emphasized the necessity for coordinated effort that incorporates a variety of strategies, including legislation, fiscal measures, taxation, and organizational transformation. The Ottawa charter recommended the need for adoption of a multisectoral approach in formulating healthy public policy including identification of barriers to its implementation and how to circumvent them in promoting the management and prevention of non-communicable diseases. Therefore, DM care organizations, community and faith-based organizations and researchers involved in DM care will need to collaborate with people in the best position to develop laws and policies that encourage wholesome environments and communities that support the best possible treatment and prevention of DM. One of such obstacles that may affect the implementation of policies promoting DM care is

the lack of provision of evidence-based information to policy makers from researchers. By using networks and intermediary bodies, it would be possible to improve direct interaction and communication between academics and decision-makers in order to get beyond these obstacles. Local, fact-based data on the dangers of DM must be provided to policymakers and the best available local option to minimize the threats. Providing policymakers with choice and flexibility that is, a range of options with varying costs and benefits instead of a single solution is more likely to inspire action. It is imperative that the available options accurately reflect the political, social, cultural, and economic landscape in which a given policy will be implemented.^{32,34} For instance, a study by Ajisegiri et al.³⁵, to understand the implementation of NCD policies in Nigeria, found that the focus of NCD national policies is “top down,” with little consideration given to decentralization to sub-national and frontline care delivery levels of the health system; NCD program coordination mechanisms are flawed, with weak regional organizational structures serving as their foundation; NCD financing is administratively onerous and dispersed; and frontline NCD service delivery for NCDs is not effectively integrated with other crucial PHC services.

Create supportive environment

This priority area focuses on people’s surroundings because it can influence how they approach their health. This component of the Ottawa charter gives the community the opportunity to collaborate in creating a wholesome atmosphere that supports, encourages, and gives resources to those who have the ability to improve their health. The WHO buttressed this point in his report on the Global Action Plan for Prevention and Control of NCDs. The report highlighted the importance of creating, sustaining and expanding health-promoting environments to reduce modifiable risk factors such as alcohol consumption, smoking of cigarette and other harmful substances injurious to the body, harmful dietary habits and physical inactivity.^{32,36}

With the current epidemiological transition in Nigeria which has led to rapid urbanization and industrialization that is contributing to the increasing prevalence of type-2 DM. There is therefore need to create a supportive environment that increases peoples’ access to resources in management of DM (glucometer, insulin and other hypoglycemic drugs), increasing opportunities for adoption of healthy lifestyles (reducing alcohol and cigarette use, healthy dietary and physical activity), reducing threats to DM complications and improving individuals ability to properly manage DM at the intra-personal level.^{37,38} Additionally, fostering a supportive environment is employed to locate organizations that could help in comprehending the characteristics of dif-

ferent approaches and practices required to get beyond typical obstacles to illness prevention.^{39,40}

In Nigeria, the national guidelines on the prevention, control and management of DM (FMOH), encouraged the promotion of creative supportive environments in the management of DM.⁴¹ It recommended whole-of-community health promotion activities in accordance with the Ottawa Charter, which includes targeted community-based activities (school-based physical activity programs and community physical activity programs like marathons, swimming, dancing, etc.) and workplace interventions (discounted vouchers for sports/gym facilities, active spaces or gyms in the workplace and periodic workplace recreation). Healthful feeding and eating programs (healthy infant and young children feeding programs, school-based feeding programs and removal of vending machines from schools and communities). The recommendations were in line with the WHO Global NCD Action Plan 2013–2020 and the Nigerian multi-sectoral action plan for NCD prevention and control.^{42,43}

Strengthen community actions

Strengthening community actions enables people to collaborate with one another and the community to guarantee that strategies and priorities are carried out in a way that promotes improved health. It strengthens community support and encouragement to take part in making sure that all services are available to everyone. Every information is accessible, and every opportunity for learning is fair. More pertinent results are obtained by communities that effectively combat DM through public involvement in prevention and control than communities who do not actively participate in prevention and control activities.³²

To guarantee that results are in line with communities' needs and resources, local expertise and skills must be given equal weight during the planning and decision-making process when bolstering community actions.^{44,45} This is because poor knowledge of causes, risk factors, complications of DM is common in most communities in Nigeria.^{46–50} Increased community access to diabetes health care and community control over the socioeconomic factors of DM should be the main goals of any diabetes community action projects.³² Furthermore, community action for diabetes mellitus is to be broadened to encompass DM screening and early detection, patient support for self-management, rehabilitation services, and community-led multisectoral diabetes prevention initiatives.³²

The World Diabetes Foundation carried out a project with the aim of strengthening DM care in Lagos State Nigeria through the establishment of 35 DM clinics across the state. The project implemented the following strategies: it developed and reviewed guidelines for

training and referrals for healthcare professionals managing diabetes; it strengthened access to diabetes care at 35 Primary Health Clinics by providing DM and DM foot screening equipment; it improved the referral process for cases involving complications; and it trained physicians, nurses, and community health workers in diabetes screening, prevention, and care.⁵¹

Additionally, research has demonstrated that community health workers' participation in diabetes treatments enhances patients' diabetes care and self-management practices. To enhance diabetes testing and monitoring, medication adherence, nutrition, physical activity, or weight control, interventions can involve coaching, teaching, or social support.^{45,52}

Develop personal skills

This is the only one of the Ottawa Charter's five priority areas for action that is at the intrapersonal level. Action at this level is necessary to help people, especially those who have chronic diseases, succeed in improving their health status and managing their illness.^{32,53} This area of action alters a person's behavior to help them realize what adjustments they can do to lower their chances of contracting DM and its consequences. Concerning DM management, it equips the patients with the most useful knowledge and abilities that are necessary to improve certain aspects of their health. This is because patient empowerment for DM self-management is necessary to maximize outcomes. The daily decisions and considerations that a patient with type 2 DM must make are part of diabetes self-management. Patients must be able to manage their resources, values, and preferences while adhering to a therapy regimen that calls for consistent exercise, a healthy diet, blood sugar self-monitoring, and medication compliance.^{32,54,55}

As a result, patients' need to be equipped with information and abilities in accordance with the Federal Ministry of Health's National Guidelines on the prevention, control, and treatment of diabetes. This is because the national guidelines align with the cultural context of Nigeria and addresses more problematic areas.^{56,57} This is pertinent in DM self-care and management because studies have shown that DM educational intervention aligning with the socio-cultural context has better management outcomes.^{58–60}

Reorient health services

Health care professionals are not the only ones who have to share responsibility for health promotion in the healthcare system; governments, community organizations, individuals, and healthcare institutions all have a part to play. To develop a healthcare system that advances the objective of health, they must work together. This means that in order to promote health, the focus of health care must be shifted from being individual and

treatment-centered to being community-centered and focusing on the promotion of a healthy community.³² Such health care services should focus on prevention, promotion and cure.

Currently, in Nigeria DM treatment and care is only operational at the tertiary and secondary level of care, with little or non-existent care at the primary level.^{61,62} This is a drawback of the Nigerian health care system because primary health care is the only setting where integrated risk reduction and prevention, treatment, and long-term management of diabetes mellitus can be successfully accomplished due to accessibility to care. The reorientation of health services in Nigeria concerning care and management of DM should focus on primary health care because primary health care is the domain where health promotion and education activities could be carried out effectively. Primary healthcare demands that all people have access to health services regardless of their location, social status, economic status, or cultural background; that the community be involved in the planning, implementation, and assessment of health services; that health and other sectors be integrated; that multidisciplinary teams be recognized as equal partners in promoting the community's health; and that a range of services, chosen by the community, be provided.³² In Nigeria studies have shown the reorientation of primary health care through interventions to improve services, drive change and overall output among health care workers.^{35,63,64}

Domains of the National Health Promotion Policy

Participation in periodic screening programs

Undiagnosed Diabetes Mellitus (UDM) remains a challenge globally, but is more common in low-and middle-income countries. According to the IDF, in 2021 almost one-in-two (44.7%) representing 239.7 million of the total adults living with diabetes (20–79 years old) were found to be unaware of their status.⁵ In low and middle income countries the prevalence of undiagnosed DM is even higher with a proportion of 50.5% representing about 9.5 million people.⁵ In the African sub-region the proportion of adults (20–79 years) with undiagnosed DM is estimated to be 53.6% representing 12.7 million people.⁵ The African sub-region does not have a standard data for UDM due to poor documentation in the health system. However, few available studies on the prevalence of UDM in Africa shows North Africa (4.2% in Egypt), South Africa (18.1%), East Africa (7.2%, 11.5%, 5%, 2.3%, 3.8%, 2.13% in Ethiopia), (9% in Tanzania), and West Africa (3.19% in Guinea), (6.3% in Cameroon), (4.64% in Senegal), (7% and 4.6% in Nigeria).⁶⁵⁻⁷⁸ Early diagnosis of people with DM is essential to prevent or delay micro and macro vascular complications; improve quality of life and avoid premature death.⁶² This is because late diagnosis of DM most

likely would have resulted in complications leading to more use of health care services; thereby placing additional burden on the health care system already struggling with known communicable diseases and other non-communicable diseases.⁶² Screening for DM remains one of the surest ways to reduce the high burden of UDM in Nigeria. The NHPP proposes participation in periodic maximum pressure campaigns activities which involve screening programs for DM to address the burden of DM in the country. Such screening programs should be organized by all levels of government (Local, State and Federal) and other non-governmental organizations regularly and should incorporate all the levels of the health care system in Nigeria (Primary, Secondary and Tertiary) to facilitate referral activities when the need arises.

Promotion of awareness and improving knowledge of DM

Creating awareness and adequate knowledge of DM remains a vital way of reducing risk of complications among diagnosed patients.⁷⁹ While previous research has documented high awareness of DM among various subgroups of the populations; the level of knowledge has been suboptimal.^{46,47,62,80-83} The NHPP proposes supporting health promotion interventions that promote awareness creation and enhancing the knowledge of DM and its prevention. This would empower the population in identifying risk factors and detecting signs and symptoms early enough to prevent DM complications and late diagnosis. In addition, the high awareness of DM among the population could be leveraged upon to increase their knowledge, attitude and practice towards DM. Both governmental and non-governmental organizations should focus on regular and continuous sensitization campaigns on the causes, signs and symptoms, risk factors, complications, management and prevention of DM in the communities, schools, religious gatherings, market places and other social gatherings in the community. This is to ensure knowledge enhancement and sustenance in health seeking behavior among the population.⁸¹

Increase access to health services by significant reduction of structural, system and societal barriers especially for the vulnerable groups

The most vulnerable groups in terms of access to DM health care services are the poor in the society who cannot afford the high cost of insulin and other hypoglycemic drugs. This is because in Nigeria there are high out-of-pocket expenses for health care services and low insurance policy especially among patients in the rural areas.^{60,75} Furthermore, weak structural and systemic factors within the health care services are hindering adequate access to health care among DM patients. For instance, in Nigeria adequate and specialized care for DM

can only be obtained from secondary and tertiary facilities as DM care is in most cases non-existent in primary care centres.⁶² Also, poor referral activities among the three tiers of health care systems and derisory implementation of health policies have compounded the problem of care among DM patients.^{84,85} Furthermore, inter-cadre rivalry among health care professionals has hindered patients from having the best possible care.⁶² Poor awareness and knowledge of DM, stigmatization and myth about DM are societal barriers that hinder access to health services.^{62,86}

Promoting sustainable healthy behavior and lifestyle

Modifiable risk factors such as smoking, alcohol consumption, and physical inactivity are major risk factors of DM.⁸⁷ Thus, sustaining healthy behavior and lifestyle is important in minimizing the risk of contracting DM. As at 2012 there were about 13 million smokers in Nigeria, with above 16,000 mortality attributable to cigarette smoking.^{88,89} As at 2020 the smoking rate was 3.70% which was a decline of 0.2% from 2015 (4.70%).⁹⁰ According to the Nigerian Demographic Health Survey (NDHS), about 6% of men smoke any type of tobacco while 94% are non-smokers and less than 1% of women smoke cigarette.⁹¹ Also, among men who smoke cigarettes daily, about 38% smoked less than 5 cigarettes each day, while 33% smoked 5–9 cigarettes and 8% of daily cigarette smokers smoked between 15 and 24 cigarettes each day. Similarly, worldwide research has demonstrated that consuming low to moderate amounts of alcohol reduces the risk of developing type-2 DM because it increases insulin sensitivity.^{92,93} On the other hand, chronic and heavy use of alcohol, however, has been shown to interfere with glucose homeostasis and cause the development of insulin resistance, which increases the chance of developing diabetes mellitus.^{94,95} Nigeria is one of the countries in the world with the highest per capita alcohol consumption.^{96,97} In Nigeria, alcohol abuse is still the most common substance. Adolescents and young adults are more likely to engage in excessive, episodic drinking, and in certain situations, alcohol beginning occurs as early as 11 years old.^{98,99} Reasons posited for increased alcohol consumption is unrestricted access to alcohol products, continued promotion and popularity of alcohol products, absence of alcohol policies and lack of implementation of a minimum drinking age by both the government and the brewers. Others are socio-cultural practices, rapidly changing lifestyles and increasing purchasing power.¹⁰⁰ Alcohol consumption is a contributing factor to most non-communicable diseases such as diabetes, cancer, liver cirrhosis, road traffic accidents among others.¹⁰¹ In Nigeria, according to reports, there are significant rates of physical inactivity (between 25% and 57%), which have been related to greater incidence of obesity, type 2 diabetes, and cancer.^{102,103} Ni-

geria has national policies to regulate the consumption of tobacco and alcohol. For instance, the National Tobacco Regulations 2019 Act was passed into law in the year 2019. Moreover, the Federal Road Safety Act, the Non-communicable Diseases Prevention and Control Policy, and the Strategic Plan of Action all contain policy measures to combat dangerous alcohol consumption. However, despite the existence of these policies in Nigeria, more still need to be done to ensure a tobacco and alcohol-free society in Nigeria. Various ways of ensuring the sustaining of these policies is to adopt a multi-sectoral approach, adoption of the framework for global monitoring to measure progress on major NCDs, their main risk factors, and their prevention and control on a global scale, decrease in the youth and young adults consumption of alcohol and tobacco, public health advocacy, partnership, technical support and capacity building.^{101,104-106} The proportion of men and women who smoke various tobacco products in Nigeria according to age and geopolitical zones is as shown in Figure 4.

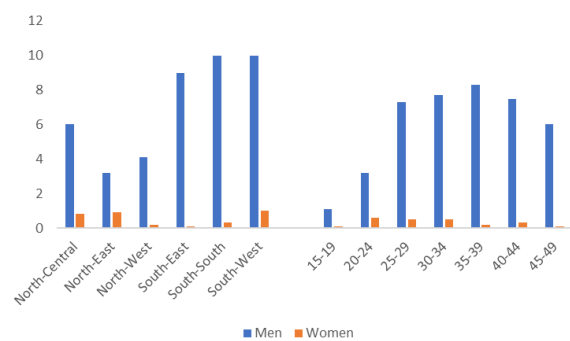


Fig. 4. Proportion of men and women who smoke various tobacco products according to age and geopolitical zone in Nigeria¹⁰¹

Strengthening school health programs to focus on the prevention of non-communicable diseases

The implementation of the guidelines on the National School Health Program was developed in the year 2006. The purpose of this school health policy was to advance students' health in order to fulfill the objectives of 'Education for All'. The need to strengthen the implementation of the National School Health Program has become more pertinent because of the increasing prevalence and burden of DM in school environment.¹⁰⁷⁻¹¹⁰ In school health programming, the NHPP suggests promoting and protecting health behaviors for children, parents, staff, and the community at large. Therefore, in line with the proposal the areas of the policy that the implementation needs to be strengthened include school feeding services, health education and school health services. In school feeding services, foods served to the pupils and students should contain high fiber diet such as fruits and vegetables which have been shown to in-

crease insulin sensitivity thereby decreasing the chances of developing type-2 diabetes.^{111,112} Also, health education on the prevention of DM and other non-communicable diseases should regularly be organized for primary school pupils, secondary school and University students and staffs. As previous studies have shown the improvement of knowledge of DM among students through health education intervention.¹¹³⁻¹¹⁵ Furthermore, the annual World Diabetes Day every 14th November could be leveraged to embark on DM awareness across primary, secondary schools and Universities in the country. Additionally, the school curriculum especially the secondary school curriculum should be revised to contain more information on the pathophysiology of DM, signs and symptoms of DM, risk factors of DM, complications, management and prevention of DM. This is important because teachers in secondary schools have affirmed the inadequacy of prevention of DM in the current secondary school curriculum.¹¹⁶ School health services centers should have glucometer, and hypoglycemic drugs, referral, follow-up services and effective counseling services. Lastly, the school health records should be made to be comprehensive for proper referral and follow-up especially of pupils or students with DM.

Establishment of effective media strategies

Effective media strategies comprising both the social and new media for DM prevention should be established by the health promotion divisions at the federal, state and local government levels. The aim of such media engagement should be to ensure:

1. Strengthening the capacity of media professionals: This could be achieved by ensuring that the capacity of media practitioners is strengthened on the reportage of issues concerning non-communicable diseases including DM and the role of social determinants of health on the onset of DM.
2. Information, enlightenment and empowerment of communities: The mass media has a wide reach therefore it could be engaged by health promotion divisions at all levels to ensure periodic and regular up-to-date information on the government activities in the organization, management and prevention of DM across communities in Nigeria. This would help in driving information to the grassroots level thereby empowering communities in adopting positive lifestyles and health seeking behavior.
3. Generation of evidence on the contribution of health promotion and education in improving diabetes care in Nigeria: Evidence based data from publications, conferences, workshops etc. on the contribution of health promotion in improving the organization, care and management of DM should be supplied to designated media practitioners periodically. This would help media practitioners with

their reportage duties in informing the public on the contribution of health promotion in improving the health of the people.

4. The media should be in cooperated as part of the team for the development of health promotion and education interventions at all levels. This would ensure adequate monitoring and coverage of health promotion programs especially as it concerns the organization, care and management of DM in Nigeria. This would help the media through the social and new media to perform its function of continuously updating the public on progress of government investment in health promotion and education activities on the organization, management and prevention of DM.

Implementation of capacity building for the delivery of health promotion and education interventions as it relates to DM care and prevention

Building organizational contexts, partnerships, and infrastructure to conduct health promotion programs, as well as developing problem-solving skills, are all elements of capacity building for health promotion.¹¹⁷ The NHPP proposes as it pertains to DM care and prevention a clear framework for transferring and scaling up staff capacity strengthening. This could be achieved by ensuring the regular organization of capacity building workshops for all categories of health professionals involved in DM care by governments at all levels. The endocrinologists, physicians, nurses and other professional bodies involved in DM care should be trained on best practices in DM care at the tertiary level. This is even more important because care at this level is constrained owing to the few diabetologists and endocrinologists providing care for DM patients.⁶² At the secondary level of care general practitioners, nurses, dieticians, pharmacists and other professional bodies involved in DM care should be targeted for such capacity building workshops, as this would help them upgrade their skills and knowledge regularly in order to manage DM more effectively and efficiently. The primary care level in Nigeria is not equipped to manage non-communicable diseases such as DM. Most primary health care in Nigeria focuses on maternal and child health care and management of communicable diseases and minor ailments.^{62,118} Previous reviews have highlighted the importance of capacity building in the management of DM in Sri Lanka and India.^{119,120} Capacity building workshops and training should be certified in form of fellowships, diplomas and certificate programs which should be institutionalized by securing buy-in of the policy with National Universities Commission (NUC) and other strategically relevant agencies for short and long term adoption. In addition, such programs should adopt a bottom-top approach where various communities and families of those affect-

ed with DM would be incorporated in the development of a National Diabetes Educational Guidelines for the management of DM.

Establishment of systems to monitor and evaluate DM care activities in Nigeria

A DM care monitoring and evaluation center should be created in the department of public health or health promotion at the national, state and local governments' levels. Such center would be saddled with the responsibility of generating evidence-based data for DM in Nigeria by establishing a national DM register consisting of all DM patients in Nigeria for easy tracking and follow-up. This will aid the generation of reliable data on prevalence of DM, morbidity and mortality, as currently such data are generated from cross sectional studies,^{11,14,33,121,122} and systematic reviews.^{7,122} Furthermore, the establishment of such center would help in tracking DM researches including interventions among various set of the population in Nigeria which will aid evidence-based data gathering. Researchers will be mandated to get approval and documentation from such offices nationwide before commencing their studies. The established DM monitoring and evaluation center will be able to work with the support of the government through the ministry of health to organize quarterly or annual national review meetings and conferences where recent researches in the management of DM will be presented and discussions on how to strengthen the system will be carried out. In addition, all health facilities in collaboration with the DM monitoring and evaluation centers would be mandated to write a monthly report of their DM activities and they will be collated and sent to the national center for documentation.

Investing in health promotion and education to improve diabetes care

Health promotion and education remains a key strategy for promoting health and wellbeing especially as it concerns prevention of DM because it empowers people to improve their mental, social and physical health. For the government to achieve increased diagnosis, better management and prevention of DM, there must be a conscious and deliberate investment in health promotion through governmental and non-governmental agencies in Nigeria. The following are areas the government could invest in improving diabetes care through health promotion and education in Nigeria.¹²³

Finance

Effective health promotion and education as it concerns DM care and prevention would need adequate financing for maximal delivery. This could be done by investment in health promotion activities through fiscal policy making and budgetary allocation to the de-

partment of health promotion through the ministry of health. Health financing for improving DM care would be channeled into subsidizing out-of-pocket payment for hypoglycemic drugs through credit allocation for indigent patients in the annual budget allocation to health care.¹²³ Also, the social insurance scheme such as the National Health Insurance Scheme and others could be funded and expanded to provide free basic insurance packages specifically for DM patients through the national and state hospital management boards as well as referral systems. Such insurance programs would be expected to cover the provision of social insurance, adequate health services and provision of drugs.¹²³

Legislation

Legislation involves having the political will to create and push through legislation and policies that enhance as well as sustain healthcare delivery. Legislation involves formulating laws that would increase the budgetary allocation to health from its current 8% in 2023 to 15% of its total budgetary allocation which was signed by African Head of States in the Abuja declaration of 2001.¹²⁴ Laws that raise the risk of diabetes mellitus should be implemented as taxes on sugar-sweetened beverages, unhealthy meals, and services. Furthermore, laws should be passed to impose higher taxes on alcoholic beverages, tax every pack of cigarettes, pipe tobacco, and ready-to-use tobacco, tax cigarette retailers, and restrict the entry of tobacco products into Nigeria by foreign visitors by collecting taxes on them. Legislation could also ensure that a percentage from Value Added Tax becomes a health tax which would be channeled into the treatment and care of patients with chronic diseases such as DM.¹²³

Health research

Investment should be made in health promotion and education research in Nigeria that promotes the prevention of non-communicable diseases such as DM.¹²⁵ Such funding should be focused on researches that are in line with the objectives of health promotion which includes prevention of DM in Nigeria, incidence and prevalence of DM, reduction of risk factors (modifiable) associated with DM, adherence and care of DM patients in preventing complications, interventions that focus on improved quality of life among DM patients. The government could also fund researches that focus on increasing individuals' knowledge of DM and skills for management of DM through information, education and communication, strengthening of community action by identifying and utilizing existing community structures, facilitating the creation of laws, regulations, and fiscal restraints that improve and support appropriate DM treatment and prevention in Nigeria. Monitor-

ing and evaluation of health promotion and education programs are also important.^{124,125}

Health system

The Nigerian government should invest heavily in the health system from the tertiary to the primary level. This is pertinent for the provision of adequate care for DM patients and timely referral. Establishment of an appropriate feedback system among the various levels of healthcare is equally important. Although, DM care at the primary level of care is non-existent considering even as it is the level of care closer to the populace and a place where DM patients are expected to present first, when in need of care.¹²⁶ This should be looked into and improved upon by the government especially the local government through the National Primary Health Care Development Agency, as these present the best opportunity for quick and timely diagnosis of DM across communities in Nigeria. If the populace is aware they can walk into any primary health center and receive adequate DM care without going to the secondary facility which might be some few kilometers away, it will go a long way to encourage residents of communities across Nigeria to seek care quickly and timely which is important to prevent DM complications.¹²⁶

At the secondary and tertiary level of care where we have professionals handling DM care. The government must ensure that trained health promotion specialist is incorporated as part of care for DM patients and are saddled with the responsibility of promoting DM awareness in communities across Nigeria.⁶²

Human resources

In line with the guidelines of the NHPP, all staffs appointed to carryout health promotion and education duties for the organization of the prevention of non-communicable diseases including DM at the federal, state and local government levels must meet the minimum requirement of a Masters' degree in public health or allied disciplines with specialization in health promotion and education at the national and state levels and a degree (BSc, HND or OND) in health promotion and education, a minimum of six months health promotion and education certification in addition to other basic professional qualification in health are required at the local government level.

Conclusion

This manuscript proposed the adoption of the Ottawa charter and the NHPP in the improvement of DM care services in Nigeria through the adoption of population-focused multi-sectoral interventions encompassing legislation, regulation, and fiscal measures which provides the populace and community options of adopting healthier choices, thereby lowering their chances of

contracting DM. Furthermore, creating sustaining and expanding health-promoting environments to reduce modifiable risk factors; ensuring community participation in the decision-making process from the planning, implementation and evaluation of intervention programs in the community and reorienting the primary health care services to aid the diagnosis, treatment and rehabilitation of DM patients. Others include, promoting screening programs, increased access to DM care services and reorientation of the school health programs to include school feeding services, health education and school health policies. Policy recommendations include the formal adoption of the NHPP as part of the DM care process in health facilities in Nigeria, strengthening HPE trained human resources as part of the DM care team in health facilities, increase budgetary allocation for health financing and strengthening the social insurance schemes, adoption of strict legislation against modifiable risk factors such as tobacco and alcoholic beverages and increased allocation and access to funds for HPE research.

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Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors used publicly available data.

Ethics approval

Not applicable

References

1. National Bureau of Statistics, 2022. <https://www.nigerianstat.gov.ng/index.php>. Accessed June 16, 2023.
2. "Nigeria Population (Demographics, Maps, Graphs)", World Population Review 2022. <https://worldpopulationreview.com>. Accessed June 16, 2023.
3. World Health Organisation 2018. Nigeria fulfils commitment, launches Plan for the Prevention and Control of Non-Communicable Diseases. <https://www.afro.who.int/news/nigeria-fulfils-commitment-launches-plan>

- prevention-and-control-non-communicable-diseases. Accessed November 20, 2023.
4. World Health Organisation 2022. Diabetes. https://www.who.int/health-topics/diabetes#tab=tab_1. Accessed April 22, 2023.
 5. International Diabetes Federation 2021. IDF Diabetes Atlas, 10th edition. Brussels, Belgium. Accessed August 10, 2023.
 6. Akinkugbe OO. Non-communicable disease in Nigeria. Final report of National Survey. Lagos: Federal Ministry of Health and Social Services. 1997:64-90.
 7. Uloko AE, Musa BM, Ramalan MA, et al. Prevalence and risk factors for diabetes mellitus in Nigeria: a systematic review and meta-analysis. *Diabetes Ther.* 2018;9(3):1307-1316. doi: 10.1007/s13300-018-0441-1
 8. Cookey SN, Gomba VE, Wariboko CM. Prevalence of Diabetes in Rural Communities in South South and South East Nigeria A Retrospective, Cross Sectional Community Based Survey. *IOSR J Dent Med Sci.* 2022;21(2):26-32. doi: 10.9790/0853-2102072632
 9. Afolalu T, Wada O, Olawade D, Suntai A. Prevalence of Diabetes Mellitus among Adult Residents of Tinda Rural Community, Nigeria. *J Biosci Med.* 2020;8:107-116. doi: 10.4236/jbm.2020.811010
 10. Arugu GM, Maduka O. Risk Factors for Diabetes Mellitus among Adult Residents of a Rural District in Southern Nigeria: Implications for Prevention and Control. *J Clin Pract.* 2017;20:1544-1549. doi: 10.4103/njcp.njcp_154_17
 11. Sabir A, Ohwovoriole A, Isezuo S, Fasanmade O, Abubakar S, Iwuala S. Type 2 Diabetes Mellitus and Its Risk Factors among the Rural Fulanis of Northern Nigeria. *Ann Afr Med.* 2013;12:217-222. doi: 10.4103/1596-3519.122689
 12. Olatunbosun ST, Ojo PO, Fineberg NS, Bella AF. Prevalence of Diabetes Mellitus and Impaired Glucose Tolerance in a Group of Urban Adults in Nigeria. *J Natl Med Assoc.* 1998;90:293-301.
 13. Sabir AA, Isezuo SA, Ohwovoriole AE. Dysglycaemia and Its Risk Factors in an Urban Fulani Population of Northern Nigeria. *West Afr J Med.* 2011;30:325-330.
 14. Agofure O, Odjimogho S, Okandeji-Barry OR, Efegbere HA, Nathan HT. Pattern of diabetes mellitus-related complications and mortality rate: Implications for diabetes care in a low-resource setting. *Sahel Med J.* 2020a;23:206-10. doi: 10.4103/smj.smj_64_19
 15. Agofure O, Okandeji-Barry OR, Ogbon P. Pattern of diabetes mellitus complications and co-morbidities in ughelli north local government area, Delta State, Nigeria. *Niger J Basic Clin Sci.* 2020b;17:123-127. doi: 10.4103/njbc.njbc_37_18
 16. Ogbera AO, Kapur A, Odeyemi K, et al. Screening for diabetes mellitus and human immune deficiency virus infection in persons with tuberculosis. *J Prev Med Hyg.* 2014;55(2):42-45.
 17. Arogundade FA. Kidney transplantation in a low-resource setting: Nigeria. *Kidney Int Suppl.* 2013;3(2):241-245. doi: 10.1038/kisup.2013.23
 18. Danesi M, Okubadejo N, Ojini F. Prevalence of stroke in an urban, mixed income community in Lagos, Nigeria. *Neuroepidemiology.* 2007;28(4):216-223. doi: 10.1159/000108114
 19. Odatuwa-Omagbemi D, Adiki O. Extremity amputations in Warri, South South Nigeria. *J West Afr Coll Surg.* 2012;2(1):14-24.
 20. Fasanmade OA, Dagogo-Jack S. Diabetes care in Nigeria. *Ann Glob Health.* 2015;81:821-829. doi: 10.1016/j.aogh.2015.12.012
 21. Adisa R, Alutundu MB, Fakeye TO. Factors contributing to nonadherence to oral hypoglycaemic medications among ambulatory type 2 diabetes patients in Southwestern Nigeria. *Pharmacy Pract.* 2009;7(3):163-169. doi: 10.4321/s1886-36552009000300006
 22. Aguocha BU, Ukpabi JO, Onyeonoro UU, Njoku P, Ukegbu AU. Pattern of diabetic mortality in a tertiary health facility in south eastern Nigeria. *African J Diabetes Med.* 2013;21(1):14-16.
 23. Unachukwu CN, Uchenna DI, Young EE. Mortality among diabetes in patients in Port Harcourt Nigeria. *African J Endocrinol Metabol.* 2008;7:1. doi: 10.4314/ajem.v7i1.57567
 24. Agofure O, Oyewole OE, Igumbor EO and Nwose EU. Diabetes care in delta state of Nigeria: An expository review. *Diabetes Updates.* 2018a;1(1):1-8. doi: 10.15761/DU.1000106
 25. World Health Organisation 2023. Country profile Nigeria. <https://www.afro.who.int/countries/nigeria/news/stakeholders-call-increased-access-diabetes-education>. Accessed March 12, 2024.
 26. World Health Organization 2016. Diabetes country profiles. https://cdn.who.int/media/docs/default-source/country-profiles/diabetes/ngaen.pdf?sfvrsn=a7a9827_38&download=true. Accessed March 12, 2024.
 27. Sixth Global Conference on Health Promotion, Bangkok, Thailand, August, 2005.
 28. Cheld 2022. Addressing the Diabetes Burden in Nigeria through policy and health education-Report. <https://cheld.org/addressing-the-diabetes-burden-in-nigeria-through-policy-and-health-education>. Accessed February 27, 2024.
 29. United Nation general assembly. Political declaration of the high-level meeting of the general assembly on the prevention and control of noncommunicable diseases. New York: United Nations, 66th sess. <https://digitallibrary.un.org/record/720106>. Accessed November 6, 2023.
 30. Chinenye S, Ogu R, Korubo I. Diabetes Advocacy and Care in Nigeria: A Review. *The Nigerian Health Journal.* 2015;15(4).
 31. Peimani M, Nasli-Esfahani E, Shakibazadeh E. Ottawa charter framework as a guide for type 2 diabetes prevention and control in Iran. *J Diabetes Metab Disord.* 2019;18:255-261. doi: 10.1007/s40200-018-0381-3

32. De Silva AP, De Silva SHP, Haniffa R, et al. A survey on socioeconomic determinants of diabetes mellitus management in a lower-middle-income setting. *Int J Equity Health.* 2016;15(1):74. doi: 10.1186/s12939-016-0363-3
33. Bowman S, Unwin N, Critchley J, et al. Use of evidence to support healthy public policy: a policy effectiveness-feasibility loop. *Bull World Health Organ.* 2012;90(11):847-853. doi: 10.2471/BLT.12.104968
34. Ajisegiri WS, Abimbola S, Tesema AG, Odusanya OO, Peiris D, Joshi R. The organisation of primary health care service delivery for non-communicable diseases in Nigeria: A case-study analysis. *PLOS Glob Public Health.* 2022;2(7):e0000566. doi: 10.1371/journal.pgph.0000566
35. Chimeddamba O, Peeters A, Walls HL, Joyce C. Noncommunicable disease prevention and control in Mongolia: a policy analysis. *BMC Public Health.* 2015;15:660. doi: 10.1186/s12889-015-2040-7
36. Pan SY, Cameron C, DesMeules M, Morrison H, Craig CL, Jiang X. Individual, social, environmental, and physical environmental correlates with physical activity among Canadians: a cross-sectional study. *BMC Public Health.* 2009;9:21. doi: 10.1186/1471-2458-9-21
37. Preventing and Managing Chronic Disease: Ontario's Framework. Ministry of Health and Long-Term Care. 2007. http://www.health.gov.on.ca/en/pro/programs/cdpm/pdf/framework_full.pdf. Accessed February 27, 2024.
38. Agide FD, Shakibazadeh E. Contextualizing Ottawa Charter Frameworks for Type 2 Diabetes Prevention: A Professional Perspective as a Review. *Ethiop J Health Sci.* 2018;28(3):355-364. doi: 10.4314/ejhs.v28i3.14
39. Infanti JJ, O'Dea A, Gibson I, et al. Reasons for participation and non-participation in a diabetes prevention trial among women with prior gestational diabetes mellitus (GDM) *BMC Med Res Methodol.* 2014;14(1):13. doi: 10.1186/1471-2288-14-13
40. Federal Ministry of Health. National guideline on the prevention, control and management of diabetes mellitus. [https://www.health.gov.ng/doc/National%20Guideline%20for%20the%20prevention,%20control%20and%20management%20of%20Diabetes%20Mellitus%20in%20Nigeria%20\(3\).pdf](https://www.health.gov.ng/doc/National%20Guideline%20for%20the%20prevention,%20control%20and%20management%20of%20Diabetes%20Mellitus%20in%20Nigeria%20(3).pdf). Accessed February 27, 2024.
41. World Health Organization 2013. Global action plan for the prevention and control of non-communicable diseases 2013-2020 Internet. Geneva, Switzerland: World Health Organization. http://www.who.int/nmh/events/ncd_action_plan/en/. Accessed February 27, 2024.
42. Federal Ministry of Health 2019. National Multi-Sectoral Action Plan for the prevention and control of non-communicable diseases (2019-2025). https://www.iccp-portal.org/system/files/plans/NCDs_Multisectoral_Action_Plan.pdf. Accessed December 11, 2023.
43. Kongats K. 2014. Diabetes prevention & management through a health equity lens. Canada: Wellesley Institute. <http://www.deslibris.ca/ID/240390>. Accessed December 11, 2023.
44. Javanparast S, Baum F, Labonte R, Sanders D, Rajabi Z, Heidari G. The experience of community health workers training in Iran: a qualitative study. *BMC Health Serv Res.* 2012;12:291. doi: 10.1186/1472-6963-12-291
45. Agofure O, Okandeji-Barry RO, Okporu UC, et al. Knowledge of diabetes mellitus: An aggregate qualitative study of students, teachers, market women, religious organization and community youths. *Ibom Med J.* 2021b;14(2):161-169.
46. Agofure O, Oghenerume H. Knowledge of Diabetes Mellitus among Students of a Public Secondary School in Southern Nigeria: A Cross-Sectional Study. *Stud J health Res Afr.* 2022;3:3. doi: 10.51168/sjhrafrica.v3i3.108
47. Ardeña GJ, Paz-Pacheco E, Jimeno CA, Lantion-Ang FL, Paterno E, Juban N. Knowledge, attitudes and practices of persons with type 2 diabetes in a rural community: phase I of the community-based Diabetes Self-Management Education (DSME) Program in San Juan, Batangas, Philippines. *Diabetes Res Clin Pract.* 2010;90:160-166. doi: 10.1016/j.diabres.2010.08.003
48. Odenigbo MA, Inya-Osuo J. Knowledge, attitudes and practices of people with type 2 diabetes mellitus in a tertiary health care centre, Umuahia, Nigeria. *J Diabetes Metab.* 2012;3:187. doi: 10.4172/2155-6156.1000187
49. Sabo SY, Moh'd AS, Emenike VI. Assessment of diabetic patients' knowledge and understanding of diabetes mellitus in a north-eastern Nigeria tertiary hospital. *SAJ Pharma Pharmacol.* 2019;6:104.
50. World Diabetes Foundation. Strengthening diabetes care in Lagos State through 35 diabetes clinics, Nigeria, WDF 16-1433. <https://www.worlddiabetesfoundation.org/projects/nigeria-wdf16-1433>. Accessed December 11, 2023.
51. Guide to community preventive services. Diabetes management: Interventions engaging community health workers. <https://www.thecommunityguide.org/findings/diabetes-management-intervention-engaging-community-health-workers.html>. Accessed December 11, 2023.
52. Flynn MAT. Empowering people to be healthier: public health nutrition through the Ottawa charter. *Proc Nutr Soc.* 2015;74(3):303-312. doi: 10.1017/S002966511400161X.
53. Rafii F, Fatemi NS, Danielson E, Johansson CM, Modanloo M. Compliance to treatment in patients with chronic illness: A concept exploration. *Iran J Nurs Midwifery Res.* 2014;19(2):159-167.
54. Tol A, Baghbanian A, Mohebbi B, et al. Empowerment assessment and influential factors among patients with type 2 diabetes. *J Diabetes Metab Disord.* 2013;12(1):6. doi: 10.1186/2251-6581-12-6
55. Colagiuri R, Girgis S, Eigenmann C, Gomez M, Griffiths R. National evidence-based guideline for patient education in type 2 diabetes. Canberra: Diabetes Australia and the NHMRC; 2009. <http://static.diabetesaustralia.com.au/s/fileassets/diabetes-australia/b9b8789d-c7ba-473d-bd49-0b7d793a0835.pdf>. Accessed December 11, 2023.
56. Beck J, Greenwood DA, Blanton L, et al. National standards for diabetes self-management education and sup-





- port. *Diabetes Care*. 2017;40(10):1409-1419. doi: 10.2337/dci17-0025
57. Okafor CN, Ezenduka PO, Onyenekwe CC, et al. Effect of Educational Intervention Programme on Self-Management Practices of Individuals with Type 2 Diabetes Mellitus in South-East, Nigeria. *Int J Diabetes Clin Res*. 2021;8:145. doi: 10.23937/2377-3634/1410145
 58. Okafor CN, Akosile CO, Nkechi CE, et al. Effect of educational intervention programme on the health-related quality of life (HRQOL) of individuals with type 2 diabetes mellitus in South-East, Nigeria. *BMC Endocr Disord*. 2023;23:75. doi: 10.1186/s12902-023-01329-y
 59. Ozioma IG. Development of Culture-Centered Diabetes Education Program for Nigerian Immigrants 2017. Nursing Masters. Paper 39. https://fisherpub.sjf.edu/nursing_etd_masters/39. Assessed December 11, 2023.
 60. Akande TM. Referral system in Nigeria: Study of a tertiary health facility. *Ann Afr Med*. 2004;3:130-133.
 61. Okumagba M. Improving access to health care in rural communities by re-orienting and integrating patent medicine sellers into primary health care service delivery in Nigeria. *South American Journal of Public Health*. 2015;3(2).
 62. Egwu IN. Reorientation in Primary Health Care Implementation: An Educational Intervention. *Int. Q. Community Health Educ*. 1988;9(3):231-242. doi: 10.2190/51E2-0FQU-NGDN-3J59
 63. Zahran AM, Salama AA, Beddah AS. Undiagnosed diabetes among adult attendants of a rural primary health-care center in Menoufia Governorate. *Menoufia Med J*. 2017;30(3):800.
 64. Erasmus RT, Soita DJ, Hassan MS, et al. High prevalence of diabetes mellitus and metabolic syndrome in a South African coloured population: baseline data of a study in Bellville, Cape Town. *S Afr Med J*. 2012;102(11):841-844. doi: 10.1046/j.1464-5491.2003.00782.x
 65. Animaw W, Seyoum Y. Increasing prevalence of diabetes mellitus in a developing country and its related factors. *PLoS One*. 2017;12(11):e0187670. doi: 10.1371/journal.pone.0187670.
 66. Abebe SM, Berhane Y, Worku A, Assefa A. Diabetes mellitus in North West Ethiopia: a community-based study. *BMC Public Health*. 2014;14(1):97. doi: 10.1186/1471-2458-14-97.
 67. Megerssa YGM, Birru S, Goshu A, Tesfaye D. Prevalence of undiagnosed diabetes mellitus and its risk factors in selected institutions at Bishoftu town, East Shoa, Ethiopia. *Diabetes Metab J*. 2013;S12(008):2-7.
 68. Wondemagegn AT, Bizuayehu HM, Abie DD, Ayalneh GM, Tiruye TY, Tessema MT. Undiagnosed diabetes mellitus and related factors in East Gojjam (NW Ethiopia) in 2016: a community-based study. *J Public Health Res*. 2017;6(1):834. doi: 10.4081/jphr.2017.834
 69. Worede A, Alemu S, Gelaw YA, Abebe M. The prevalence of impaired fasting glucose and undiagnosed diabetes mellitus and associated risk factors among adults living in a rural Koladiba town, northwest Ethiopia. *BMC Res. Notes*. 2017;10(1):251. doi: 10.1186/s13104-017-2571-3.
 70. Seifu W, Woldemichael K, Tsehaine B. Prevalence and risk factors for diabetes mellitus and impaired fasting glucose among adults aged 15-64 years in Gilgel Gibe Field Research Center, Southwest Ethiopia, 2013: through a WHO step wise approach. *MOJ Public Health*. 2015;2(5):136-143. doi: 10.15406/mojph.2015.02.00035
 71. Ludwig C, Streicher M, Habicht SD, Swai ME, Krawinkel MB. Targeted screening reveals high numbers of prediabetes and diabetes mellitus in Moshi, Tanzania. *Diabetes Metab J*. 2017;8(1):720. doi: 10.4172/2155-6156.1000720
 72. Balde NM, Camara A, Diallo AA, et al. Prevalence and awareness of diabetes in Guinea: findings from a WHO STEPS. *JEMDSA*. 2017;22(3):36-42.
 73. Echouffo-Tcheugui JB, Dzudie A, Epacka ME, et al. Prevalence and determinants of undiagnosed diabetes in an urban Sub-Saharan African population. *Prim Care Diabetes*. 2012;6(3):229-234. doi: 10.4102/ajlm.v11i1.1433
 74. Seck SM, Dia DG, Doupa D, et al. Diabetes burden in urban and rural Senegalese populations: a cross-sectional study in 2012. *Int J Endocrinol*. 2015;6:163641. doi: 10.1155/2015/163641
 75. Enang OE, Out AA, Essien OE, et al. Prevalence of dysglycemia in Calabar: a cross-sectional observational study among residents of Calabar, Nigeria. *BMJ Open Diabetes Res Care*. 2014;2(1):e000032. doi: 10.1136/bmj-drc-2014-000032
 76. Sabir A, Isezuo S, Ohwovoriole A. Dysglycaemia and its risk factors in an urban Fulani population of northern Nigeria. *West Afr J Med*. 2011;30(5). doi: 10.11604/pamj.2016.23.19.5806
 77. Abiodun OO, Olaogun AAE, Oladayo Akinpelu AO. Educational Intervention Impacts on Knowledge and Performance of Self-Care Practices among Type 2 Diabetes Mellitus Patients in Selected Hospitals in Southwestern, Nigeria. *Int J Diabetes Clin Res*. 2020;7:124. doi: 10.23937/23773634/1410124
 78. Ubangha LO, Odugbemi TO, Abiola AO. Diabetes mellitus: Identifying the knowledge gaps and risk factors among adolescents attending a public school in Lagos State. *J Clin Sci*. 2016;13:193-198. doi: 10.4103/2468-6859.192302
 79. Anyanti J, Akuiyibo SM, Fajemisin O, Idogho O, Amoo B. Assessment of the level of knowledge, awareness and management of hypertension and diabetes among adults in Imo and Kaduna states, Nigeria: a cross-sectional study. *BMJ Open*. 2021;11:e043951. doi: 10.1136/bmjopen-2020-043951
 80. Odili VU, Isiboge PD, Eregie A. Patients' Knowledge of Diabetes Mellitus in a Nigerian City. *Trop J Pharm Res*. 2011;10(5):637-642. doi: 10.4314/tjpr.v10i5.13
 81. Agofure O, Oyewole OE, Okandeji-Barry RO. Health Seeking Behaviour among patients with type-2 diabetes mellitus in Warri, Delta Sate, Nigeria. *Journal of Agric Bio and App Sci*. 2015;4:161-171.

82. Awosusi A, Folaranmi T, Yates R. Nigeria's new government and public financing for universal health coverage. *Lancet Glob Health*. 2015;3:514-515. doi: 10.1016/S2214-109X(15)00088-1
83. Oтовwe A, Baba A. Knowledge of referral and feedback system among health workers in billiri local government area of Gombe state, Nigeria. *European J Pharm Med Res*. 2016;3:111-155.
84. Oтовwe A, Henry EA, Ese OA. Knowledge of dietary and medical management of type-2 diabetes in an urban and rural community of Delta State Nigeria. *AJDM*. 2018;26(1).
85. Ng R, Sutradhar R, Yao Z, Wodchis WP, Rosella LC. Smoking, drinking, diet and physical activity-modifiable lifestyle risk factors and their associations with age to first chronic disease. *Int J Epidemiol*. 2020;49(1):113-130. doi: 10.1093/ije/dyz078
86. World Health Organization 2015. WHO global report on trends in tobacco smoking 2000–2025. Geneva: World Health Organization. <https://www.who.int/tobacco/publications/surveillance/reportontrendstobaccosmoking/en/>. Accessed June 13, 2023.
87. Oyewole BK, Animasahun VJ, Chapman HJ. Tobacco use in Nigerian youth: A systematic review. *PloS One*. 2018;13(5):e0196362. doi: 10.1371/journal.pone.0196362
88. World Bank Group. World Development Indicators. <https://datatopics.worldbank.org/world-development-indicators>. Accessed June 13, 2023.
89. National Population Commission (NPC) Nigeria and ICF. *Nigeria Demographic and Health Survey 2018*. Abuja, Nigeria, and Rockville, Maryland, USA: NPC and ICF 2019.
90. Schrieks IC, Heil AL, Hendriks HF, Mukamal KJ, Beulens JW. The effect of alcohol consumption on insulin sensitivity and glycemic status: a systematic review and meta-analysis of intervention studies. *Diabetes Care*. 2015;38(4):723-732. doi: 10.2337/dc14-1556
91. Kim SJ, Kim DJ. Alcoholism and diabetes mellitus. *Diabetes Metab J*. 2012;36(2):108-115. doi: 10.4093/dmj.2012.36.2.108
92. Wan Q, Liu Y, Guan Q, Gao L, Lee KO, Zhao J. Ethanol feeding impairs insulin stimulated glucose uptake in isolated rat skeletal muscle: role of Gs alpha and cAMP. *Alcohol Clin Exp Res*. 2005;29(8):1450-1456. doi: 10.1097/01.alc.0000174768.78427.f6
93. World Health Organization 2004. Global status report on alcohol and health. Geneva: World Health Organization. Accessed June 13, 2023.
94. Adeloye D, Olawole-Isaac A, Auta A, et al. Epidemiology of harmful use of alcohol in Nigeria: a systematic review and meta-analysis. *Am J Drug Alcohol Abuse*. 2019;1-13. doi: 10.1080/00952990.2019.1628244
95. Bennett LA, Campillo C, Chandrashekar CR, Gureje O. Alcoholic beverage consumption in India, Mexico, and Nigeria: a cross-cultural comparison. *Alcohol Health Res World*. 1998;22:243-252.
96. Agofure O, Okandeji-Barry O, Odjimogho S. Prevalence of Alcohol Consumption among Primary and Secondary School Adolescents in Obiaruku Community in Delta State, Southern Nigeria. *Afr J Biomed Res*. 2020;23:35-40.
97. Adekeye OA, Adeusi SO, Chenube OO, Ahmadu FO, Sholarin MA. Assessment of alcohol and substance use among undergraduates in selected private universities in Southwest Nigeria. *IOSR-JHSS*. 2015;20:1-7. doi: 10.9790/0837-20320107
98. World Health Organization 2018. Global status report on alcohol and health. Geneva: World Health Organization WHO Press; 2018. https://apps.who.int/iris/bitstream/handle/10665/112736/9789240692763_eng.pdf;sequence=1. Accessed June 13, 2023.
99. Oduwole AA, Ladapo TA, Fajolu IB, Ekure EN, Adeniyi OF. Obesity and elevated blood pressure among adolescents in Lagos, Nigeria: a cross-sectional study. *BMC Public Health*. 2012; 12(1):616. doi: 10.1186/1471-2458-12-616
100. Abubakari A, Bhopal R. Systematic review on the prevalence of diabetes, overweight/obesity and physical inactivity in Ghanaians and Nigerians. *Public Health*. 2008; 122(2):173-182. doi: 10.1016/j.puhe.2007.06.012
101. Abiona O, Oluwasanu M, Oladepo O. Analysis of alcohol policy in Nigeria: multi-sectoral action and the integration of the WHO “best-buy interventions. *BMC Public Health*. 2019;19:810. doi: 10.1186/s12889-019-7139-9
102. Global status report on alcohol and health 2018. Geneva: World Health Organization. Licence: CC BY-NC-SA 3.0 IGO.
103. Livingston M 2015. Understanding recent trends in Australian alcohol consumption. Canberra: Foundation for Alcohol Research and Education & Centre for Alcohol Policy Research. <http://fare.org.au/wp-content/uploads/Understanding-recent-trends-in-Australian-alcohol-consumption.pdf>. Accessed August 12, 2023.
104. Jaja T, Yarhere IE. Risk factors for type-2 diabetes mellitus in adolescents secondary school students in Port Harcourt, Nigeria. *Niger J Paediatr*. 2015;42(2):137-141. doi: 10.4314/njp.v42i2.13
105. Okpere AN, Anochie IC, Eke FU. Prevalence of Microalbuminuria among secondary school children. *Afr Health Sci*. 2012;12(2):140-147. doi: 10.4314/ahs.v12i2.10
106. Oluwayemi IO, Brink SJ, Oyenusi EE, Oduwole OA, Oluwayemi MA. Fasting Blood Glucose Profile among Secondary School Adolescents in Ado-Ekiti, Nigeria. *J Nutr Metab*. 2015;417859:4. doi: 10.1155/2015/417859
107. Agofure O, Akpojobaro EH. Diabetes mellitus in primary and secondary schools in Africa: an exploratory review. *Alexandria J Med*. 2020;56(1):166-172. doi: 10.1080/20905068.2020.1833278
108. Dong Y, Chen L, Gutin B, Zhu H. Total, insoluble, and soluble dietary fiber intake and insulin resistance and blood pressure in adolescents. *Eur J Clin Nutr*. 2019;73(8):1172-1178. doi: 10.1038/s41430-018-0372-y
109. Weickert MO, Pfeiffer AFH. Impact of Dietary Fiber Consumption on Insulin Resistance and the Preven-

- tion of Type 2 Diabetes. *J Nutr.* 2018;148(1):7-12. doi: 10.1093/jn/nxx008
110. Agofure O, Okporu UC. Effects of Teachers-led educational intervention on Knowledge and Attitude towards the prevention of diabetes mellitus among students of a Secondary School in Southern Nigeria: a one group quasi-experimental study. *Rwanda Medical J.* 2023;80(2):23-34. doi: 10.4314/rmj.v80i2.3
111. Srinivas SC, Wrench WM, Bradshaw K, Dukhi. Diabetes mellitus: preliminary health-promotion activity based on service-learning principles at a South African national science festival. *JEMDSA.* 2011;16(2):101-106. doi: 10.1080/22201009.2011.10872258
112. Mhlongo M, Marara P, Bradshaw K, Srinivas S. Health education on diabetes at a South African national science festival. *Afr J Health Professions Educ.* 2018;10(1):26-30. doi: 10.7196/AJHPE.2018.v10i1.887
113. Agofure O, Okandeji-Barry RO, Okporu UC, Odjimogho S, Agofure K, Abuh I. Opinion of teachers on perceived deficiencies in the current secondary school curriculum in the prevention and control of non-communicable diseases: a qualitative study. *Port Harcourt J Educ Stud.* 2021b;6(1).
114. Hawe P, King L, Noort M, Jordens C, Lloyd B. Indicators to help with capacity building in Health Promotion. Australian Centre for Health Promotion. 2000. <https://iseralaska.org/static/akpfs/IndicatorsForCapacityBuilding.pdf>. Accessed June 28, 2023.
115. Mehra R, Vats S, Kumar R, et al. Emergence of diabetes education and capacity-building programs for primary care physicians in India. *J Family Med Prim Care.* 2022;11(3):839-846. doi: 10.4103/jfmpc.jfmpc_669_21
116. Wijeyaratne C, Arambepola C, Karunapema P, et al. Capacity building of the allied health workforce to prevent and control diabetes: lessons learnt from the National Initiative to Reinforce and Organize General Diabetes Care in Sri Lanka (NIROGI) Lanka project. *WHO South-East Asia J Public Health.* 2016;5(1):34-39. doi: 10.4103/2224-3151.206550
117. Ojobi JE, Odoh G, Aniekwensi E, Dunga J. Mortality among type 2 diabetic in patients in a Nigerian tertiary hospital. *Afr J Diab Med.* 2016;24:17-20.
118. Unadike BC, Essien I, Akpan NA, Peters EJ, Assien OE. Profile and outcome of diabetic admissions at the university of Uyo teaching hospital, Uyo. *Int J Med Med Sci.* 2013;5:286-289. doi: 10.5897/IJMMS09.376
119. Oshilonya HU, Ijioma SN, Ibeh IN. Prevalence of type-2 diabetes mellitus amongst suspected subjects in Agbor, Delta State, Nigeria and its relationship with age and gender. *Arch Appl Sci Res.* 2015;7:18-20.
120. Adeloye D, Ige JO, Aderemi AV, et al. Estimating the prevalence, hospitalisation and mortality from type 2 diabetes mellitus in Nigeria: A systematic review and meta-analysis. *BMJ Open.* 2017;7:e015424. doi: 10.1136/bmjopen-2016-015424
121. Javadinasab H, Masoudi Asl I, Vosoogh-Moghaddam A, Najafi B. Sustainable financing of health promotion services in selected countries: Best experience for developing countries. *Med J Islam Repub Iran.* 2019;5:33:52. doi: 10.34171/mjiri.33.52
122. World Health Organization 2013. Regional Office for Africa. State of health financing in the African region. Geneva: WHO. <https://www.afro.who.int/sites/default/files/2017-06/state-of-health-financing-afro.pdf>. Accessed November 21, 2023.
123. Abubakar I, DalGLISH SL, Angell B, et al. The Lancet Nigeria Commission: investing in health and the future of the nation. *Lancet.* 2022; 399(10330):1155-1200. doi: 10.1016/S0140-6736(21)02488-0
124. Eze AE. Health Promotion and Its Challenges to Public Health Delivery System in Africa. Public Health in Developing Countries - Challenges and Opportunities. IntechOpen 2020 doi: 10.5772/intechopen.91859
125. World Health Organization 2001. Health Promotion: A Strategy for the African Region. Geneva: WHO. <https://www.afro.who.int/sites/default/files/2017-06/Health%20Promotion%20Strategy%20inside%20English.pdf>. Accessed June 29, 2023.
126. Nwatu CB. Improving access to diabetes care in Nigeria – The GIFSHIP opening. *Int J Med Health Dev.* 2022;27:319-325. doi: 10.4103/ijmh.ijmh_33_22



Phototherapy in the management of vitiligo – an updated narrative review

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ABSTRACT

Introduction and aim. Vitiligo is a chronic skin disease characterized by progressive loss of melanocytes. Various treatment options have been developed to manage vitiligo, however, phototherapy has emerged as one of the most effective treatment options. Therefore, this review has been written to examine the mechanisms of this particular treatment approach and its optimal implementation.

Material and methods. A review of the literature regarding combination of word vitiligo with the following: psoralen ultraviolet A (PUVA), narrowband ultraviolet B (NB-UVB) and excimer laser (EL) was performed using the PubMed database.

Analysis of the literature. NB-UVB has demonstrated safety and efficacy in stimulating melanocyte proliferation and melanin synthesis, making it an attractive treatment option for both localized and generalized vitiligo. PUVA therapy, combining psoralen photosensitization with UVA irradiation, has shown remarkable efficacy in repigmentation, particularly in refractory or extensive vitiligo. However, because of possible side effects, it is not recommended as a first line phototherapy. With its targeted and precise approach, EL offers a localized treatment and has produced impressive results in localized and segmented vitiligo.

Conclusion. Despite limitations, phototherapy continues to evolve, offering hope for individuals with vitiligo. Further research and advancements in treatment protocols are needed.

Keywords. NB-UVB, phototherapy, vitiligo

Introduction

Vitiligo is a common depigmentation disorder affecting about 1–2% of the world's population. It is characterized by the formation of hypopigmented patches on the skin corresponding to the dysfunction and loss of epidermal melanocytes.¹ Vitiligo is more prevalent in female patients. As for geographic region and ethnicity, evidence suggests that people on the African continent are more affected by this condition.² The lesions may be localized or generalized, although they most commonly affect vis-

ible parts of the body, namely skin of palms, soles and head. Pathophysiology of the disease is complex and includes a genetic predisposition, an autoimmune response or oxidative stress, and autoinflammatory mechanisms.¹ To date, options for vitiligo treatment remain limited, with therapeutic strategies targeting inflammation and immune responses, such as topical or systemic steroids, topical calcineurin inhibitors alongside topical and systemic Janus kinase inhibitors or surgical procedures. One of the options gaining ground in recent years

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is phototherapy, which promotes reduction of inflammation and melanocyte regrowth. In general, efficacy of phototherapy can be assessed after at least six months, and its effect depend on the type of phototherapy, duration of treatment, and body site. However, phototherapy should be considered as ineffective if no repigmentation (mainly perifollicular) is seen during the first 3 months of treatment or the degree of repigmentation is less than 25% after 6 months of therapy.^{3,4} The main phototherapy methods include psoralen-UV-A (PUVA) and narrow band UV-B (NB-UVB) therapies, which are used for large lesions. In contrast, relatively new excimer laser is used mainly for small lesions. Currently, NB-UVB is considered as first-line treatment for body surface area (BSA) > 10–20%, while PUVA is used as a second-choice treatment, mainly in adults.^{4,5} While achieving good clinical results with a lower total cumulative UV dose than the other methods, the excimer laser is limited by high acquisition and maintenance costs, limited availability, and time-consuming procedure.⁵

Aim

The purpose of this paper is to assess the treatment response of vitiligo to phototherapy.

Material and methods

A comprehensive research was carried out on the PubMed databases, covering period between 2000 and 2024. Search terms included phototherapy, vitiligo, psoralen ultraviolet A, narrowband ultraviolet B, and excimer laser. A thorough analysis of literature was conducted, focusing on the most recent articles published within the last five years. However, older papers were also considered if they presented noteworthy findings. Findings from a total of 68 selected papers were compiled and organized in this review.

Analysis of the literature

Psoralen ultra-violet A

PUVA photochemotherapy (Fig. 1), which is the use of psoralens as a photosensitizer in combination with ultraviolet (UVA) radiation (320–400 nm), have been used to treat vitiligo since the 1950s and was the main type of phototherapy until the development of NB-UVB.^{6,7} Psoralens are natural phototoxic furanocoumarins found in plants.⁸ They are administered systemically or topically, followed by exposure to UVA radiation.⁹ This combination triggers a strong phototoxic reaction that allows the skin to repigment. The most commonly used photosensitizer is 8-methoxy psoralen (8-MOP), usually taken at 0.6–0.8 mg/kg.⁵ Photosensitivity develops after 1 hour, peaks after approximately 2 hours and disappears after roughly 8 hours.¹⁰ Psoralens rapidly enter the cell and intercalate between DNA base pairs and, upon absorption of photons, undergo chemical activation to

crosslink DNA. This causes a range of antiproliferative, antiangiogenic, apoptotic and immunosuppressive effects. Through some unknown mechanism, melanogenesis is also stimulated and the expression of vitiligo-associated antigens on melanocyte cell membranes is reduced.^{6,11} Nevertheless, the exact mechanism of action of pigmentation induction by PUVA in acquired vitiligo is still unknown. Anbar et al. showed that PUVA therapy increases the number and activity of epidermal melanocytes in all areas and reduces degenerative changes in both melanocytes and keratinocytes. The reversal of degeneration in depigmented and seemingly normal skin after PUVA indicates the role of this modality in both repigmentation and protection against further depigmentation.¹² Indications for using PUVA in vitiligo treatment include BSA of more than 10% of the body surface area of vitiligo, for which other treatments, including NB-UVB, have not guaranteed satisfactory results.¹⁰ It is crucial to evaluate the patient's condition carefully for long-term treatment. When evaluating a patient before treatment, key elements are age, skin type (according to Fitzpatrick types) and past medical history (including the history of skin cancer, immunosuppression, and current medications).⁷ The best effects of PUVA therapy are achieved on the face, trunk and proximal limbs¹³ with acral areas most resistant to treatment¹⁴ and requires 1 year to achieve a maximal treatment.³ More than 25% repigmentation occurred in 51.4% of patients at 6 months, 61.6% at 12 months after receiving PUVA therapy, and ≥75% repigmentation occurred in 8.5% of patients at 6 months and 13.6% at 12 months.¹⁴ There was no effect of disease elapsed duration on the response rate to PUVA.¹⁰ Although PUVA therapy is effective, it has many limitations. It is associated with, higher risk of skin cancer compared to other forms of phototherapy. In addition, non-specific side effects such as erythema, dryness, pruritus, blistering, and hyperpigmentation or photoaging may occur.^{10,15} Due to the systemic use of psoralen, exclusion criteria for PUVA treatments include pregnancy and lactation, premenstrual photosensitivity disorders and age (children below 12 shall be excluded). After UVA irradiation, psoralens generate photosensitizing reactions and reactive oxygen species (ROS). Certain transient receptor potential (TRP) channels, such as TRP Ankyrin type 1 (TRPA1) and TRP Vanilloid type 1 (TRPV1) in peripheral nerve endings, which are involved in pain and itch signaling, as well as neurogenic inflammation, are assumed to be sensitive detectors of ROS.¹⁶ The mechanisms above underlie some of the adverse effects of PUVA therapy, including the most serious one known as PUVA pricks. This sensation has been reported as a persistent severe burning pain deep under the skin, of a degree more severe than renal colic.¹⁷ There is a variant of PUVA therapy called PUVA sol therapy, in which the radiation

source is sunlight. However, in a study comparing the efficacy of these two therapies in the treatment of vitiligo, it was found that oral PUVA was more effective than PUVA sol in terms of early onset of repigmentation, speed of repigmentation, total repigmentation achieved after nine months of therapy, and improvement in quality of life (QOL). Nonetheless, phototoxicity was higher with oral PUVA therapy.¹⁸ In patients who experienced gastrointestinal side effects after taking a photosensitizer, topical PUVA therapy can be considered by applying psoralen in cold cream, solution, or emulsion only to the lesions.¹⁹ The effects of vitamin D analogs such as calcipotriol or tacalcitol on the effects of phototherapy have also been analyzed. However, none of the vitamin D analogs enhanced the efficacy of PUVA.²⁰



Fig. 1. Equipment used to perform PUVA therapy, A: whole body cabinet, B: body part machine

Narrow-band ultraviolet B

Narrow-band ultraviolet B (NB-UVB) therapy was first used in vitiligo treatment in 1997 by Westerhof and Nieuweboer-Krobotova.²¹ NB-UVB uses light beam of 311 nm wavelength and is significantly more broadly used due to its weaker radioactive effect. In recent years, NB-UVB has established itself as the standard treatment for vitiligo (Fig. 2). Before initiating therapy, patients with history of taking medications with photosensitizing potential should be ruled out, considering that regardless of radiation dosage, this is associated with a higher risk of erythema as a complication of therapy.²² The dose is selected by establishing the so-called MED, which is the lowest dose that causes marked erythema. Usually, therapy is started with a dose equal to 70% of MED, and with subsequent sessions, dosage would be increased by 10–20%. Caution should be maintained as $\frac{1}{3}$ of patients are photo resistant, and in these patients, doses should not be increased. Alternatively, the dose can be determined by skin phototype according to Fitzpatrick scale, although a safe and practical option is to start therapy with a dose of 200 mJ/cm² regardless of skin type.²³ Maximum

permissible dose for the face per m² of a given treatment is 1500 mJ/cm², while the maximum dose for the body is 3000 mJ/cm².²³ The most significant effect is noticeable after about 12–24 h. The appropriate skin reaction to this therapy is a pink, symptom-free erythema that lasts for 24 hours. Once this reaction is observed, the current dosage should be maintained until the erythema subsides. Following this, the subsequent dosage can be raised by 10% to 20%. Treatments are applied 2–3 times a week until remission or stabilization of the clinical condition is achieved.²³ Once stabilization is achieved, treatments are performed twice a month for the first month, once a week for the next month, once every two weeks for the third month, and then therapy can be discontinued in the fourth month.²³ Approximately 15% of patients experience a relapse within one year after discontinuation.²⁴ The effectiveness of vitiligo treatment with NB-UVB can be estimated after 18–36 irradiations and its ineffectiveness after 48.²³ In case of some patients being slow responders 72 sessions may be considered before stopping phototherapy. NB-UVB therapy can be combined with topical treatment achieving better clinical results; however, 4 hours before skin irradiation, no topical products should be applied to the skin other than mineral oil.²³ It is common for patients to miss a dose in case of patients receiving hospital phototherapy. If the treatment intervals are between 4 to 7 days, the dosage should stay the same. However, if the intervals are longer, the management strategy will differ.²³ It is important for patient to take photos of the lesions throughout the treatment to provide the doctor with a reference point for comparison. To guarantee the therapy's efficacy, follow-up appointments every 3 months are recommended to evaluate the treatment's progress. Early initiation of NB-UVB is crucial due to its ability to halt disease progression and promote repigmentation. The longer vitiligo persists, the less effective treatment tends to be.²⁵ This is especially significant in cases of segmental and acral vitiligo, where achieving repigmentation becomes increasingly challenging as the condition progresses.²⁶ It is important to assess specific factors that can impact the success of therapy. Factors such as difficult-to-treat anatomical sites (e.g., fingers, toes, bony areas) and areas lacking melanocyte reservoirs (e.g., patches with leukotrichia) can pose limitations to treatment effectiveness.²⁶ The mechanisms of UVB phototherapy involve immunosuppression induction of keratinocyte T-lymphocyte apoptosis and stimulation of peri-follicular cells to migrate and differentiate into melanocytes.^{11,27} In addition, there has been noticed an increase in acetylcholinesterase levels.²⁸ NB-UVB increases the activity of proteins responsible for the production of tyrosine, whose metabolism is impaired in the melanocytes of vitiligo patients. NB-UVB therapy not only leads to the stimulation of melanocytes but also leads to a decrease in

CD4+ and CD8+ lymphocytes and level decrease of chemokines CXCL9 and CXCL10 in the peripheral blood.²⁹ A positive therapeutic response to NB-UVB phototherapy in patients with vitiligo is often observed when lesions are localized to the face, and perifollicular pigmentation is present on dermatoscopic examination.³⁰ This phenomenon is explained by the reservoir of stem cells in hair follicles which, stimulated by radiation, differentiate into melanocytes. Among the most stable repigmentation patterns are the marginal and perifollicular mechanisms, hence NB-UVB therapy is more effective on the scalp in favor of less effective on the skin of the hands and feet.³¹ NB-UVB phototherapy in patients with vitiligo is not associated with an increased risk of melanoma, basal cell carcinoma (BCC), or squamous cell carcinoma (SCC); regardless, patients who have had 200 or more treatment sessions have an increased risk of solar keratosis.³² In the treatment of vitiligo, combination therapies have been found to be more beneficial than monotherapies. For instance, the combination of narrowband ultraviolet B with topical medications like tacrolimus 0.1%, calcipotriol/betamethasone dipropionate, Er: YAG laser, and micro-needling has shown to be more effective compared to using only one treatment method.^{25,33} Studies have also explored the use of off label medications, such as methotrexate gel, which has demonstrated positive effects when combined with NB UVB but not when used alone.³⁴ Another combination currently being investigated is the intradermal injections of prostaglandins the PGE2 or PGF2 α .³⁵ However, focus of researchers in dermatology lies on Jak Inhibitors, which are being considered as a valuable treatment option for vitiligo. Hongbin Song et al. conducted a research study to evaluate the efficacy of combining tofacitinib with NB UVB in comparison to a control group treated with betamethasone cream, tacrolimus 0.1% ointment, or pimecrolimus cream, in combination with NB-UVB therapy.³⁶ The results of the study demonstrated a significant increase in repigmentation starting from eighth week in the tofacitinib group when compared to NB-UVB therapy alone. Moreover, the level of repigmentation was notably higher in the tofacitinib group when compared to control group. These findings suggest that combination of tofacitinib and NB-UVB therapy is a safe and effective treatment for refractory vitiligo, including lesions on acral areas.³⁶ On the other hand, Xiu-kun Sun highlighted in a case report that while tofacitinib is a valid treatment option, it is important to note that it primarily acts as an inhibitor of the inflammatory pathway, suppressing the autoimmune response of vitiligo by targeting IFN- γ signaling and reducing T cell numbers in the skin. Therefore, tofacitinib alone may not be able to restore melanocytes and should be used in conjunction with NB UVB phototherapy.³⁷ Additionally, ruxolitinib, another JAK inhibitor, is also

considered a viable treatment option when combined with NB UVB for patients with extensive and progressive vitiligo lesions.³⁸ We compared effectiveness of therapies used in mentioned studies (Table 1). The advantages of NB-UVB compared to PUVA are the higher levels of repigmentation, shorter treatment, no use of psoralens, and possibility of use during pregnancy and for children. Combining psolarin with NB UVB, so-called P-NBUVB allows for faster repigmentation on the Vitiligo Area Scoring Index (VASI) scale, especially when lesions involve the lower extremities, but at the cost of increased risk of side effects.³⁹ El Mofty et al. first stated that use of psoralen plus broadband UVB (P-NBUVB) can be as effective as PUVA in the treatment of vitiligo.⁴⁰ P-NBUVB has been shown to be effective especially for facial lesions. In a randomized clinical trial (RCT), 45 Indian patients with vitiligo involving more than 5% of the body. The extent of repigmentation in the P-NBUVB group was statistically significantly more pronounced in the face, neck, and hands than in the NBUVB group. Also, erythema and perifollicular pigmentation appeared earlier at a lower cumulative dose in the P-NBUVB group compared to the NB-UVB group.⁴¹ Similarly, in RCT from Iran the P-NBUVB group showed more remarkable VASI improvement in the lower extremities.⁴² Given the cost and maintenance involved, phototherapy equipment is currently mostly accessible in dermatology clinics located in larger cities. This limited availability poses a challenge for patients seeking treatment. As a result, the concept of home phototherapy has gained significant attention over the years despite that according to studies few doctors including dermatologists know about home phototherapy and even fewer prescribe it.⁴³ For patients who frequently commute before work for phototherapy sessions, purchasing home phototherapy equipment can be a viable option to reduce travel expenses and enhance convenience. One study found that 7 weeks of therapy made it more financially viable to have a home device than to go to the hospital.⁴⁴ Nevertheless, not everyone who can afford the equipment will qualify for NB-UVB home phototherapy. Certain exclusion factors, such as history of photosensitivity disorders (xeroderma pigmentosum, lupus erythematosus, dermatomyositis, porphyria) and use of photosensitizing medications like thiazide diuretics, amiodarone, and antibiotics (tetracyclines, sulfonamides, fluoroquinolones), need to be taken into account.⁴³ Additionally, patient's BSA is another factor that needs to be considered. Patients requiring whole-body in-office phototherapy may prefer in-hospital treatment, as the multi-panel three-dimensional devices used at home require changes in body position during treatment, resulting in uneven illumination of the skin surface. Patients receiving home phototherapy should schedule a follow-up appointment every 3 months to assess potential side effects such as erythema,

burning sensation, pruritus, nausea, blistering, ocular damage, theoretical risk of skin cancer, and accidental overexposure.⁴³ Additionally, the device used for home phototherapy needs to be recalibrated every 3 months due to a decrease in irradiance.⁴⁵ The biggest advantage of home phototherapy is its convenience, as patients can receive treatment every other day. This allows for a faster cumulative dose and quicker results compared to hospital treatment.⁴⁵ The requirement for a prescription for such a device varies by country.⁴³ Patients undergoing home phototherapy should attend a follow-up visit once every 3 months for evaluation of potential erythema, burning sensation, pruritus, nausea, blistering, ocular damage, theoretical risk of skin cancer, and death from accidental overexposure. During those appointments the device requires periodic recalibration, that is, due to decay in irradiance.⁴⁵ The matter of a prescription for such a device depends on the country – in Canada it is not needed, but insurance companies ask for it for reimbursement purposes.⁴³ The question arises whether home phototherapy is as effective as hospital procedure. Singh et al. conducted a study which found that the percentage of repigmentation was similar between the two methods at each follow-up visit and after 4 months of therapy.⁴⁵ It is worth noting that patients using home NB UVB devices had fewer missed treatment sessions. This finding was consistent with other studies as well.^{31,44}

Excimer laser

Excimer lasers (ELs) combine a noble inert gas and a halogen, forming excited dimers when activated. These

dimers are created using a high-energy electrical current and have a short lifespan. Upon dissociation, they emit ultraviolet photons, releasing the stored energy post.^{46,47} There has been growing interest in the 308 nm xenon chloride laser as an exceptionally effective treatment option for various dermatological conditions.



Fig. 2. Equipment used to perform NB UVB therapy, A and B: body part machines

Excimer 308-nm light is a type of targeted phototherapy that utilizes a specific wavelength of UVB radiation through the use of an excimer laser.⁴⁸ Baltás et al. first introduced an excimer laser in 2001 to treat vitiligo patients' loss of pigmentation.⁴⁹ Excimer therapy offers several advantages compared to other phototherapy approaches. These advantages include a lower overall

Table 1. Comparison of repigmentation rates and therapeutic responses of NB-UVB treatment combined with other vitiligo medications (0 – no response, I – poor, II – moderate, III – good, IV – excellent)

Authors and year	Intervention	Mean percentage (%) of repigmentation after treatment	Therapeutic response visual analog system score (VAS) grade					Conclusion
			0	I	II	III	IV	
Alshiyab et al., 2023	Tacrolimus 0.1% ointment + NBUVB	45.6	0%	28%	43%	10%	19%	There were no significant differences between interventions in efficacy at three and six-month follow-up points.
	Calcipotriol/betamethasone + NBUVB	54.7	0%	10%	30%	45%	15%	
Gharib et al., 2023	Methotrexate gel	19.3	37.5%	37.5%	18.8%	6.3%	0%	Methotrexate gel could increase the therapeutic effect of NB-UVB and excimer laser.
	Methotrexate gel + NB-UVB	49.7	18.8%	12.5%	12.5%	31.3%	25%	
	Methotrexate gel + excimer light	39.9	25%	18.8%	18.8%	25.0%	12.5%	
Neinaa et al., 2023	PGE2 + NBUVB	54.4	0%	23.3%	20%	26.7%	30%	The intradermal injection of either PGE2 or PGF2α in association with NB-UVB is considered therapeutically successful for vitiligo with non-significant difference between them.
	PGF2α + NBUVB	48.67	0%	33.3%	16.7%	23.3%	26.7%	
	Saline (as placebo) + NBUVB	39.9	0%	76.7%	13.3%	10.0%	0%	
Song et al., 2022	Tofacitinib + halometasone + tacrolimus + NBUVB	No data	0%	0%	6.6%	6.6%	86.6%	Tofacitinib in combination with NB-UVB phototherapy may be an effective and safe alternative modality for refractory vitiligo.
	Halometasone + tacrolimus + NBUVB	No data	5.2%	57.9%	26.3%	10.5%	0%	

UV exposure, a shorter treatment time, and the capacity to target specific lesions while limiting side effects on healthy skin nearby.⁵⁰ The 308-nanometer excimer laser has proven to be a highly effective treatment option in restoring pigmentation in individuals with vitiligo. However, it has some limitations. It is recommended for depigmented BSA that are lower than 10%.⁵¹ There is a lack of clear clinical guidelines regarding the frequency, dosage, and duration of excimer laser therapy. Two studies compared the effectiveness of therapy with this laser administered 2 and 3 times a week. However, there wasn't enough evidence to conclusively determine the extent of repigmentation between these two dosage frequencies. The degree of repigmentation was found to correlate with the overall number of treatment sessions, showing an earlier onset of pigmentation with a dosage administered three times a week.^{52,53} Bae et al. proposed excimer laser treatment protocols based on their published experiences. The initial therapeutic dose ranges from 100 to 300 mJ/cm² and varies depending on the skin phototype. Subsequently, the dose is increased by 50 mJ/cm² during each therapeutic session until erythema appears post-treatment. The suggested optimal dose by the team is one that induces asymptomatic erythema, which persists for 24–48 hours. Radiation sessions can be conducted from 1 to 3 times a week. However, researchers emphasize that the ultimate effect of achieved repigmentation seems to depend on the total number of treatment sessions rather than their frequency.⁵⁴ The therapeutic mechanism of EL involves inducing apoptosis in T cells and stimulating the proliferation of melanocytes.⁵⁵ The efficacy of the 308-nm excimer laser in treating non-segmental vitiligo is confirmed by significant research. The 308-nm excimer laser displayed equal efficacy to the NB-UVB control group in attaining 75% repigmentation of vitiligo patches, according to a systematic review of seven randomized controlled trials (RCTs).⁴⁹ Bae et al., evaluating the long-term use of a 308-nanometer EL for localized vitiligo, found no significant increase in the risks of actinic keratosis, non-melanoma skin cancers, or melanoma. This suggests that EL treatment is a safe option for patients with vitiligo and does not pose an elevated risk of skin cancer.⁵⁶ Recently, EL treatment's safety has been confirmed in a substantial group of 25,694 patients diagnosed with vitiligo.⁵⁷ A notable association exists between the disease's location and duration and repigmentation's effectiveness. UV-sensitive areas such as face and neck tend to respond more rapidly to treatment, leading to an earlier reduction of lesions than UV-resistant areas like joints and extremities.⁵⁸ The application of EL is considered permissible for pediatric patients, indicating that this treatment modality can also be safely extended to children. Among the anticipated long-term skin photodamage associated with this treatment, the most frequent side effects include burns, perilesional hyper-

pigmentation, and folliculitis.⁵⁹ The EL can also be used with topical therapy, which translates into improved treatment outcomes. Based on the analysis of 8 randomized controlled trials involving 425 patches/patients, the combination of EL treatment with topical calcineurin inhibitors demonstrated superior efficacy compared to EL monotherapy for treating vitiligo. However, based on the existing evidence, there is inadequate support for the efficacy of combining topical vitamin D₃ analogs and corticosteroids with EL treatment.⁶⁰ On the other hand, Deng et al. demonstrated the application of a combination of intradermal platelet-rich plasma (PRP) injections with a 308 nm EL, resulting in positive therapy outcomes and a shortened duration of treatment.⁶¹ The meta-analysis conducted by Chen et al., which included 6 studies involving 302 patients, provided further evidence supporting the superiority of combining PRP with EL therapy compared to laser monotherapy.⁶² Moreover, Chang et al. performed a meta-analysis to evaluate the outcomes of combining topical therapy with an EL.⁶³ The meta-analysis included three RCTs involving 40 patients with vitiligo. The findings demonstrated significantly greater efficacy in achieving ≥75% repigmentation when utilizing the combination of topical therapy with tacrolimus and EL.⁶⁴⁻⁶⁶ Recently, Liu et al conducted a meta-analysis on various therapeutic combinations with excimer laser. The combination of excimer laser with antioxidants achieved the best therapeutic effects, while the weakest therapeutic effects were observed when the laser was used alone. Thus, it appears that combined therapeutic methods with various points of intervention will be of interest to researchers in the future in order to obtain the most effective form of treatment for vitiligo.⁶⁷ This treatment option appeals to individuals who want to prevent the darkening of their skin resulting from NB-UVB therapy. While NB-UVB is successful in repigmenting stable patches, it often doesn't stabilize vitiligo because it doesn't treat clinically unaffected skin. For segmental vitiligo, early use of excimer laser appears to offer the most advantageous treatment.⁶⁸

Conclusion

Despite new therapeutic options for vitiligo emerging, phototherapy (especially NB-UVB) remains as preferred treatment option due to its effectiveness and safety. Acknowledging that phototherapy alone may not be sufficient for complete repigmentation in all cases is essential. Combining phototherapy with other treatments can accelerate repigmentation process and reduce number of required phototherapy sessions. This approach is beneficial as it minimizes the risk of potential side effects while boosting the overall efficacy of the treatment. The advantage of phototherapy as a primary or maintenance therapy is also that it can be performed at home. Despite its proven benefits, usage

of phototherapy has limitations. Treatment requires adherence to the prescribed regimen and multiple sessions over an extended time period. Additionally, certain patient groups may not be suitable for phototherapy, such as those suffering from photosensitivity disorders or having a history of skin cancer. In summary, phototherapy is a valuable tool in treating vitiligo, as it provides significant repigmentation results and improves patient quality of life. With ongoing research and treatment protocol advances, phototherapy may evolve and bring hope to those with this chronic skin condition.

Declarations

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Author contributions

Conceptualization, A.W.; Validation, R.C.; Resources, A.W., A.B. and B.K.; Data Curation, A.W., A.B. and B.K.; Writing – Original Draft Preparation, A.W., A.B. and B.K.; Writing – Review & Editing, A.W., A.B. and B.K.; Supervision, R.C.; Project Administration, A.W., A.B. and B.K.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability

Not applicable.

References

1. Diotallevi F, Gioacchini H, De Simoni E, et al. Vitiligo, from Pathogenesis to Therapeutic Advances: State of the Art. *Int J Mol Sci.* 2023;24(5):4910. doi:10.3390/ijms24054910
2. Zhang Y, Cai Y, Shi M, et al. The Prevalence of Vitiligo: A Meta-Analysis. *PLoS One.* 2016;11(9):e0163806. doi:10.1371/journal.pone.0163806
3. Bae JM, Jung HM, Hong BY, et al. Phototherapy for Vitiligo: A Systematic Review and Meta-analysis. *JAMA Dermatol.* 2017;153(7):666-674. doi:10.1001/jamadermatol.2017.0002
4. Czajkowski R, Placek W, Flisiak I, et al. Vitiligo. Diagnostic and therapeutic recommendations of the Polish Dermatological Society. *Dermatology Review.* 2019;106(1):1-15. doi:10.5114/dr.2019.83440
5. Post NF, Ezekwe N, Narayan VS, et al. The use of lasers in vitiligo, an overview. *J Eur Acad Dermatol Venereol.* 2022;36(6):779-789. doi:10.1111/jdv.18005
6. Esmat S, Hegazy RA, Shalaby S, Hu SC, Lan CE. Phototherapy and Combination Therapies for Vitiligo. *Dermatol Clin.* 2017;35(2):171-192. doi:10.1016/j.det.2016.11.008
7. Richard EG. The Science and (Lost) Art of Psoralen Plus UVA Phototherapy. *Dermatol Clin.* 2020;38(1):11-23. doi:10.1016/j.det.2019.08.002
8. Vieyra-Garcia PA, Wolf P. A deep dive into UV-based phototherapy: Mechanisms of action and emerging molecular targets in inflammation and cancer. *Pharmacol Ther.* 2021;222:107784. doi:10.1016/j.pharmthera.2020.107784
9. Ibbotson SH. A Perspective on the Use of NB-UVB Phototherapy vs. PUVA Photochemotherapy. *Front Med (Lausanne).* 2018;5:184. doi:10.3389/fmed.2018.00184
10. Shenoj SD, Prabhu S; Indian Association of Dermatologists, Venereologists and Leprologists. Photochemotherapy (PUVA) in psoriasis and vitiligo. *Indian J Dermatol Venereol Leprol.* 2014;80(6):497-504. doi:10.4103/0378-6323.144143
11. Krenitsky A, Ghamrawi RI, Feldman SR. Phototherapy: a Review and Update of Treatment Options in Dermatology. *Curr Derm Rep.* 2020;9:10-21. doi:10.1007/s13671-020-00290-6
12. Anbar TS, El-Sawy AE, Attia SK, et al. Effect of PUVA therapy on melanocytes and keratinocytes in non-segmental vitiligo: histopathological, immuno-histochemical and ultrastructural study. *Photodermatol Photoimmunol Photomed.* 2012;28(1):17-25. doi:10.1111/j.1600-0781.2011.00631.x
13. Zhang Y, Mooneyan-Ramchurn JS, Zuo N, Feng Y, Xiao S. Vitiligo nonsurgical treatment: a review of latest treatment researches. *Dermatol Ther.* 2014;27(5):298-303. doi:10.1111/dth.12143
14. Cunningham KN, Rosmarin D. Vitiligo Treatments: Review of Current Therapeutic Modalities and JAK Inhibitors. *Am J Clin Dermatol.* 2023;24(2):165-186. doi:10.1007/s40257-022-00752-6
15. Bertolani M, Rodighiero E, de Felici Del Giudice MB, Lotti T, Feliciani C, Satolli F. Vitiligo: What's old, what's new. *Dermatol Reports.* 2021;13(2):9142. doi:10.4081/dr.2021.9142
16. Babes A, Kichko TI, Selescu T, et al. Psoralens activate and photosensitize Transient Receptor Potential channels Ankyrin type 1 (TRPA1) and Vanilloid type 1 (TRPV1). *Eur J Pain.* 2021;25(1):122-135. doi:10.1002/ejp.1654
17. Wyckmans M, Bervoets A. A review on PUVA pricks-A debilitating adverse event. *Photodermatol Photoimmunol Photomed.* 2023;39(3):185-192. doi:10.1111/phpp.12824
18. Singh S, Khandpur S, Sharma VK, Ramam M. Comparison of efficacy and side-effect profile of oral PUVA vs. oral PUVA sol in the treatment of vitiligo: a 36-week prospective study. *J Eur Acad Dermatol Venereol.* 2013;27(11):1344-1351. doi:10.1111/jdv.12002
19. Barros NM, Sbroglio LL, Buffara MO, Baka JLCES, Pessoa AS, Azulay-Abulafia L. Phototherapy. *An Bras Dermatol.* 2021;96(4):397-407. doi:10.1016/j.abd.2021.03.001
20. Liu X, Yao Z, Wang Y, Chai L, Zhou X. Vitamin D analogs combined with different types of phototherapy in the treatment of vitiligo: A systematic review of randomized trials and within-patient studies. *Int Immunopharmacol.* 2022;109:108789. doi:10.1016/j.intimp.2022.108789


21. Khanna U, Khandpur S. What Is New in Narrow-Band Ultraviolet-B Therapy for Vitiligo?. *Indian Dermatol Online J*. 2019;10(3):234-243. doi:10.4103/idoj.IDOJ_310_18
22. Harrop G, Dawe RS, Ibbotson S. Are photosensitizing medications associated with increased risk of important erythematous reactions during ultraviolet B phototherapy?. *Br J Dermatol*. 2018;179(5):1184-1185. doi:10.1111/bjd.16800
23. Mohammad TF, Al-Jamal M, Hamzavi IH, et al. The Vitiligo Working Group recommendations for narrowband ultraviolet B light phototherapy treatment of vitiligo. *J Am Acad Dermatol*. 2017;76(5):879-888. doi:10.1016/j.jaad.2016.12.041
24. Silpa-Archa N, Weerasubpong P, Junsuwan N, Yothachai P, Supapueng O, Wongpraparut C. Treatment outcome and persistence of repigmentation from narrow-band ultraviolet B phototherapy in vitiligo. *J Dermatolog Treat*. 2019;30(7):691-696. doi:10.1080/09546634.2018.1544409
25. Alshiyab D, Al-Qarqaz F, Ba-Shammakh S, et al. Comparison of the efficacy of tacrolimus 0.1% ointment vs calcipotriol/betamethasone in combination with NB-UVB in treatment of vitiligo. *J Dermatolog Treat*. 2023;34(1):2252119. doi:10.1080/09546634.2023.2252119
26. Seneschal J, Speeckaert R, Taieb A, et al. Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the international Vitiligo Task Force-Part 2: Specific treatment recommendations. *J Eur Acad Dermatol Venereol*. 2023;37(11):2185-2195. doi:10.1111/jdv.19450
27. Yang TT, Chiu SH, Lan CE. The effects of UVB irradiance on vitiligo phototherapy and UVB-induced photocarcinogenesis. *Photodermatol Photoimmunol Photomed*. 2020;36(4):257-262. doi:10.1111/phpp.12536
28. Said ER, Nagui NAER, Rashed LA, Mostafa WZ. Oxidative stress and the cholinergic system in non-segmental vitiligo: Effect of narrow band ultraviolet b. *Photodermatol Photoimmunol Photomed*. 2021;37(4):306-312. doi:10.1111/phpp.12653
29. Lin F, Sun X, Lei J, Xu AE. Altered circulating memory T cells in vitiligo cases followed NB-UVB therapy. *Photodermatol Photoimmunol Photomed*. 2022;38(1):76-82. doi:10.1111/phpp.12719
30. Errichetti E, Zelin E, Pinzani C, Kyrgidis A, Lallas A, Stinco G. Dermoscopic and Clinical Response Predictor Factors in Nonsegmental Vitiligo Treated with Narrowband Ultraviolet B Phototherapy: A Prospective Observational Study. *Dermatol Ther (Heidelb)*. 2020;10(5):1089-1098. doi:10.1007/s13555-020-00431-6
31. Zhang L, Wang X, Chen S, et al. Comparison of efficacy and safety profile for home NB-UVB vs. outpatient NB-UVB in the treatment of non-segmental vitiligo: A prospective cohort study. *Photodermatol Photoimmunol Photomed*. 2019;35(4):261-267. doi:10.1111/phpp.12462
32. Bae JM, Ju HJ, Lee RW, et al. Evaluation for Skin Cancer and Precancer in Patients With Vitiligo Treated With Long-term Narrowband UV-B Phototherapy. *JAMA Dermatol*. 2020;156(5):529-537. doi:10.1001/jamadermatol.2020.0218
33. Zhu B, Liu C, Zhang L, Wang J, Chen M, Wei Y. Comparison of NB-UVB combination therapy regimens for vitiligo: A systematic review and network meta-analysis. *J Cosmet Dermatol*. 2023;22(3):1083-1098. doi:10.1111/jocd.15534
34. Gharib K, Ibrahim A, El Sharkawi Y, Elmegrab N, Attia M. Methotrexate Gel Either Alone or Combined with Narrow Band Ultraviolet B or Excimer Light for the Treatment of Vitiligo. *J Clin Aesthet Dermatol*. 2023;16(3):32-36.
35. Neinaa YME, Mahmoud MAE, El Maghraby GM, Ibrahim ZAE. Efficacy of prostaglandin E2 versus prostaglandin F2 alpha assisted with narrowband-UVB in stable vitiligo. *Arch Dermatol Res*. 2023;315(9):2647-2653. doi:10.1007/s00403-023-02700-8
36. Song H, Hu Z, Zhang S, Yang L, Liu Y, Wang T. Effectiveness and safety of tofacitinib combined with narrowband ultraviolet B phototherapy for patients with refractory vitiligo in real-world clinical practice. *Dermatol Ther*. 2022;35(11):e15821. doi:10.1111/dth.15821
37. Sun XK, Xu AE. Repigmentation of acral vitiligo with tofacitinib combined with NB-UVB phototherapy: A case report. *Australas J Dermatol*. 2023;64(4):571-572. doi:10.1111/ajd.14147
38. Yousefian F, Yadlapati S, Browning JC. The use of Janus kinase inhibitors and narrowband ultraviolet B combination therapy in non-segmental vitiligo. *J Cosmet Dermatol*. 2023;22(3):1105-1107. doi:10.1111/jocd.15537
39. Zabolinejad N, Maleki M, Salehi M, Ashrafi Z, Molkara S, Layegh P. Psoralen and narrowband UVB combination provides higher efficacy in treating vitiligo compared with narrowband UVB alone: A randomised clinical trial. *Australas J Dermatol*. 2020;61(1):65-69. doi:10.1111/ajd.13184
40. Hum M, Kalia S, Gniadecki R. Prescribing Home Narrowband UVB Phototherapy: A Review of Current Approaches. *J Cutan Med Surg*. 2019;23(1):91-96. doi:10.1177/1203475418800947
41. Liu B, Sun Y, Song J, Wu Z. Home vs hospital narrowband UVB treatment by a hand-held unit for new-onset vitiligo: A pilot randomized controlled study. *Photodermatol Photoimmunol Photomed*. 2020;36(1):14-20. doi:10.1111/phpp.12495
42. Singh S, Khandpur S, Sharma VK, Bhari N, Pandey RM. An Open-Label Non-Randomized Preliminary Noninferiority Study Comparing Home-Based Handheld Narrow-Band UVB Comb Device with Standard Hospital-Based Whole-Body Narrow-Band UVB Therapy in Localized Vitiligo. *Indian Dermatol Online J*. 2023;14(4):510-515. doi:10.4103/idoj.idoj_604_22
43. Mofty ME, Zaher H, Esmat S, et al. PUVA and PUVB in vitiligo--are they equally effective?. *Photodermatol Photoimmunol Photomed*. 2001;17(4):159-163. doi:10.1034/j.1600-0781.2001.170403.x

44. Bansal S, Sahoo B, Garg V. Psoralen-narrowband UVB phototherapy for the treatment of vitiligo in comparison to narrowband UVB alone. *Photodermatol Photoimmunol Photomed*. 2013;29(6):311-317. doi:10.1111/phpp.12072
45. Zabolinejad N, Maleki M, Salehi M, Ashrafi Z, Molkara S, Layegh P. Psoralen and narrowband UVB combination provides higher efficacy in treating vitiligo compared with narrowband UVB alone: A randomised clinical trial. *Australas J Dermatol*. 2020;61(1):65-69. doi:10.1111/ajd.13184
46. Ly K, Smith MP, Thibodeaux QG, Beck KM, Liao W, Bhutani T. Beyond the Booth: Excimer Laser for Cutaneous Conditions. *Dermatol Clin*. 2020;38(1):157-163. doi:10.1016/j.det.2019.08.009
47. Yeon J, Doolan BJ, Schultz A, Gupta M. Australian experience and practical approach to the 308-nm excimer light therapy in dermatology. *Australas J Dermatol*. 2022;63(2):240-243. doi:10.1111/ajd.13842
48. Park KK, Liao W, Murase JE. A review of monochromatic excimer light in vitiligo. *Br J Dermatol*. 2012;167(3):468-478. doi:10.1111/j.1365-2133.2012.11008.x
49. Baltás E, Csoma Z, Ignác F, Dobozy A, Kemény L. Treatment of vitiligo with the 308-nm xenon chloride excimer laser. *Arch Dermatol*. 2002;138(12):1619-1620.
50. Mavilia L, Mori M, Rossi R, Campolmi P, Puglisi Guerra A, Lotti T. 308 nm monochromatic excimer light in dermatology: personal experience and review of the literature. *G Ital Dermatol Venereol*. 2008;143(5):329-337.
51. Rodrigues M, Ezzedine K, Hamzavi I, Pandya AG, Harris JE; Vitiligo Working Group. Current and emerging treatments for vitiligo. *J Am Acad Dermatol*. 2017;77(1):17-29. doi: 10.1016/j.jaad.2016.11.010
52. Noborio R, Nomura Y, Nakamura M, et al. Efficacy of 308-nm excimer laser treatment for refractory vitiligo: a case series of treatment based on the minimal blistering dose. *J Eur Acad Dermatol Venereol*. 2021;35(4):287-289. doi:10.1111/jdv.17047
53. Kim JC, Kim HR, Park JS, et al. Vitamin D supplementation can enhance therapeutic effects of excimer laser in patients with vitiligo. *J Cosmet Dermatol*. 2024;23(3):839-848. doi:10.1111/jocd.16043
54. Bae JM, Hann S-K. Laser Treatments for Vitiligo. *Med Lasers*. 2016;5:63-70. doi:10.25289/ML.2016.5.2.63
55. Fenniche S, Zaouak A, Tanfous AB, Jrad M, Hammami H. Successful Treatment of Refractory Vitiligo with a Combination of Khellin and 308-nm Excimer Lamp: An Open-Label, 1-Year Prospective Study. *Dermatol Ther (Heidelb)*. 2018;8(1):127-135. doi:10.1007/s13555-017-0218-x
56. Bae JM, Eun SH, Oh SH, et al. The 308-nm excimer laser treatment does not increase the risk of skin cancer in patients with vitiligo: A population-based retrospective cohort study. *Pigment Cell Melanoma Res*. 2019;32(5):714-718. doi:10.1111/pcmr.12781
57. Ju HJ, Han JH, Kim MS, et al. The long-term risk of lymphoma and skin cancer did not increase after topical calcineurin inhibitor use and phototherapy in a cohort of 25,694 patients with vitiligo. *J Am Acad Dermatol*. 2021;84(6):1619-1627. doi:10.1016/j.jaad.2021.01.067
58. Mehraban S, Feily A. 308nm excimer laser in dermatology. *J Lasers Med Sci*. 2014;5(1):8-12.
59. Gianfaldoni S, Tchernev G, Wollina U, et al. Vitiligo in Children: What's New in Treatment?. *Open Access Maced J Med Sci*. 2018;6(1):221-225. doi:10.3889/oamjms.2018.060
60. Bae JM, Hong BY, Lee JH, Lee JH, Kim GM. The efficacy of 308-nm excimer laser/light (EL) and topical agent combination therapy versus EL monotherapy for vitiligo: A systematic review and meta-analysis of randomized controlled trials (RCTs). *J Am Acad Dermatol*. 2016;74(5):907-915. doi:10.1016/j.jaad.2015.11.044
61. Deng Y, Li J, Yang G. 308-nm Excimer Laser Plus Platelet-Rich Plasma for Treatment of Stable Vitiligo: A Prospective, Randomized Case-Control Study. *Clin Cosmet Investig Dermatol*. 2020;13:461-467. doi:10.2147/CCID.S260434
62. Chen J, Yu N, Li H, Tang Y, Zhu H. Meta-analysis of the efficacy of adding platelet-rich plasma to 308-nm excimer laser for patients with vitiligo. *J Int Med Res*. 2022;50(9):3000605221119646. doi:10.1177/03000605221119646
63. Chang HC, Sung CW. Efficacy of combination therapy of narrowband-ultraviolet B phototherapy or excimer laser with topical tacrolimus for vitiligo: An updated systematic review and meta-analysis. *Photodermatol Photoimmunol Photomed*. 2021;37(1):74-77. doi:10.1111/phpp.12593
64. Kawalek AZ, Spencer JM, Phelps RG. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: a pilot study. *Dermatol Surg*. 2004;30(2 Pt 1):130-135. doi:10.1111/j.1524-4725.2004.30058.x
65. Nisticò S, Chiricozzi A, Saraceno R, Schipani C, Chimenti S. Vitiligo treatment with monochromatic excimer light and tacrolimus: results of an open randomized controlled study. *Photomed Laser Surg*. 2012;30(1):26-30. doi:10.1089/pho.2011.3029
66. Passeron T, Ostovari N, Zakaria W, et al. Topical tacrolimus and the 308-nm excimer laser: a synergistic combination for the treatment of vitiligo. *Arch Dermatol*. 2004;140(9):1065-1069. doi:10.1001/archderm.140.9.1065
67. Li C, Hu Y, Mu Z, et al. Comparison of various excimer laser (EL) combination therapies for vitiligo: a systematic review and network meta-analysis. *J Dermatolog Treat*. 2024;35(1):2302064. doi:10.1080/09546634.2024.2302064
68. Zhou F, Chen S, Jin W, Lu Y, Gao Y, Wu J. Comparison of the efficacy and safety of 308-nm excimer laser as monotherapy and combination therapy with topical tacrolimus in the treatment of periorcular vitiligo. *Dermatol Ther*. 2022;35(7):e15556. doi:10.1111/dth.15556



CASUISTIC PAPER

Atypical presentation of extra-skeletal Ewing's sarcoma in a 57-year-old female – a case report

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ABSTRACT

Introduction and aim. Malignant soft tissue tumors exhibiting similar histological and immunohistochemical characteristics to Ewing sarcoma of the bones are referred to as extra-skeletal Ewing sarcoma within the pathology research domain. These tumors fall under the broader classification of Ewing sarcoma family of tumors, which encompasses Ewing sarcoma of the bones, extra-skeletal Ewing sarcoma, and primitive neuroectodermal tumor, the latter demonstrating a more pronounced neural differentiation compared to Ewing sarcoma of the bone. Extra-skeletal Ewing sarcoma stands out as a rare, aggressive, and rapidly growing malignant soft tissue tumor characterized by a notable recurrence rate and a predilection for occurrence in males. The roots of recognizing extra-skeletal Ewing sarcoma trace back to 1975 when Angervall and Enzinger reported the inaugural case. This study aims to underscore the significance of recognizing diverse clinical presentations for precise diagnosis and effective patient care of Extra-skeletal Ewing sarcoma in an elderly patient.

Case description. In the context of our pathology research, a noteworthy case involves a 57-year-old female presenting with a mass in the left iliac fossa. The diagnosis, established through a comprehensive approach involving Imaging, histopathological examination, immunohistochemistry, and molecular studies such as fluorescence in situ hybridization, confirms the nature of the tumor as extra-skeletal Ewing sarcoma. This case adds to the understanding and documentation of this distinct variant through a multi-modal investigative process.

Conclusion. This case report contributes to the existing literature by shedding light on an atypical presentation of extra-skeletal Ewing sarcoma in an older patient. Understanding the varied clinical manifestations and incorporating advanced diagnostic techniques, such as fluorescence in situ hybridization and immunohistochemistry, is pivotal for accurate diagnosis and optimal patient management.

Keywords. Ewing sarcoma, Ewing sarcoma family of tumors primitive neuroectodermal tumor, extra skeletal Ewing sarcoma

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Introduction

Ewing Sarcoma stands as a highly malignant bone tumor primarily affecting long bones, a condition notably prevalent in children and young adults. The pioneering description of this pathology traces back to James Ewing in 1921.¹ Despite its primarily osseous manifestation, instances of malignant soft tissue tumors exhibiting indistinguishable features from Ewing sarcoma have been documented, termed as extra-skeletal Ewing's Sarcoma. These tumors are presently categorized under the Ewing sarcoma family of tumors, encompassing Ewing sarcoma, extra-skeletal Ewing sarcoma, and the primitive neuroectodermal tumor, the latter demonstrating heightened neural differentiation compared to Ewing sarcoma.²

Extra-skeletal Ewing sarcoma, characterized by rarity and aggressiveness, represents a malignant soft tissue tumor with a notable recurrence rate, predominantly affecting adolescents and young adults within the age range of 10 to 30 years. The initial recognition of extra-skeletal Ewing sarcoma dates back to 1975 when Angervall and Enzinger reported the inaugural case.³ Common sites of occurrence include the chest wall, paravertebral region, retroperitoneal space, lower extremities, and gluteal region. Uncommonly, cases have been reported in various locations such as the kidney, breast, gastrointestinal tract, prostate, endometrium, adrenal glands, brain, and lungs.⁴

Extra-skeletal Ewing sarcoma remains a challenging entity within the realm of medical literature, often posing diagnostic and therapeutic dilemmas. Diagnostic endeavors primarily rely on magnetic resonance imaging (MRI) and fluorodeoxyglucose-positron emission tomography (FDG-PET) imaging techniques, allowing for initial diagnosis and the detection of potential metastases.⁵ Extra-skeletal Ewing sarcoma emerges as a swiftly progressing tumor, primarily afflicting the young demographic, often posing a poor prognosis with notably high mortality rates, especially in cases of metastasis to the lungs, bones, and bone marrow. This pathology develops within the soft tissues of diverse anatomical regions, with the upper thigh, upper arms, shoulders, and buttocks being common sites.⁶ The lack of specific clinical signs often contributes to delayed diagnosis, underscoring the importance of imaging in diagnosis, staging, preoperative assessment, and surveillance. Early diagnosis is imperative for effective management and intervention in this challenging medical condition.⁷

Aim

This study aims to underscore the significance of recognizing diverse clinical presentations for precise diagnosis and effective patient care of extra-skeletal Ewing sarcoma in an elderly patient.

Description of the case

A 57-year-old female sought evaluation in the Outpatient Department due to severe abdominal pain. Upon examination, a palpable mass was identified in the left iliac fossa. Ultrasonography revealed a substantial solid cystic intraperitoneal mass measuring 12.9×12.3×8.7 cm. The mass exhibited invasion of the left rectus muscle anteriorly and close proximity to small bowel loops posteriorly. Potential differentials were considered, with neoplasm (likely small bowel Gastro Intestinal Stromal Tumor) being the primary consideration, and hematoma deemed less likely. Biopsy was recommended for further confirmation.

Magnetic Resonance Imaging of the abdomen unveiled a large, heterogeneous, relatively defined solid cystic mass originating from the peritoneal surface of the left rectus muscle. Its superior extension reached from the level of the umbilicus, while its inferior extension reached into the left iliac fossa. Notably, no omental thickening or deposits were observed, with mild fluid present in the pelvis. Positron emission tomography-computed tomography imaging findings suggested a soft tissue or small bowel gastro intestinal stromal tumor.

Histopathological examination revealed features consistent with an abdominal wall malignant round cell neoplasm. Immunohistochemistry further indicated characteristics aligning with the Ewing sarcoma family of tumors. This comprehensive diagnostic approach underscores the complexity of the pathology and guides further management decisions.

Gross examination

Upon receipt, the mass exhibited adherence to fat and an attached ellipse of skin. A tag was identified, and the specimen was appropriately oriented. The mass with attached fibro-fatty tissue, measured 12×10×9 cm, while the attached skin measured 3.5×1 cm (Fig. 1).

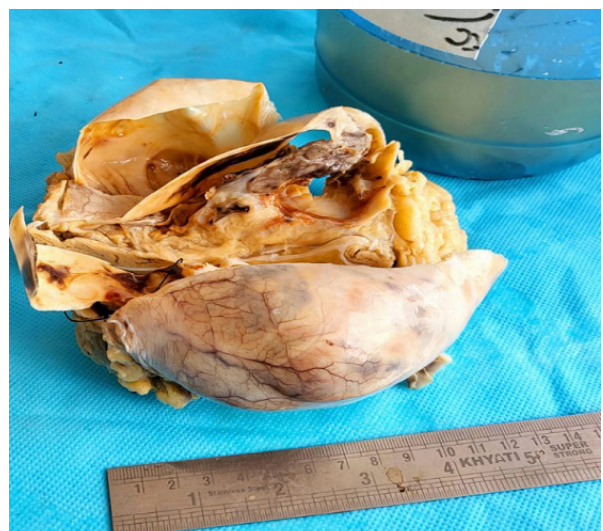


Fig. 1. Gross examination: Solid to cystic mass with areas of necrosis

Upon cutting, as shown in the Figure 1, the cut surface showed a tumor which displayed a combination of solid and cystic areas, cysts extruded hemorrhagic serous fluid. The largest solid area within tumor, measuring 9×4×6 cm, exhibited a variegated appearance with necrosis and hemorrhagic areas. Notably, the tumor displayed adjacency to the right lateral margin. This detailed gross examination provides a comprehensive overview of the specimen's macroscopic features, informing further pathological analysis and interpretation.

Microscopic examination

Upon microscopic examination, sections of the anterior abdominal mass revealed sheets of malignant-looking small round cells characterized by hyperchromatic nuclei, indistinct nucleoli, occasional mitosis, and scant to moderate eosinophilic cytoplasm (Fig. 2).

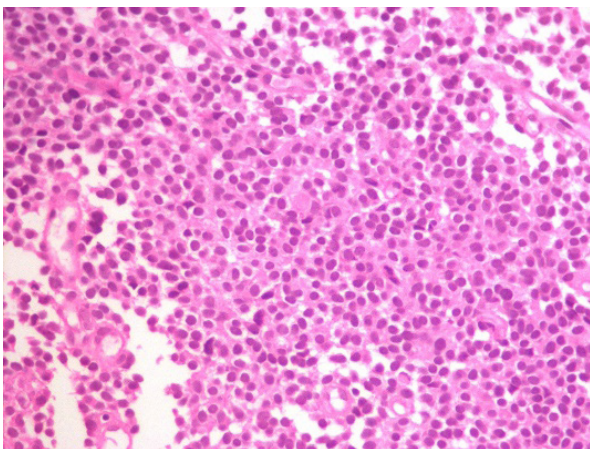


Fig. 2. Histopathology under high power view showed malignant small round cells (Hematoxylin & Eosin, 40×)

Figures 2 shows the microscopic examination in high-power view providing detailed visualizations of the cellular composition and structural characteristics. Initial impressions were that the features observed in the anterior abdominal mass are indicative of a malignant small round cell tumor. To confirm and subtype the tumor, immunohistochemistry (IHC) is recommended. The comprehensive immunohistochemistry (IHC) panel was conducted on the anterior abdominal wall mass, yielding the following results: cytokeratin (CK): negative; vimentin: diffuse positive; leukocyte common antigen (LCA): negative; synaptophysin: weak positive; proliferation index marker – Ki-67: 10–15%; desmin: negative; muscle markers-MYOD1: negative; CD99: positive (membranous); FLI-1: positive; B-COR: negative; NKX2.2: positive. The respective Figures 3–8 illustrate the immunohistochemistry results, visually highlighting the expression of specific markers.

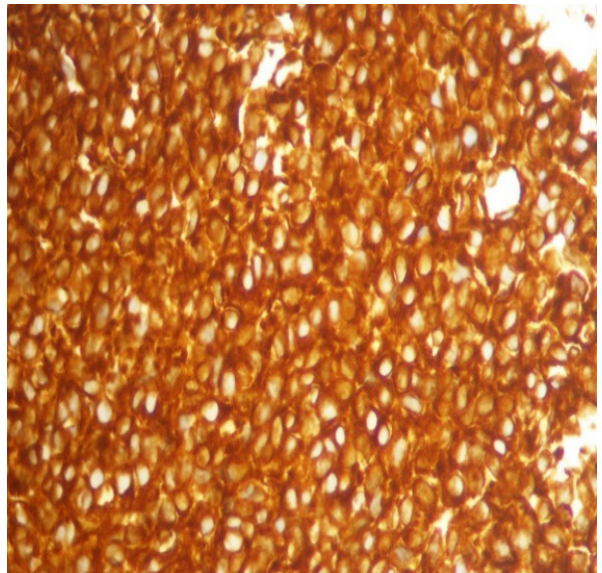


Fig. 3. Vimentin IHC staining showed diffuse cytoplasmic positivity

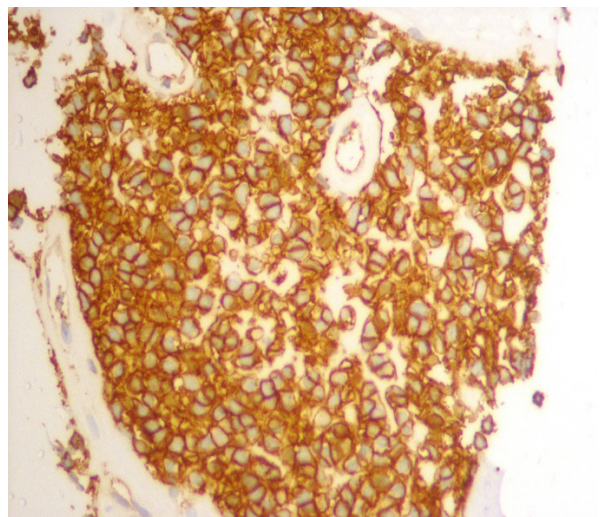


Fig. 4. CD-99 IHC staining showed strong membranous positivity

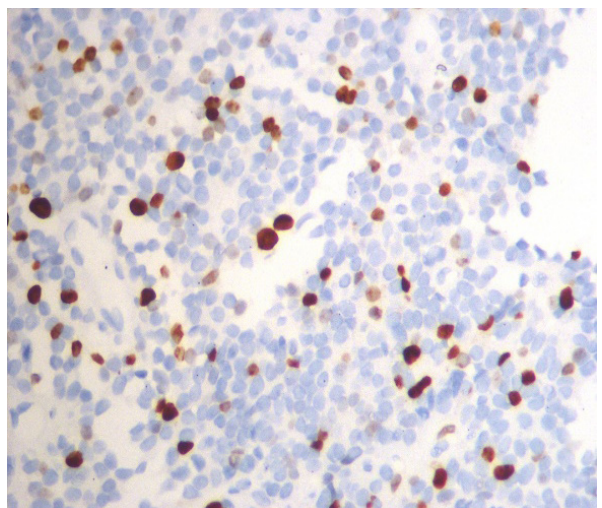


Fig. 5. Ki-67 IHC staining showed 10–15% nuclear positivity

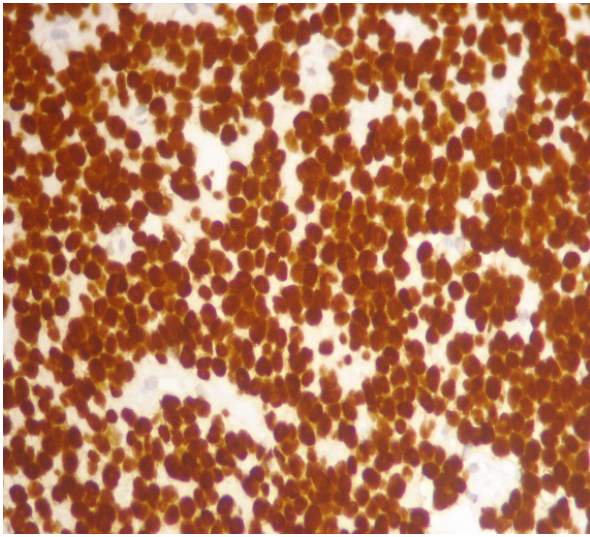


Fig. 6. NKX 2.2 IHC staining showed strong positivity

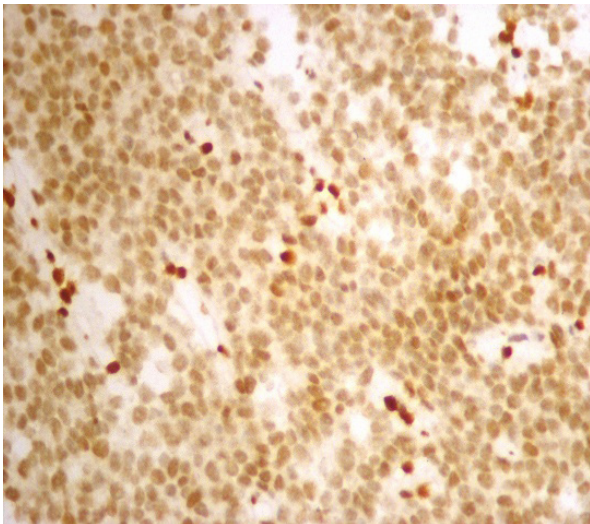


Fig. 7. FLI-1 IHC staining showed strong positivity

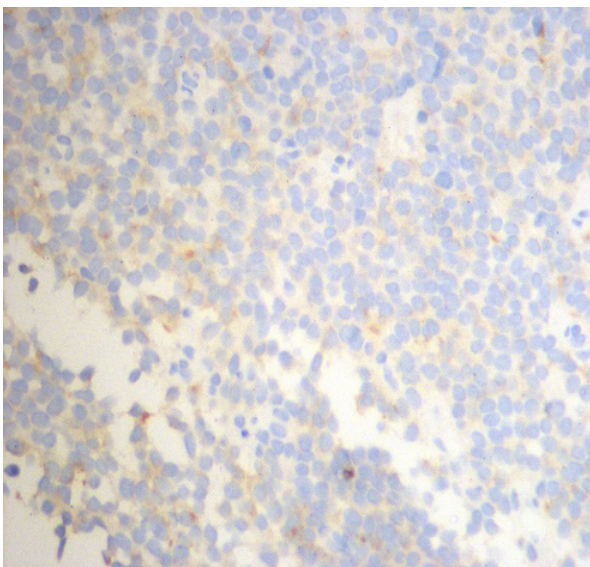


Fig. 8. Synaptophysin IHC staining showed weak positivity

Further genetic analysis using fluorescence in situ hybridization (fluorescence in situ hybridization) of tumor nuclei in a representative section (Fig. 9) revealed positivity for Ewing sarcoma breakpoint region-1 (EWSR1) in chromosome 22q12 gene rearrangement, confirming a positive result for EWSR1 gene rearrangement.⁸

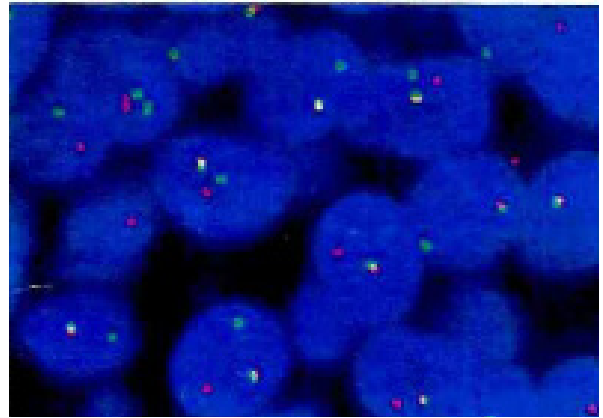


Fig. 9. fluorescence in situ hybridization analysis showed EWSR1 (22q12) gene rearrangement

The final diagnosis was obtained in association with molecular studies of the anterior abdominal wall mass strongly suggest the presence of the Ewing sarcoma family of tumors. This comprehensive analysis, encompassing histopathology, immunohistochemistry, and molecular studies, contributes to a nuanced understanding of the tumor's nature and aids in guiding further diagnostic and therapeutic considerations.

Discussion

Extra skeletal Ewing's sarcoma is an exceedingly rare and aggressive soft tissue malignancy with distinct clinicopathological features.⁹ Our case report highlights a 57-year-old female presenting with a left iliac fossa mass, ultimately diagnosed as extra skeletal Ewing sarcoma through a comprehensive diagnostic approach. The rarity of this condition in an older age group underscores the importance of recognizing atypical presentations and conducting thorough investigations. Microscopically, the tumor exhibited sheets of malignant small round cells with hyperchromatic nuclei, indistinct nucleoli, and occasional mitosis. The IHC panel, including markers like vimentin, CD99, synaptophysin, and FLI-1, provided crucial insights into the tumor's characteristics, confirming its affiliation with the Ewing sarcoma family of tumors. The positive result for EWSR1 gene rearrangement via fluorescence in situ hybridization further supported the diagnosis.

The clinical presentation of extra-skeletal Ewing sarcoma is often nonspecific, contributing to diagnostic challenges. In our case, the mass was initially iden-

tified due to severe abdominal pain, emphasizing the importance of considering extra-skeletal Ewing sarcoma in the differential diagnosis of abdominal masses, even in older individuals. The management of extra-skeletal Ewing sarcoma involves a multidisciplinary approach, integrating surgery, chemotherapy, and sometimes radiation therapy. Prognosis remains guarded, with a high recurrence rate and metastatic potential, particularly to the lungs and bones. The tenacious nature of this tumor necessitates close follow-up and vigilant monitoring to detect recurrence or metastasis promptly.^{7,10}

This case report contributes to the existing literature by shedding light on an atypical presentation of extra-skeletal Ewing sarcoma in an older patient. Understanding the varied clinical manifestations and incorporating advanced diagnostic techniques, such as fluorescence in situ hybridization and IHC, is pivotal for accurate diagnosis and optimal patient management.

Declarations

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Author contributions

Conceptualization, K.N.; Methodology, K.N., N.P.R., S.L.N. and A.S.; Software, K.N. and M.P.B.; Validation, K.N., M.P.B.; Formal Analysis, K.N.; Investigation, K.N., N.P.R., S.L.N. and A.S.; Resources, K.N.; Data Curation, K.N.; Writing – Original Draft Preparation, K.N. and M.P.B.; Writing – Review & Editing, K.N. and M.P.B.; Visualization, K.N.; Supervision, K.N., N.P.R., S.L.N. and A.S.; Project Administration, K.N.; Funding Acquisition, K.N., N.P.R., S.L.N., A.S. and M.P.B.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Data availability

Data available on request due to privacy/ethical restrictions.

Ethics approval

Approved by Bharat Heavy Electricals Limited, Power Sector Southern Region, Chennai, Tamilnadu, India.

References

1. Wang CC, Schulz MD. Ewing's sarcoma: a study of fifty cases treated at the Massachusetts General Hospital, 1930-1952 inclusive. *N Engl J Med.* 1953;248(14):571-576. doi: 10.1056/NEJM195304022481401
2. Balamuth NJ, Womer RB. Ewing's sarcoma. *Lancet Oncol.* 2010;11(2):184-192. doi: 10.1016/S1470-2045(09)70286-4
3. Angervall L, Enzinger FM. Extraskeletal neoplasm resembling Ewing's sarcoma. *Cancer.* 1975;36(1):240-251. doi: 10.1002/1097-0142(197507)36:1<240::aid-cncr2820360127>3.0.co;2-h
4. Applebaum MA, Worch J, Matthay KK, et al. Clinical features and outcomes in patients with extraskeletal Ewing sarcoma. *Cancer.* 2011;117(13):3027-3032. doi: 10.1002/cncr.25840
5. Juurikka K, Butler GS, Salo T, Nyberg P, Åström P. The Role of MMP8 in Cancer: A Systematic Review. *Int J Mol Sci.* 2019;20(18):4506. doi: 10.3390/ijms20184506.
6. Pankratjevaite L, Eskandarani HA, Lizdenis P, Saladzinskas Z. Challenges in diagnosing an extraosseous Ewing sarcoma: A case report. *Int J Surg Case Rep.* 2022;91(106708):106708. doi: 10.1016/j.ijscr.2021.106708
7. Gaspar N, Hawkins DS, Dirksen U, et al. Ewing sarcoma: Current management and future approaches through collaboration. *J Clin Oncol.* 2015;33(27):3036-3046. doi: 10.1200/JCO.2014.59.5256
8. MCGOWAN-JORDAN J, HASTINGS R, MOORE J. *ISCN2020: An International System for Human Cytogenomic Nomenclature (2020) (Cytogenetic and Genome Research)*. 2020.
9. Chai J, Hyuk MD, Phd, Ro JY. PhD The 2020 WHO Classification of Tumours of soft tissue: selected changes and new entities. *Adv Anat Pathol.* 2021;28(1):44-58. doi: 10.1097/PAP.0000000000000284
10. Thacker MM, Humble S, Zhang C, Gokaslan ZL, Galindo RL, Wadhwa R. Surgical outcomes for Ewing sarcoma of the spine: A systematic review. *Spine.* 2010;35:1400-1410.



CASUISTIC PAPER

Wunderlich syndrome – report of a rare case with comments on clinical implications

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ABSTRACT

Introduction and aim. Spontaneous renal hemorrhage, known as Wunderlich syndrome, is a rare clinical condition that occurs without any history of trauma. The most common causes of this syndrome are both benign and malignant renal tumors. The treatment strategy is determined based on the patient's hemodynamic stability.

Description of the case. We report a case where a patient was admitted to the emergency department experiencing persistent pain in the right flank for three days. A diagnosis of spontaneous renal hemorrhage, secondary to an angiomyolipoma, was established through CT imaging. In this case study, we detail the diagnostic process and management of a patient who, due to the absence of hemodynamic instability, did not require surgical intervention. Instead, the patient was monitored and managed with conservative treatment.

Conclusion. This case highlights the importance of prompt diagnosis, implementation of appropriate treatment, and the relevance of active follow-up in hemodynamically stable patients receiving conservative treatment.

Keywords. angiomyolipoma, flank pain, renal hematoma, spontaneous renal hemorrhage, Wunderlich syndrome

Introduction

Wunderlich syndrome (WS), also known as spontaneous renal hemorrhage is a rare condition in which there is bleeding into the subcapsular and/or perirenal space without the presence of trauma as a causative factor.¹ The most common cause of WS is renal tumors, with both malignant and benign tumors serving as etiological factors, among which angiomyolipoma (AML) represent the most significant alteration.² Other causes of this rare condition include vasculitis,

arteriovenous malformations, and aneurysms.³ WS is a severe condition which may require urgent nephrectomy.

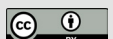
Aim

We report the case of a 46-year-old female patient who presented to the emergency department with acute abdominal pain mainly localized in the right flank. This work has been reported in line with the CARE (for CASE Reports) criteria.⁴ This case enriches the existing data

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on rare kidney abnormalities and consolidates the information published on the topic to date.

Description of the case

A 46-year-old female patient presented herself to emergency department, reporting a persistent right flank pain that had lasted for three days and radiated to the right lower quadrant. She had no history of hematuria, fever, or trauma. Vomiting occurred only on the first day of the reported pain. The patient denied any medical history. Upon her arrival, the cardiopulmonary examination was within normal limits.

Table 1. Relevant initial blood work results*

Parameter	Value of our patient	Reference range
Leukocytes (10 ³ /μL)	8.5	4–10
Hemoglobin (g/dL)	12.4	12–16
Hematocrit (%)	36	38–45
Platelets (10 ³ /μL)	293	150–400
hsCRP (mg/dL)	2.64	0–0.5
APTT (s)	32.4	25.4–36.9
Prothrombin time (s)	13.3	9.4–12.5
Creatinine (mg/dL)	0.6	0.55–1.02
eGFR (mL/min/1.73m ²)	114	>60
Sodium (mmol/L)	137	136–145
Potassium (mmol/L)	4	3.5–5.2

* hsCRP – high sensitivity C-reactive protein, APTT – activated partial thromboplastin time

Table 2. Relevant urinalysis results

Parameter	Value of our patient	Reference range
Dipstick urinalysis		
Color	yellow	–
Clarity	turbid	–
pH	6	5–7
Specific gravity (g/mL)	1.020	1.015–1.025
Glucose	negative	negative
Blood	positive	negative
Protein	positive	negative
Bilirubin	negative	negative
Ketones	negative	negative
Ascorbic acid	positive	negative
Nitrate	negative	negative
Urine microscopy		
White blood cells (cells/hpf)	many per hpf	2–5
Red blood cells (cells/hpf)	singular per hpf	2
Bacteria	many	negative
Squamous epithelial cells (cells/hpf)	few	15–20

The abdomen was soft with tenderness in the right side and pain radiating to the right flank. Costovertebral angle tenderness (Goldflam's sign) on the right side was questionable and on the left side was negative. Initial blood tests revealed elevated levels of high-sensitivity C-reactive protein. The hemoglobin level was found to be within the normal range (Table 1). Urinalysis showed

the presence of blood cells, leukocytes and numerous bacteria in the urine (Table 2).

An abdominal and pelvic computed tomography (CT) scan, urological and gynecological examinations were performed to evaluate the cause of the pain.

The CT image was performed in spiral acquisition with 1.5 mm layers in native phase and after contrast enhancement (multiphase). Both kidneys with the presence of numerous heterogeneous fat lesions about 4 cm in size on the right side and 6 cm on the left side – lesions indicative of an angiomyolipoma (AML) (Fig. 1, Fig. 2 and Fig. 3).



Fig. 1. The right kidney with numerous heterogeneous fat lesions up to 4 cm in size - AML-like lesions, right kidney visibly displaced forward by hematoma and AML-like lesions



Fig. 2. Perinephric hematoma associated with one of the AMLs of this kidney

In the perinephric fatty space on the right side, mainly on the dorsal side, numerous hyper dense bands 2.5x8.3 cm wide, with a density of about 60 HU, not enhancing after contrast – a perinephric hematoma associated with one of the AMLs of this kidney was diagnosed (Fig. 4).

Right kidney markedly displaced anteriorly by hematoma and AML-like lesions. The kidneys secrete

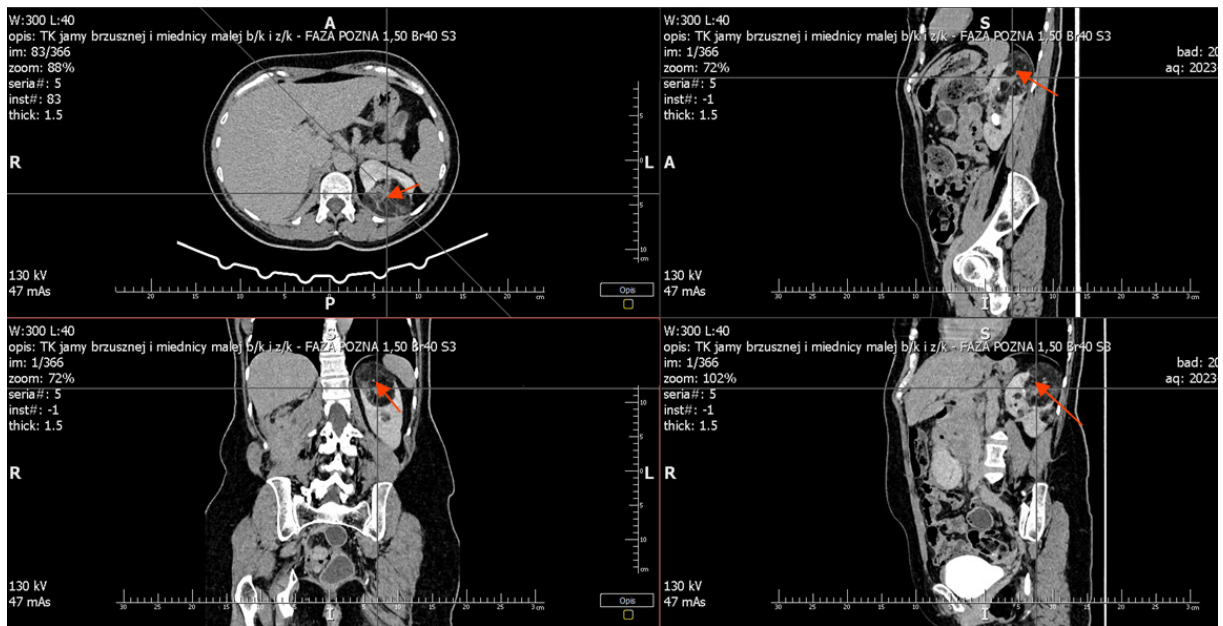


Fig. 3. The left kidney with numerous heterogeneous fat lesions up to 6 cm in size – AML-like lesions

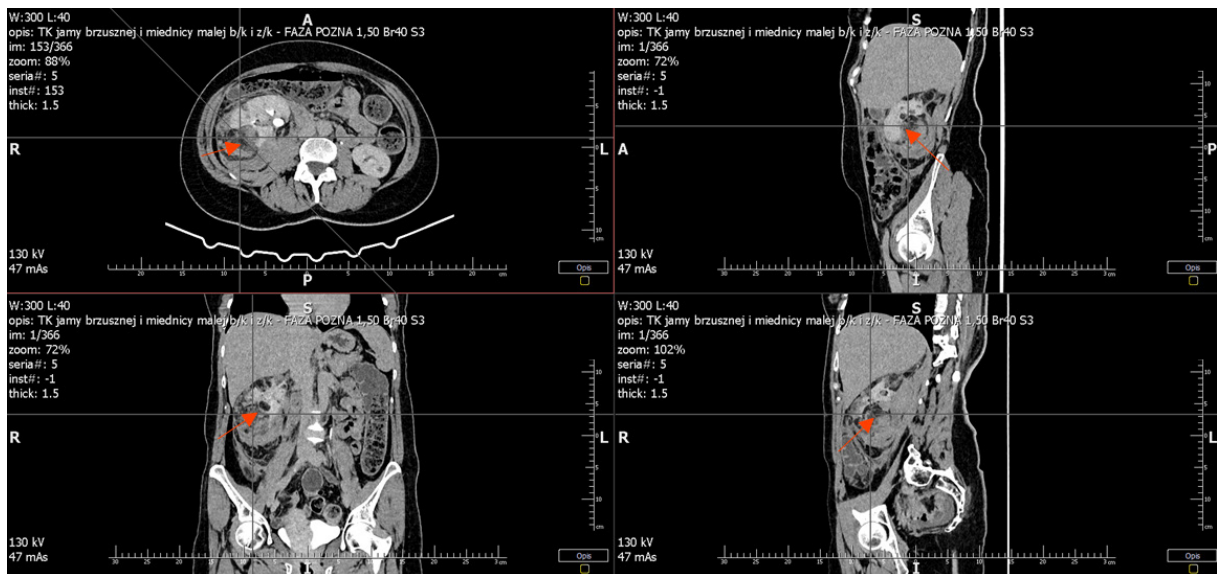


Fig. 4. In the perirenal fat space on the right side mainly on the dorsal side, numerous hyperdense bands up to 2.5x8.3 cm wide, with a density of about 60 UH, not enhancing after contrast – a perinephric hematoma associated with one of the AMLs of this kidney

urine bilaterally, without any signs of stasis or urine leakage. No calcified deposits were observed in the kidneys. Adrenal glands, ureters, urinary bladder were without pathology. Visible fluid in the sinus of Douglas on the right side was about 19 mm wide. No pathological changes were found in other abdominal organs, the imaged lymph nodes were not enlarged.

A diagnosis of Wunderlich syndrome associated with spontaneous rupture of an AML was made. The patient refused hospitalization. Due to the patient's refusal of further hospital treatment, she was discharged from the emergency department in accordance with the

doctor's recommendation. She was prescribed a strict bed rest, an antibiotic containing sulfamethoxazole + trimethoprim for a genitourinary infection. In addition, a follow-up visit to the general practitioner and the urology clinic was recommended. In the follow-up CT scan conducted 4 weeks after diagnosis, a regression of the hematoma was observed, the patient's clinical condition was assessed as good, and the patient reported no abdominal complaints. At the next follow-up visit, 8 weeks from diagnosis, further regression of the hematoma was observed in the control ultrasound of the abdominal cavity.

Discussion

Spontaneous, nontraumatic renal bleeding limited to subcapsular and/or perirenal space, WS was described for the first time in 1856 by Carl Reinhold August Wunderlich.¹ Known causes of WS range from neoplasms such as AML, renal cell carcinoma, sarcomas, lymphomas or pheochromocytomas to non-neoplasm like acquired cystic kidney disease, simple and/or hemorrhagic renal cysts, infections (acute and chronic pyelonephritis, renal abscess, emphysematous pyelonephritis, nephritis), ureteropelvic junction obstruction (Kliknij tutaj, aby wprowadzić tekst. vascular diseases (vasculitis, renal artery arteriosclerosis, renal artery aneurysm rupture, polyarteritis nodosa and renal vein thrombosis), undiagnosed or new occurring (like microangiopathic hemolytic anemia) hematological disorders and anatomical lesions.⁵⁻¹⁰ A case of WS caused by pancreatic pseudocyst has also been described.⁶ The presence of multiple unilateral or bilateral AMLs has been linked to tuberous sclerosis (TS), making TS a potential risk factor for Wunderlich syndrome. Therefore, TS should be considered when diagnosing a patient with this condition. Among patients with suspected WS, factors preceding trauma, anticoagulant treatment, hemorrhagic diathesis, arteritis, tuberous sclerosis and chronic hemodialysis should be excluded.¹² In addition, a rare case of Wunderlich Syndrome was described, which was diagnosed by prenatal ultrasound and manifested bilateral hydronephrosis and fetal bladder dysfunction.¹³ However, the most common cause of Wunderlich syndrome is rupture of tumor, with AML accounting for the majority.⁵⁻⁷ The second leading cause of WS syndrome is diseases of vascular etiology, such as polyarteritis nodosa (PAN), with smaller contributions from aneurysms, arteriovenous malformations, renal vein thrombosis and myocardial infarction accounting for about 20–30%.^{2,14} Among patients without previously diagnosed tuberous sclerosis, PAN should be considered if bilateral or recurrent WS is present.² Sometimes the cause of the syndrome cannot be determined.^{5,15}

Clinical presentation of patients with WS varies depending on the extent, duration and cause of bleeding. The most commonly reported symptom is unilateral flank pain that may radiate medially or downwards,^{5,15} which may be accompanied by hematuria, vomiting, weakness, fever, renal failure, anemia. Hemorrhagic shock may occur in 11–26.5% of patients. The classic presentation (Lenk's triad) includes flank or abdominal pain, palpable tender mass and hemorrhagic shock but only 20% of patients present those three together.^{5,16} Preliminary diagnosis of WS can be based on ultrasound, however a method with 92–100% sensitivity is contrast-enhanced CT, furthermore, performed during the time of hemorrhage enables us to identify all WS caused by AML.^{5,10,15} Combining CT with MRI enables detection of approximately 80% WS causes additionally providing 100% sen-

sitivity. In other cases, selective renal angiography may be useful in determining the source of bleeding.⁷

Management of patients with spontaneous, non-traumatic renal bleeding will be determined by the cause and hemodynamic stability of patients. Currently, patients are eligible for initial treatment by three methods i.e. conservative/medical management involving only hemodynamic stabilization using fluids and blood products with monitoring of the patient's clinical condition; transarterial embolization, which is the most common treatment of choice and surgery, which is generally based on performing a total nephrectomy, but can also involve exploration/wash out, ureteric stenting or partial nephrectomy.¹⁷ In hemodynamically stable patients, observation and conservative treatment can be used along with regular follow-up visits.¹⁸ Patients who presented with hemorrhagic shock in the clinical picture are more likely to require surgical management, but even in patients in severe hypovolemic shock, improvement can be achieved with conservative/medical management alone.^{8,9,15,17} Initial surgical treatment is also used in patients with suspected malignant lesions.^{9,17} Embolization, on the other hand, is the treatment of choice more often when patients cannot be stabilized with conservative management or instead of it, and when the causes are AML or vascular lesions.^{10,16,17}

However, there are no rigidly established management protocols, and the final choice of management will depend on the patient's condition, the technical capabilities of the staff and their experience.

Conclusion

Wunderlich syndrome is a rare but important condition to take into consideration when diagnosing a patient with sudden flank pain and hematuria. If not recognized quickly enough, it can lead to hemodynamic instability which is a life-threatening condition. Consequently, in patients with spontaneous non-traumatic renal hemorrhage, it is important to perform a contrast-enhanced CT scan without delay and implement proper conservative or surgical treatment, depending on the patient's hemodynamic stability. Our case highlights the importance of timely diagnosis and active follow-up in hemodynamically stable patients treated conservatively.

Declarations

Funding

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Author contributions

Conceptualization, K.K and K.B.; Methodology, K.K. and A.K.; Software, S.R.; Resources, S.R. and K.B.; Data Curation, S.R. and A.R.; Writing – Original Draft Preparation, K.K. and A.K.; Writing – Review & Editing, S.R. and A.R. and K.K.; Visualization, K.B.; Supervision, K.B.

Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Data availability

Not applicable.

Ethics approval

Written informed consent for publication was obtained from the patient. We complied with the policy of the journal on ethical consent.




References

1. Wunderlich CR. Handbuch der Pathologie und Therapie. Stuttgart: Ebner and Seubert. 2nd ed. 1856.
2. Parmar N, Langdon J, Kaliannan K, Mathur M, Guo Y, Mahalingam S. Wunderlich Syndrome: Wonder What It Is. *Curr Probl Diagn Radiol*. 2022;51(2):270-281. doi: 10.1067/j.cpradiol.2020.12.002
3. Ramirez-Limon DA, Gonzaga-Carlos N, Angulo-Lozano JC, Miranda-Symes O, Virgen-Gutierrez F. Wunderlich Syndrome Associated With Angiomyolipomas. *Cureus*. 2022;14(4): e23861. doi: 10.7759/cureus.23861
4. Riley DS, Barber MS, Kienle GS, et al. CARE guidelines for case reports: explanation and elaboration document. *J Clin Epidemiol*. 2017;89:218-235. doi: 10.1016/j.jclinepi.2017.04.026
5. Kim JW, Kim JY, Ahn ST, et al. Spontaneous perirenal hemorrhage (Wunderlich syndrome): An analysis of 28 cases. *Am J Emerg Med*. 2019;37(1):45-47. doi: 10.1016/j.ajem.2018.04.045
6. Albi G, del Campo L, Tagarro D. Wunderlich's Syndrome: Causes, Diagnosis and Radiological Management. *Clin Radiol*. 2002;57(9):840-845. doi: 10.1053/crad.2002.0981
7. Katabathina VS, Katre R, Prasad SR, Surabhi VR, Shanbhogue AKP, Sunnapwar A. Wunderlich Syndrome. *J Comput Assist Tomogr*. 2011;35(4):425-433. doi: 10.1097/RCT.0b013e3182203c5e
8. Bayraktar N. Wunderlich syndrome secondary to ureteropelvic junction obstruction. *Ulus Travma Acil Cerrahi Derg*. 2023;29(5):641-643. doi: 10.14744/tjtes.2022.54502
9. Swaminathan N, Sedhom R, Shahzad A, Azmaiparashvili Z. Post-partum occurrence of Wunderlich syndrome and microangiopathic haemolytic anaemia (MAHA): a case report. *J Community Hosp Intern Med Perspect*. 2021;11(2):277-279. doi: 10.1080/20009666.2021.1883812
10. Medda M, Picozzi S, Bozzini G, Carmignani L. Wunderlich's syndrome and hemorrhagic shock. *J Emerg Trauma Shock*. 2009;2(3):203. doi: 10.4103/0974-2700.55346
11. Samuels JA. Treatment of Renal Angiomyolipoma and Other Hamartomas in Patients with Tuberous Sclerosis Complex. *Clinical Journal of the American Society of Nephrology*. 2017;12(7):1196-1202. doi: 10.2215/CJN.08150816
12. García-Chairez LR, Montelongo-Rodríguez FA, Moreno-Arquieta IA, Ayala MM, Gutierrez-González A. Unusual Presentation of Wunderlich Syndrome. *Ochsner Journal*. 2022;22(3):273-276. doi: 10.31486/toj.21.0120
13. Jia Y, Gao J. Spontaneous perirenal hemorrhage (Wunderlich syndrome) in the fetus: a case report. *J Med Case Rep*. 2023;17(1):204. doi: 10.1186/s13256-023-03867-4
14. Vercelli A, Pagani L, Christodoulakis K, et al. Hypovolemic shock due to Wunderlich syndrome (spontaneous renal haemorrhage): a case report and literature review. *Acta Biomedica*. 2023;94(3):e2023073. doi: 10.23750/abm.v94i3.14087
15. Simkins A, Maiti A, Cherian S V. Wunderlich Syndrome. *Am J Med*. 2017;130(5):e217-e218. doi: 10.1016/j.amjmed.2016.11.031
16. Grubb SM, Stuart JJ, Harper HM. Sudden onset flank pain: Spontaneous renal rupture. *Am J Emerg Med*. 2017;35(11):1787e1-1787e3. doi: 10.1016/j.ajem.2017.07.095
17. Ahn T, Roberts MJ, Navaratnam A, Chung E, Wood S. Changing etiology and management patterns for spontaneous renal hemorrhage: a systematic review of contemporary series. *Int Urol Nephrol*. 2017;49(11):1897-1905. doi: 10.1007/s11255-017-1694-8
18. Cubillos JD, Mejia DR, Cañas EE, Serrano J, Casas O. A Subacute Presentation of Wunderlich Syndrome in a Young Woman: A Case Report. *Cureus*. 2023;15(7): e41385. doi: 10.7759/cureus.41385



CASUISTIC PAPER

Lung abscess with pneumonia after SARS-CoV-2 infection – a case report

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ABSTRACT

Introduction and aim. Some patients after the SARS-CoV-2 infection may be at higher risk of consequent bacterial or fungal infections even if they have no risk factors (advanced age, obesity, metabolic diseases). A possible complication of SARS-CoV-2 infection is lung abscess with pneumonia what requires further examination and specialized treatment as well as the pulmonary rehabilitation.

Description of the case. This report presents all stages of the diagnosis and treatment of lung abscess with pneumonia of male patient, aged 42 years in course of COVID-19. The article emphasizes the role of pulmonary rehabilitation in decreasing the number of postoperative pulmonary complications. Presented case report includes a description of a rehabilitation program conducted during the patient's hospitalization.

Conclusion. Lung abscess is a serious disease with an often unpredictable course, complications and an uncertain prognosis. However, most patients can be treated conservatively, and the priority in treatment is antibiotic therapy and physiotherapy treatments.

Keywords. brain fog, COVID-19, lung abscess, respiratory failure, SARS-CoV-2

Introduction

SARS-CoV-2 is a cause of COVID-19 pandemic. The most common symptoms of SARS-CoV-2 infection include fever, cough, shortness of breath, difficulty breathing as well as diarrhea, nausea and vomiting.¹⁻³ The condition may be accompanied with muscle pain, fatigue, loss of taste and smell.⁴ Chest X-ray examinations show typical features of viral pneumonia with diffuse bilateral infiltrations. Computed tomography scans of the chest initially show an image of “hazy/milky glass.”⁵

The above serious symptoms are identified in a growing number of patients with severe form of COVID-19 requiring treatment in hospital and at in-

tensive care units (ICU). Onset of acute respiratory failure reflects progress of this life-threatening disease.⁶ Patients brought to ICUs generally are at an advanced stage of COVID-19, frequently presenting with serious complications resulting from the infection. They commonly require breathing support.⁷

Acute respiratory syndrome develops in approximately 33% of patients hospitalized due to COVID-19, whereas 26% have to be moved to ICUs, 16% must be connected to respirators, and 16% of the patients die.⁸

The disease affects people of all ages, including young and middle-aged individuals, as well as athletic people with no pre-existing conditions, and it leads

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to long-lasting effects. In the first half of 2021 we have many patients aged 40 years or younger who are severely affected by the infection which leads to complications and long-term damage.⁴

Aim

The aim of the study was to present the effects of early rehabilitation in a patient with diagnosed lung abscess and pneumonia after SARS-COV-2. This report presents a case of a patient with SARS-CoV-2 infection which led to pleural effusion, right-sided and left-sided pneumothorax and acute respiratory failure. The patient needed intensive therapy and breathing support based on high flow oxygen therapy.

Description of the case

A male patient, aged 42 years, was admitted into the Thoracic Surgery Unit at Hospital, in Poland, due to complications associated with a severe case of COVID-19. Three weeks earlier diagnosed with SARS-CoV-2 infection, the patient was assigned to category 3 of care, and had a diagnosis of lung abscess with pneumonia. Overall condition of the patient was very serious, with O₂ saturation of 70% while on breathing support, shortness of breath at rest, tachypnoea up to 40/min, and central cyanosis. The patient received oxygen from the first day at a rate of 15 L/min., and from the 14th day at 10 L/min. He presented poor nutritional status. No swelling was found in the peripheral lymph nodes. A drain was placed along the right paravertebral line into the pleural cavity resulting in serosanguineous drainage with no leakage (Fig. 1, 2) ASM approximately 150/min. On the second day of hospitalization acute respiratory failure occurred due to left-sided pneumothorax, as a result the patient was transferred to ICU and pleural drainage was applied on the left side.

After treatment at ICU, on the third day at hospital the patient returned to the Thoracic Surgery Unit where at a later time undrained pleural fluid locules were identified on the right and left sides (Fig. 3). After subsequent thoracocentesis and videothoracoscopy, on the left side expansion of the parenchyma was observed, with improved X-ray image. The drainage was removed. During the hospital stay the patient had *Clostridium difficile* infection, which was treated with an antibiotic. The treatment included a dairy-free diet and equalization of water and electrolyte balance. Oral treatment with metronidazole 3×500 mg for 14 days was initiated. Electrolyte imbalance, observed in the patient, was managed on an ongoing basis. During the entire hospitalization the patient required continuous oxygen therapy, and periodically presented fever or subfebrile temperature. Cultures collected from both pleurae showed no increase in bacteria count.

The following treatments were administered during hospitalization:

1. Procedures: right- and left-sided pleural cavity drainage, videothoracoscopy,
2. Pharmacotherapy,
3. Inhalations, pulmonary and general rehabilitation programs.

During his stay at the Thoracic Surgery Unit, the patient received complex treatment, including a rehabilitation program. The therapeutic procedures carried out daily included: tracheobronchial toilet, general exercise, exercise intended to relax chest muscles, breathing exercise with the use of Triflo and Acapella apparatuses. Admission to Thoracic Surgery Unit. The lesion was diagnosed as a lung abscess after a severe case of COVID-19. Drainage was applied due to tension pneumothorax on the right side (Fig. 1). Saturation during 15 L/min. Oxygen therapy was 70%. After two days, patient transferred to ICU. It was found acute respiratory failure as well as left-sided pneumothorax. Suction drain was applied (Fig. 1). After another two days, patient transferred from ICU to Thoracic Surgery Unit. Drainage of pleural cavities on both sides. On 3 November of 2020 – drain was removed from the left pleura. The drain from the right pleura was replaced; bloody pleural fluid was identified. Puncture of the left pleura – removal of 200 mL hematoma (Fig. 2). Chest ultrasound – right side: no excess pleural fluid. Left side: two separate fluid locules, one in the region of the angle of the scapula – puncture 300 mL. hematoma, the other one below the supradiaphragmatic region – puncture 300 mL of serous fluid. Cultures were sampled. Saturation during 10L/min. oxygen therapy was 85%. On ultrasound on November 12 left-side videothoracoscopy. Removal of fluid collections. Bloody pleural fluid drained with no air leakage. After one week, patient in stable condition. Serous fluid drained from the left pleura. Oxygen therapy is still needed. Saturation during 2 L/min. oxygen therapy was 93%. On 2 December of 2020, patient was in a stable condition with mild respiratory insufficiency, was transferred to Internal Medicine Department for continued treatment.

Discussion

The course of the disease is adversely affected by various factors, such as age >65 years, cardiovascular diseases, diabetes, lung diseases, hypertension, neoplastic diseases, as well as kidney, liver, metabolic and neurological disorders, obesity, smoking, pregnancy, impaired immunity, post-transplantation conditions and HIV infection.⁹ Serious, complicated cases of COVID-19 presenting risk of death, are particularly frequently observed in obese male smokers, aged 50–60 years.¹⁰ The range of consequences of SARS-CoV-2 infection is very wide, from asymptomatic to typical symptoms such as: fever, dry cough, fatigue, muscle pain, sore throat, headache, diarrhea, conjunctivitis, loss of taste or smell.^{4,11}

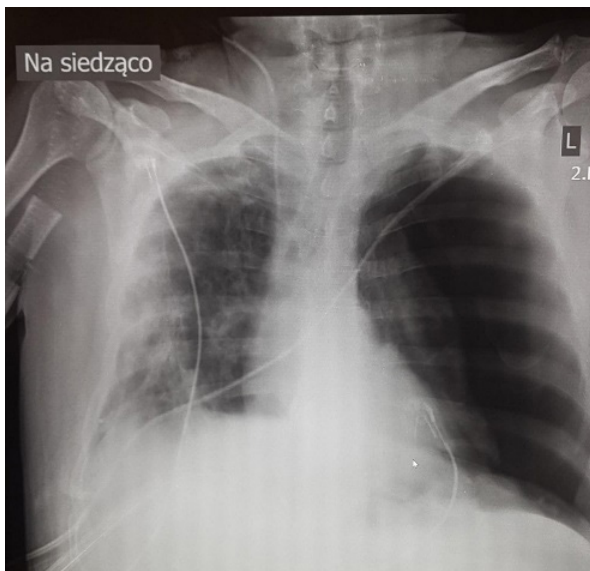


Fig. 1. Imaging examinations – chest X-ray from November 28, 2020 – right pleura drainage, abscess on the left side

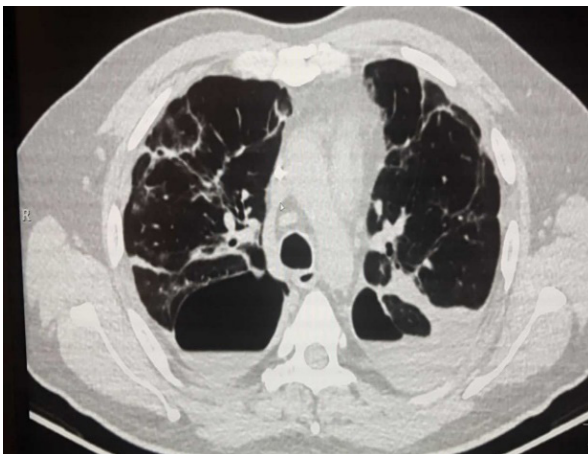


Fig. 2. Computed tomography – November 6, 2020 – excess fluid in pleural cavities R-1.8 cm, L 1.6 cm; both cavities contain air constituting a single fluid/gas layer

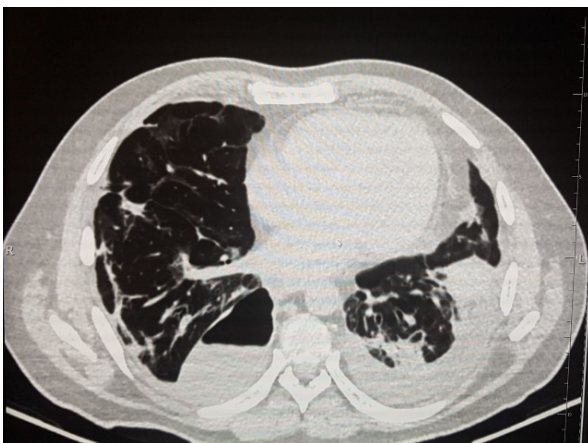


Fig. 3. Computed tomography – November 16, 2020 – excess fluid in pleural cavities R-3.8 cm, L 2.6 cm, both cavities contain air constituting a single fluid/gas layer

Sudden deterioration of the condition, and development of certain complications are characteristic for this disease. Onset of such symptoms as difficulty breathing, chest pain, loss of speech or impaired motor abilities reflects severe course of the disease which is associated with deterioration of various functions, mainly the respiratory, nervous, urinary and circulatory systems. SARS-CoV-2 infection may also induce immune response which is manifested with increased levels of cytokines, or the so-called cytokine storm. Its symptoms include high fever, nausea, extreme fatigue, and damage to many organs. These symptoms are life threatening and frequently lead to death. The type of complications and timing of their onset are extremely varied. More and more patients are diagnosed with loss of smell and taste which are associated with loss of memory, the so-called COVID-19 brain fog.⁴ In neurology departments there is an increasing number of COVID-19 patients who are diagnosed with stroke or TIA, and in the most severe cases cerebrovascular disease involving the brain stem, associated with nausea, state of confusion and disturbed consciousness. Other complications, related to the cardiovascular system, include venous thrombosis, post-thrombotic syndrome as well as acute heart failure.¹² Patients frequently present with acute kidney injury and acute respiratory failure.¹³ Complications associated with SARS-CoV-2 infection lead to irreversible multiple organ damage, which in turn leads to health loss, lower quality of life and permanent disability.⁴ In the literature, we find cases after SARS-CoV-2 with lung abscess with a similar course as our patient. Our patient's description included the rehabilitation program conducted during his stay in the department.

A lung abscess is a local, limited area of purulent necrosis of the lung parenchyma, which is a complication of a bacterial, viral, fungal or parasitic infection or a cancer process. When infection occurs, multiple small abscesses <2 cm in diameter develop in the lung. This condition is called necrotizing pneumonia or pulmonary gangrene.¹²

The incidence of lung abscess in the general population is not precisely known. The literature reports that thanks to advances in antibiotic therapy and treatment of pneumonia, the number of abscesses has decreased more than tenfold.¹³

The causes of lung abscess may be diseases of the oropharynx and aspiration of infected contents from the mouth or gastrointestinal tract. 85% of lung abscesses are located in the upper segments of the lower lobe of the right lung, sometimes in the lower lobe of the left lung or in both segments of the middle lobe of the right lung. Another cause of an abscess may be the appearance of a foreign body in the lungs after aspiration or penetration from the outside, for example a bullet fragment. Sometimes the cause of lung abscess is infection

of the chest wall, inflammation of the mediastinum or abdominal cavity.¹²

Abscesses often become secondarily infected by anaerobic bacteria or fungi, which may cause lung gangrene. Lung abscesses largely contain anaerobic bacteria such as Gram (+) and Gram (-) anaerobes, such as *Peptococcus* sp., *Peptostreptococcus* sp., *Fusobacterium necrophorum*, *Fusobacterium nucleatum*, *Bacteroides* sp., *Porphyromonas* sp., *Prevotella melaninogenica*. Fungal infections (*Aspergillus*, *Candida*, *Histoplasma*) occur rarely, almost exclusively in chronic abscesses drained by the bronchi. Lung abscesses can also be caused by bronchial infections with *Actinomyces*. Occasionally, lung abscesses caused by parasites and protozoa (*Paragonimus westernami*, *Entamoeba histolytica*) may be encountered.¹⁴

The diagnosis of abscesses is based on the clinical picture, radiological tests and peripheral blood morphology, which usually shows leukocytosis, as well as the measurement of ESR and CRP. Additionally, patients undergo a microbiological examination to determine the type and drug sensitivity of pathogens. The microbiological examination assesses blood and material from the respiratory tract. In the late stage of an abscess, material for culture is obtained by puncturing the abscess cavity through the chest wall or bronchial wall, or by bronchofiberscopy.¹⁵

In the treatment of acute lung abscesses, regimens of combined administration of 2 or 3 intravenous antibiotics, such as synthetic penicillins and metronidazole in combination with clindamycin or amoxicillin, are used. In case of anaerobic infections, imipenem or meropenem is used. Treatment is modified depending on the clinical effect and drug sensitivity of the isolated pathogens. Treatments play an important role in supportive care in the field of physiotherapy such as bronchial toilet and respiratory kinesiotherapy. Surgical treatment should be considered if conservative treatment is ineffective or if abscess complications occur. Surgical treatment using drainage consists of activities aimed at emptying the abscess cavity of the infected contents and rinsing it with solutions of antiseptics or antibiotics. Surgical treatment involves resection of the lung parenchyma and abscess via thoracotomy. Our patient's description included a rehabilitation program conducted during the patient's hospitalization.¹⁶

Conclusion

The case presented here shows in what way COVID-19 may progress in a person below 45 years of age, with normal body weight, and no pre-existing conditions or bad habits, regularly engaging in sports. The case report shows how severe may be the complications and the functional condition in individuals with SARS-CoV-2 infection. Consequences of the disease may be tragic for well-being and life of individuals of all ages. Lung

abscess is a serious disease with an often unpredictable course, complications and an uncertain prognosis. However, most patients can be treated conservatively, and the priority in treatment is antibiotic therapy and physiotherapy treatments.

Declarations

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Author contributions

Conceptualization, E.S. and R.B.; Methodology, R.B.; Investigation, K.W.; Resources, A.K.; Data Curation, R.B.; Writing – Original Draft Preparation, R.B and E.S.; Writing – Review & Editing, E.S and K.S.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The datasets used and/or analyzed in the present study are available from the respective author.

Ethics approval

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee (protocol code No. 10/01/2021). The patient gave his written consent to the publication of his case report.

References

- Mehraeen E, Behnezhad F, Salehi MA, Noori T, Harandi H, SeyedA-linaghi S. Olfactory and gustatory dysfunctions due to the corona-virus disease (COVID-19): a review of current evidence. *Eur Arch Otorhinolaryngol*. 2021;278(2):307-312. doi: 10.1007/s00405-020-06120-6
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-30185
- Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet*. 2020;395(10223):470-473. doi: 10.1016/S 0140-6736(20)30185-9
- Waterboer T, Hippchen T, Simon J, et al. Persistent symptoms in adult patients one year after COVID-19: a prospective cohort study Jessica Seeßle. *Clinical Infectious Diseases*. 2022;9,74(7):1191-1198. <https://doi.org/10.1093/cid/ciab611>
- Jacobi A, Chung M, Bernheim A, Eber C. Portable chest X-ray in coronavirus disease-19 (COVID-19): Apictorial review. *Clin Imaging*. 2020;64:35-42. doi: 10.1016/j.clinimag.2020.04.001
- Młodożeniec A, Orłowska-Florek R, Czarnożycka-Wróbel A, Gargas K, Gala-Błądzińska A. Nonthyroidal illness

- syndrome as independent predictor of hospital mortality in the elderly hospitalized patients with COVID-19 pneumonia – single-center observation. *Eur J Clin Exp Med.* 2022;20(3):348-354. doi: 10.15584/ejcem.2022.3.14
7. Englisch CN, Tschernig T, Flockerzi F, Meier C, Bohle RM. Lesions in the lungs of fatal corona virus disease Covid-19. *Ann Anat.* 2021;234:151657. doi: 10.1016/j.aanat.2020.151657
 8. Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: aglobal literature survey. *Crit Care.* 2020; 24(1):516. doi: 10.1186/s13054-020-03240-7
 9. Kruszewski J. Asthma and allergic diseases and COVID-19. *Lek Wojsk.* 2021;99(1):28-35.
 10. Perini P, Nabulsi B, Massoni CB, et al. Acute limb ischaemia in two young, nonatherosclerotic patients with COVID19. *Lancet.* 2020;395:1546. doi: 10.1016/S0140-6736(20)31051-5
 11. Roy S. Journey so far with COVID 19 – a comprehensive review. *Eur J Clin Exp Med.* 2020;18(4):303-317. doi: 10.15584/ejcem.2020.4.7
 12. Feki W, Ketata W, Bahloul N, Ayadi H, Yangui I, Kamoun S. Lung abscess: Diagnosis and management. *Rev Mal Respir.* 2019;36(6):707-719.
 13. Mohapatra MM, Rajaram M, Mallick A. Clinical, Radiological and Bacteriological Profile of Lung Abscess - An Observational Hospital Based Study. *Open Access Maced J Med Sci.* 2018;23;6(9):1642-1646.
 14. Marra A, Hillejan L, Ukena D. Management of Lung Abscess. *Zentralbl Chir.* 2015;140(1):47-53.
 15. Hillejan L. Management des pulmonalen Abszesses: Diagnostik und Behandlung [Management of Lung Abscess - Diagnostics and Treatment]. *Zentralbl Chir.* 2020;145(6):597-609.
 16. Cascone R, Sica A, Sagnelli C, et al. Endoscopic Treatment and Pulmonary Rehabilitation for Management of Lung Abscess in Elderly Lymphoma Patients. *Int J Environ Res Public Health.* 2020;5;17(3):997. doi: 10.3390/ijerph17030997



CASUISTIC PAPER

Acute myocarditis mimicking ST – elevation myocardial infarction in a young adult with pharyngitis – a case report

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ABSTRACT

Introduction and aim. Acute myocarditis (AM) is a life-threatening inflammatory disease that manifests with a highly variable range of clinical symptoms, sometimes mimicking those of myocardial infarction. The aim of this report was to describe the diagnostic challenges of AM.

Description of the case. A 22-years old male previously diagnosed with pharyngitis arrived in the emergency room (ER) with retrosternal chest pain. The electrocardiogram (ECG) showed ST elevation in inferior and posterior leads and reciprocal changes with ST depression in anterolateral leads. Laboratory tests revealed elevated cardiac enzymes and bedside echocardiogram (ECHO) revealed hypokinesis of the inferior wall. Initial diagnosis of ST elevation myocardial infarction (STEMI) was made. Coronary angiogram showed normal epicardial coronary arteries and cardiac magnetic resonance imaging (CMRI) revealed sub-epicardial late gadolinium enhancement (LGE).

Conclusion. This case was proven challenging due to the unusual ECG and ECHO findings, mimicking inferoposterior STEMI. The need for available angiography and CMRI was mandatory for the final diagnosis of AM.

Keywords. CMRI, myocardial infarction, myocarditis

Introduction

Acute myocarditis (AM) is a life-threatening disease caused by viral, and less frequently bacterial infection, autoimmune diseases or exposure to drugs that elicit an inflammatory response in cardiac myocytes. In the emergency setting, patients with the suspicion of AM are usually evaluated based on their symptoms, electrocardiogram (ECG), echocardiogram (ECHO) and laboratory test markers. The clinical presentation is usually nonspecific and can be misinterpreted especially in rare cases which mimics ST elevation myocardial infarction (STEMI).¹ We report a young male, previously diagnosed with pharyngitis, that presented in the emergency room (ER) with a clinical presentation of inferoposterior STEMI.

Aim

The aim of this report was to describe the diagnostic challenges of AM.

Description of the case

A 22-years old male presented in the ER with continuous, non-radiating retrosternal crushing chest pain and diaphoresis lasting for three hours. Five days prior to the admission the patient was diagnosed with pharyngitis. However, one day ago, he visited a private physician with complaints of chest pain of similar character with his present symptoms. The ECG at the time showed nonspecific ST abnormalities in leads II, III, AVE, V5, V6 and his cardiac ECHO was normal. From past med-

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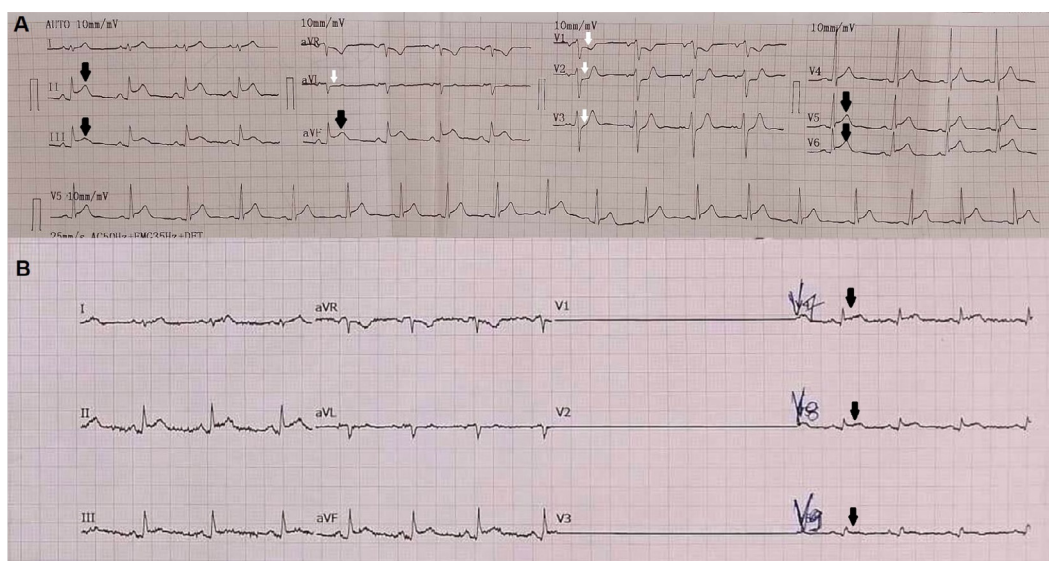


Fig. 1. A: PR depression, ST elevation in leads II, III, aVF, V5 and V6 (black arrows) and reciprocal changes with ST depression in leads V1, V2, V3, aVL (white arrows), B: ST elevation in posterior placed leads V7-V9 (black arrows)

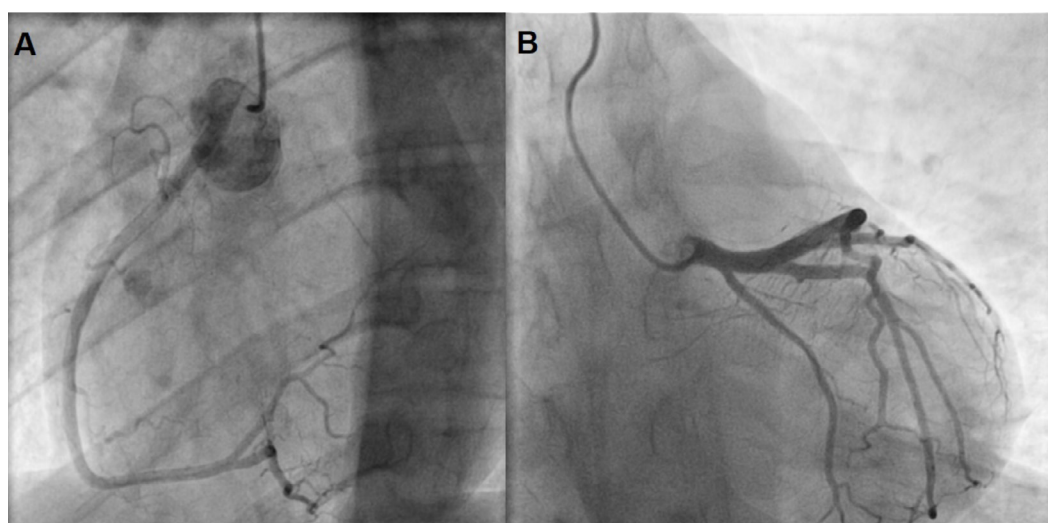


Fig. 2. A: Right coronary artery, B: Left coronary artery

ical history the patient had no allergies, no usage of recreational drugs, no chronic illnesses or cardiovascular risk factors. The family history revealed the incidence of myocarditis in his father and sister a few years prior. Additionally, due to the recent COVID-19 pandemic, the vaccination status was acquired, and the patient proved to be fully vaccinated.

At presentation his heart rate was 83/min and his blood pressure 151/59 mmHg. The temperature was 37.3°C and SaO₂ 99. The initial clinical exam showed normal heart sound S1, S2 and absence of any audible murmurs, gallops or rubs.

Laboratory test showed elevated cardiac markers, creatinine kinase (CK) of 1032 IU/l (reference range [rr]: 39–308), troponin hs of 11502 pg/mL (ng/l) (rr: <72), and lactate dehydrogenase (LDH) of 395 IU/l (rr: 81–230). Further results included, white blood cell (WBC)

8,10 K/ μ l (rr: 4–10), hemoglobin (Hg) of 13.1 g/dL (rr: 11.7–15.7), platelets (PLT) of 295 K/ μ L (rr: 140–440), blood glucose (BG) of 109 mg/dL (rr: 74–106), creatinine (Cr) of 1.1 (rr: 0.6–1.3), urea (BUN) of 21 mg/dL (rr: 10–45), prothrombin time (PT) of 11.8 sec (rr: 10–13), fibrinogen (Fg) of 470 mg/dL (rr: 200–400) and C-reactive protein (CRP) of 4.3 mg/dL (rr: 0–0.5). The ECG revealed sinus rhythm 1:1, PR depression, ST elevation in leads II, III, aVF, V5 to V9 and reciprocal changes with ST depression in leads V1, V2, V3, aVL (Fig. 1A and 1B) indicating regional ischemic injury of the inferoposterior segments supplied by the posterior descending artery (PDA). A bedside ECHO was also conducted and showed hypokinesis of the inferior wall, left ventricular ejection fraction (LVEF) >60%, E>A, mild mitral regurgitation, inferior vena cava (IVC) diameter 1.6 cm with normal inspiratory collapse, and

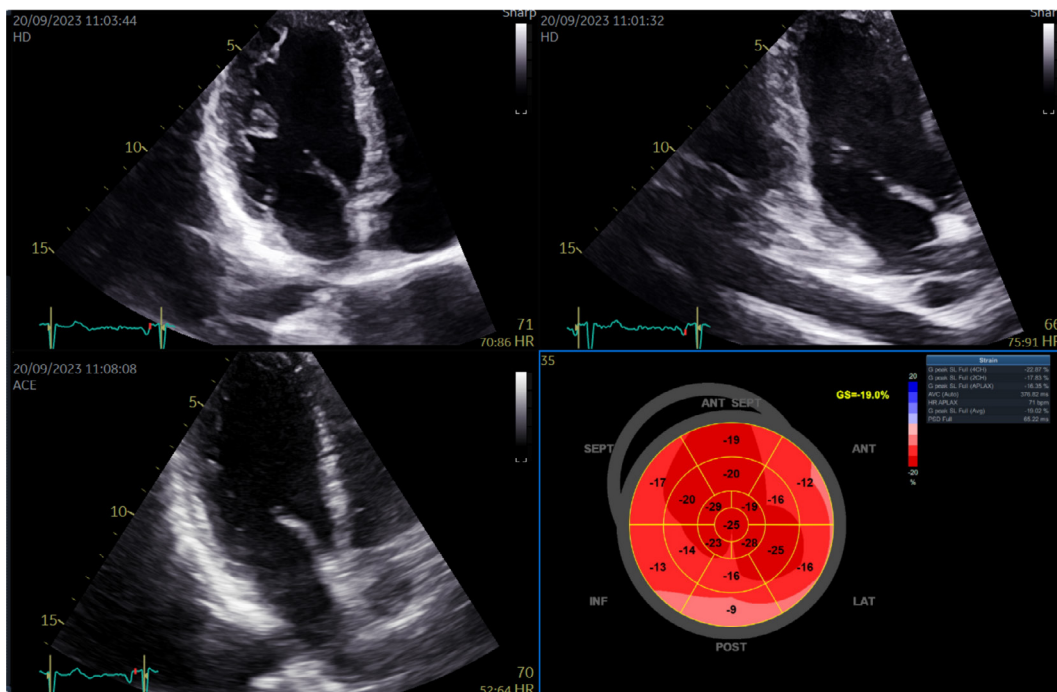


Fig. 3. Two-dimensional speckle tracking echocardiography

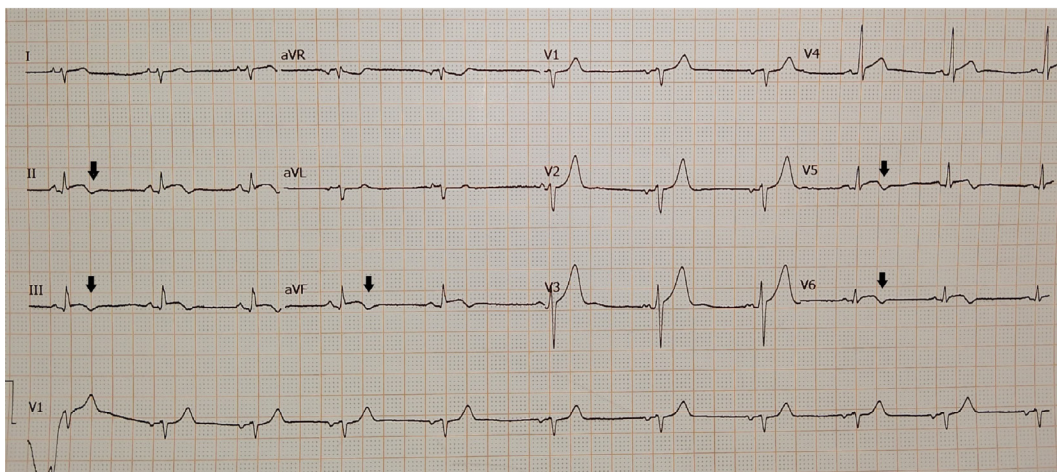


Fig. 4. ECG evolution with ST normalization and T inversion in leads II, III, AVF, V5, V6 (black arrows) 24h after the admission

no pericardial fluid buildup. The chest x-ray showed a normal size heart, clear lung fields and sharp costodiaphragmatic angles.

Based on the clinical presentation of chest pain, elevated cardiac markers, ECG and ECHO abnormalities initial diagnosis of inferoposterior myocardial infarction was made. The patient received a loading dose of 250 mg of aspirin and was transferred for primary coronary intervention (PCI). Coronary angiography was performed but revealed normal epicardial coronary arteries (Fig. 2).

In respect to the earlier results of angiography and the history of pharyngitis, acute coronary syndrome (ACS) was excluded and differential diagnosis of AM was made.

On the second day of hospitalization two-dimensional speckle tracking echocardiography was per-

formed. Global longitudinal strain (GLS) curves using semi-automatic algorithm (GE Healthcare) reveal peak systolic strain equal to -19% (Fig. 3). Basal inferior and basal inferolateral segments were affected, areas that electrocardiographically had already been characterized by ischemic changes. Additional ECG 24 hours later showed resolving of ST changes with normalization of ST segments and inversion of T waves, mimicking the ECG evolution of an ACS after reperfusion of the culprit artery (Fig. 4).

Cardiac magnetic resonance imaging (CMRI) for confirmation of AM was performed. T2-weighted short time recovery (STIR) image showed increased subepicardial signal in inferior and posterior wall of the left ventricle (LV) suggestive of myocardial edema. In post

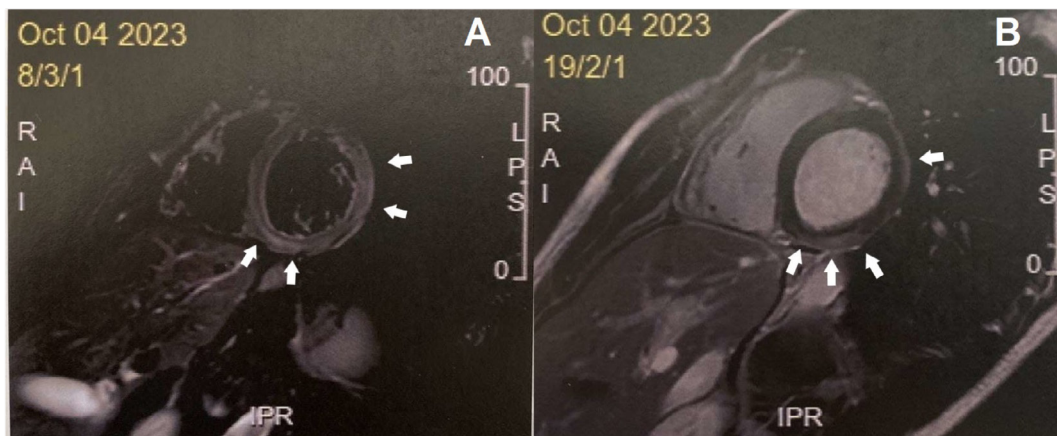


Fig. 5. A: T2-W STIR image showing intense subepicardial rim (white arrows) representing myocardial edema in the inferior and posterior wall of the LV, B: LGE image showing subepicardial scarring with intense signal in inferior and posterior wall of LV (white arrows)

contrast late gadolinium enhancement (LGE) images acquired with a T1- weighted segment inversion recovery gradient echo sequence, an increased subepicardial signal was also observed in the inferior and posterior wall of the LV indicative of myocardial scarring (Figure 5). Finally, the hypothesis was confirmed, and the final diagnosis was made.

Furthermore, etiological causes were investigated throughout the duration of hospitalization. Upon admission influenza A/B rapid diagnostic test and Covid 19 rapid antigen test were negative. Serological testing revealed negative results for cytomegalovirus (CMV) and hepatitis C virus (HCV) but positive IgM with negative IgG antibodies for Epstein Barr virus (EBV). Due to the recent diagnosis of pharyngitis antistreptolysin O titer and throat swab culture test were also conducted but both were negative.

The patient was treated with beta blockers and angiotensin converting enzyme (ACE) inhibitors. During the hospitalization a 24-hour Holter was implanted but did not reveal any abnormalities. At the follow-up one week later there was remission of the symptoms and the patient was discharged from the hospital.

Discussion

This case represents an AM, resembling a STEMI, in the setting of pre-diagnosed pharyngitis in a 22-year-old male patient. Myocarditis is an inflammatory condition, that can be caused by viral or less commonly by bacterial agents. Virus genomes that have been most identified in western countries are adenovirus, enterovirus, CMV, parvovirus B19, human immunodeficiency virus (HIV), as well as influenza and HCV.^{2,3} Bacteria such as group A streptococcus (GAS) infections had been well documented as a causative agent of AM with clinical presentation of myocardial infarction, but rarely in absence of rheumatic fever.⁴

The presentation of AM is heterogeneous and overlapping with other clinical entities, ranging from asymptomatic to arrhythmias and even acute heart failure.⁵ Clinical characteristics often include fever, diaphoresis, dyspnea, fatigue, cardiac arrhythmias, palpitations and chest pain being the most frequent symptom.⁶⁻⁸ In general, recent infections or related symptoms should always be forewarned during history taking. Already published case series regarding cases of GAS related myocarditis found prevalence, especially in males with a mean age of 27.8 and latency period of pharyngitis to chest pain of 4.2 days.¹⁰⁻¹² Cardiac enzymes are elevated in most cases proving that these findings can be often misleading in these patients.⁸

Diagnostic modalities, such as ECG shows non-specific ST changes, T inversion, q waves, and even, atrioventricular (AV) blocks.¹² More specifically, in myocarditis, two ST elevation patterns have been described; a pericarditis pattern with elevation less than 5 mm, involving diffusely both limb and precordial leads, with the exception of AVR and V1, which often presents with reciprocal ST depression, and a typical myocardial infarction like pattern, characterized by J-point elevation and an flat or convex ST segment, in at least two contiguous leads, often without reciprocal ST depression.^{13,14} It was found that no correlation between ST elevation and regional necrosis in CMRI was present, although in our case of myocardial infarction like type, the affected segments were related to the ECG leads that showed ischemic changes.^{15,16} Regarding T wave inversion, the prevalence in AM is 9–48%, and a late manifestation in leads with previous ST elevation. T wave inversion was found to be independently related to the extent of both myocardial necrosis, as assessed later by CMRI.^{17,18}

Transthoracic ECHO is generally not useful for the differentiation between myocardial infarction and myocarditis. In previous studies patients with AM showed,

regional movement abnormalities, reduced left ventricular ejection fraction and pericardial effusion.¹²

CMRI with LGE, has emerged as the cornerstone in the diagnosis of AM, especially in cases which mimics STEMI, being able to diagnose ischemic from non-ischemic pattern. In ischemic pattern, LGE always involves subendocardial layers with or without transmural extent, whereas, in non-ischemic pattern, LGE doesn't have the same characteristics, being mid-wall, subepicardial, or mixed.^{11,19} The use of CMRI is of pivotal importance, but unfortunately, it is not always available in the ER. Instead, these cases are transferred for angiography, and when normal epicardial coronary arteries are found, suspicion of other etiologies are made.

Endomyocardial biopsy is considered the gold standard for diagnosis of myocarditis. Unfortunately, its invasive nature, the time needed for the results, and the likelihood of sampling errors, makes it less applicable in clinical practice.²⁰

This case report was affected by three notable limitations. First, the inability to conduct serological tests for multiple viral agents limited us to establish cause-effect relationship of the AM. Second, the case report is being conducted retrospectively, recall bias might prevent us in collecting additional information from the patient, the family or other health care professionals. Finally, better understanding of this clinical presentation and the appropriate early management could be derived by studies on larger population of patients with AM mimicking STEMI.

Conclusion

AM remains a diagnostic challenge for physicians due to the range of clinical presentations. The present case, specifically shares many similarities with inferoposterior STEMI, evidenced by regional ST segment elevation with reciprocal changes and combination with echocardiographic regional hypokinesis of the corresponding segment. In cases of young patients evaluated for ACS, with absence of predisposing factors and normal coronary angiogram, CMRI is mandatory to establish the diagnosis.

Declarations

Funding

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Author contributions

Conceptualization, A.C. and A.K.; Methodology, A.K.; Validation, A.C. and N.V.; Formal Analysis, A.C., A.K. and N.V.; Investigation, A.C. and N.V.; Resources, A.C. and N.V.; Data Curation, A.K.; Writing – Original Draft Preparation, A.K.; Writing – Review & Editing, A.K.; Visualization, A.C. and A.K.; Supervision, A.C.; Project Administration, A.C.

Conflicts of interest

The authors declare no conflict of interest in preparing this article.

Data availability

The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics approval

Informed consent was obtained from the patient.

References



- Lasica R, Djukanovic L, Savic L, et al. Update on Myocarditis: From Etiology and Clinical Picture to Modern Diagnostics and Methods of Treatment. *Diagnostics (Basel)*. 2023;13(19):3073. doi: 10.3390/diagnostics13193073
- Yajima T, Knowlton KU. Viral myocarditis: from the perspective of the virus. *Circulation*. 2009;119(19):2615-2624. doi: 10.1161/CIRCULATIONAHA.108.766022
- Nielsen TS, Hansen J, Nielsen LP, Baandrup UT, Banner J. The presence of enterovirus, adenovirus, and parvovirus B19 in myocardial tissue samples from autopsies: an evaluation of their frequencies in deceased individuals with myocarditis and in non-inflamed control hearts. *Forensic Sci Med Pathol*. 2014;10(3):344-350. doi: 10.1007/s12024-014-9570-7
- Gore I, Saphir O. Myocarditis associated with acute nasopharyngitis and acute tonsillitis. *Am Heart J*. 1947;34(6):831-851. doi: 10.1016/0002-8703(47)90148-8
- Al-Akchar M, Shams P, Kiel J. *Acute Myocarditis*. In: StatPearls. Treasure Island (FL): StatPearls Publishing; July 5, 2023.
- Grün S, Schumm J, Greulich S, et al. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. *J Am Coll Cardiol*. 2012;59(18):1604-1615. doi: 10.1016/j.jacc.2012.01.007
- Hufnagel G, Pankuweit S, Richter A, Schönián U, Maisch B. The European Study of Epidemiology and Treatment of Cardiac Inflammatory Diseases (ESETCID). First epidemiological results. *Herz*. 2000;25(3):279-285. doi:10.1007/s000590050021
- Schmutzler L, Mirna M, Hoppe UC, Lichtenauer M. From Streptococcal Pharyngitis/Tonsillitis to Myocarditis: A Systematic Review. *J Cardiovasc Dev Dis*. 2022;9(6):170. doi: 10.3390/jcdd9060170
- Talmon Y, Gilbey P, Fridman N, Wishniak A, Roguin N. Acute myopericarditis complicating acute tonsillitis: beware the young male patient with tonsillitis complaining of chest pain. *Ann Otol Rhinol Laryngol*. 2008;117(4):295-297. doi: 10.1177/000348940811700409
- Mokabberi R, Shirani J, M AH, Go BD, Schiavone W. Streptococcal pharyngitis-associated myocarditis mimicking acute STEMI. *JACC Cardiovasc Imaging*. 2010;3(8):892-893. doi: 10.1016/j.jcmg.2010.05.012

11. Upadhyay GA, Gainor JF, Stamm LM, Weinberg AN, Dec GW, Ruskin JN. Acute nonrheumatic streptococcal myocarditis: STEMI mimic in young adults. *Am J Med.* 2012;125(12):1230-1233. doi: 10.1016/j.amjmed.2012.06.016
12. Caraco J, Arnon R, Raz I. Atrioventricular block complicating acute streptococcal tonsillitis. *Br Heart J.* 1988;59(3):389-390. doi: 10.1136/hrt.59.3.389
13. Hanna EB, Glancy DL. ST-segment elevation: Differential diagnosis, caveats. *Cleve Clin J Med.* 2015;82(6):373-384. doi: 10.3949/ccjm.82a.14026
14. Chen S, Hoss S, Zeniou V, et al. Electrocardiographic Predictors of Morbidity and Mortality in Patients With Acute Myocarditis: The Importance of QRS-T Angle. *J Card Fail.* 2018;24(1):3-8. doi: 10.1016/j.cardfail.2017.11.001
15. Deluigi CC, Ong P, Hill S, et al. ECG findings in comparison to cardiovascular MR imaging in viral myocarditis. *Int J Cardiol.* 2013;165(1):100-106. doi: 10.1016/j.ijcard.2011.07.090
16. Nucifora G, Miani D, Di Chiara A, et al. Infarct-like acute myocarditis: relation between electrocardiographic findings and myocardial damage as assessed by cardiac magnetic resonance imaging. *Clin Cardiol.* 2013;36(3):146-152. doi: 10.1002/clc.22088
17. De Lazzari M, Zorzi A, Baritussio A, et al. Relationship between T-wave inversion and transmural myocardial edema as evidenced by cardiac magnetic resonance in patients with clinically suspected acute myocarditis: clinical and prognostic implications. *J Electrocardiol.* 2016;49(4):587-595. doi: 10.1016/j.jelectrocard.2016.04.002
18. de Bliet EC. ST elevation: Differential diagnosis and caveats. A comprehensive review to help distinguish ST elevation myocardial infarction from nonischemic etiologies of ST elevation. *Turk J Emerg Med.* 2018;18(1):1-10. doi: 10.1016/j.tjem.2018.01.008
19. Aquaro GD, De Gori C, Faggioni L, et al. Diagnostic and prognostic role of late gadolinium enhancement in cardiomyopathies. *Eur Heart J Suppl.* 2023;25(Suppl C):C130-C136. doi: 10.1093/eurheartjsupp/suad015
20. Kang M, Chippa V, An J. *Viral Myocarditis.* In: StatPearls. Treasure Island (FL): StatPearls Publishing; November 20, 2023.



CASUISTIC PAPER

ST-segment elevation in anterior leads secondary to electric shock – a diagnostic dilemma

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ABSTRACT

Introduction and aim. Electrical injuries can be life-threatening and prompt interventions can save lives. Cardiac complications like arrhythmias and sudden cardiac death are common after electric shock. Certain ECG abnormalities can persist after successfully reviving the patient which can mimic ST-Elevation occlusive myocardial infarction. This case report aims to inform the treating emergency physicians about this rare association of ST-Elevation in anterior leads after electric shock.

Description of the case. After obtaining proper consent from the patient, we describe here an interesting case of a 19-year-old boy who was presented to the emergency room with cardiac arrest after sustaining electrical injury. The patient was revived after cardiopulmonary resuscitation; ECG, as well as echocardiographic findings, were consistent with ST-elevation myocardial infarction of the anterior wall. A diagnostic dilemma was there between occlusive and non-occlusive causes of this condition. A coronary angiogram and conservative management of the patient helped in decision making and he was discharged with a Glasgow coma scale of 15/15 after recovery.

Conclusion. ST-Elevations in ECG can occur after electric shock injury and their cause is rarely due to occlusion of the coronaries. Hence thrombolysis in such cases is rarely needed and supportive management is required.

Keywords. cardiac arrest, electrical injury, non-occlusive MI

Introduction

Electrical injuries are very heterogeneous depending on multiple factors and their presentations can be varied ranging from small skin burns to extensive injuries of internal organs, which could be life-threatening.¹ Cardiovascular effects of electrical injuries can be arrhythmias or myocardial injuries. Arrhythmias are the most common cardiac complications of electrical injury but ECG pattern of myocardial infarction can also be present and lead to diagnostic challenges in the emergency room.²

Aim

Here we discuss a case of a 19-year-old male who was brought to the emergency room with cardiac arrest after sustaining electrical injuries and revived with post-return of spontaneous circulation (ROSC) ECG showing ST-segment elevation, a sign that could point to the diagnosis of occlusive myocardial infarction. This case report highlights the importance of the fact that most of the myocardial ischemic changes after electrocution injuries are related to vasospasm instead of thrombotic occlusion of the coronaries. Even ST-Elevations in the anterior lead in ECG, though rare, can

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be present without occlusive Myocardial infarction in this group of patients.

Description of the case

We report a case of a 19-year-old male, a resident of Jodhpur city in India, brought to the emergency room in an unresponsive state for 10 minutes following contact with an electric current at the workplace with a history of falling from a height of 5 feet. The patient was a handicraft factory worker and accidentally got shocked while fixing the power supply of a drill machine. The electric supply of the factory receives AC 220 Volt and 50 Hertz. There was no prior history of any comorbid conditions like diabetes, hypertension, ischemic heart disease, epilepsy etc. On examination, the carotid pulse was not palpable so code blue was activated and he was immediately shifted to the resuscitation bay. Cardiopulmonary resuscitation (CPR) was started according to advanced cardiac life support (ACLS) protocol. The initial rhythm on the monitor was ventricular fibrillation so defibrillation was done with 200 joules of energy. Defibrillation was repeated 2 times and an injection of amiodarone 300 mg intravenous was also given. After 2 cycles of CPR, ROSC was achieved and the airway was secured with a 7.5 mm endotracheal tube. ABG was suggestive of lactic acidosis with PH of 7.18, PCO_2 44 mmHg, PO_2 58 mmHg, Na^+ 132 mmol/L, K^+ 5.1 mmol/L, HCO_3^- 19 mmol/L and lactate levels were 6 mmol/L (Normal value 0.8–1.2 mmol/L) (Table 1). Post-ROSC vitals were stable with a blood pressure of 120/70 mmHg and a heart rate of 70/minute, regular. His GCS remained low, that is E1V1M1 with Bilateral pupils mid-dilated and non-reactive. On further examination, a wound mark was present on the left hand which was the entry wound, and the left foot was the exit wound (Fig. 1). Post-ROSC ECG taken after 30 minutes, showed ST segment elevation in leads V2 to V6, I, aVL (Fig. 2), and troponin I was 1.13 ng/mL (Normal is 0–0.03 ng/mL). The troponin I test was done by using a point-of-care Nanochecker machine, with 4-in-1 immunoassay-based kits for quantitative analysis of cardiac biomarkers. Bedside 2-dimensional Echocardiography (2D Echo) showed hypokinesia in the territory of the left anterior descending artery and E-FAST was negative. Blood gas showed Primary metabolic acidosis appropriately compensated by respiratory alkalosis. The patient was given loading doses of dual antiplatelets suspecting the possibility of acute ST-elevation myocardial infarction following electrical injury. Given a poor Glasgow Coma Scale (GCS) of 7/15 post-ROSC, a non-contrast CT head was done which was normal. The patient was shifted to the ICU where serial ECGs were obtained which showed persistently the same changes. Serial Trop levels were also done, which were decreasing and became normal within 3 days. Cardiologist consultation was taken for ECG changes and given no regional wall motion abnormality on 2D Echocardiography, per-

sistently stable vitals, and improvement in the general condition of the patient, conservative management was advised. The patient was managed conservatively in the ICU for the next 3 days, after which he gained consciousness and was extubated. A coronary angiogram was done to rule out occlusive myocardial infarction but it was normal. The patient was monitored for complications and later was discharged with a cerebral performance score of 1 and GCS E4V5M6. Repeat ECG on day 5 of ICU admission showed biphasic t waves in lead V3, and V4, and the 2-dimensional echocardiography repeated was also normal.



Fig. 1. Entry wound in the left hand (black arrow) and exit wound in left foot (white arrow)

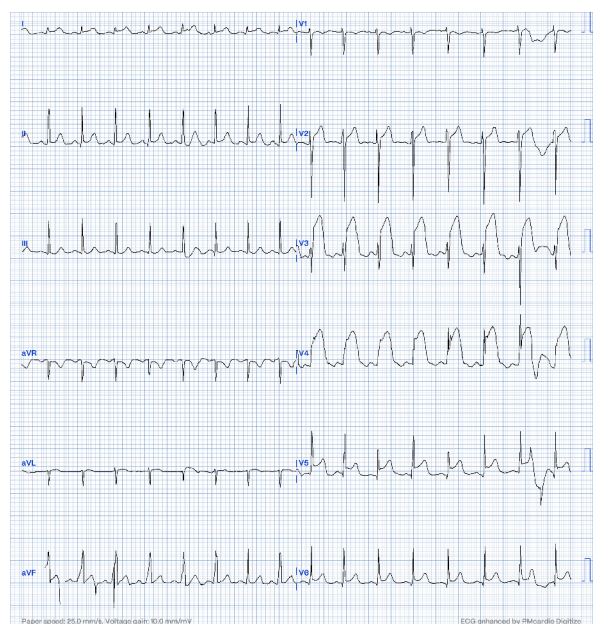


Fig. 2. ECG showing ST segment elevations in leads V2–V6 and I, aVL

Table 1. Investigations done in the Emergency Room

Parameter	Value
Total leukocyte count	10×10 ³ /mm ³
Hemoglobin	12 g/dL
Platelets	200×10 ³ /μl
Urea	39 mg/dL
Serum creatinine	1.28 mg/dL
Na ⁺ /K ⁺ /Cl ⁻	134/4.5/103 meq/L
SGOT/SGPT	113/194 IU/L
PT/INR	12/1.01
CT brain + C spine	Normal
Troponin I	1.13 ng/L (Positive)
CK NAC	3011 U/L (Elevated)

Discussion

The major mechanisms of electricity-induced injury are electrical injuries causing direct tissue damage, altering cell membrane potential, conversion of electrical energy into thermal energy, causing tissue destruction, and mechanical injury resulting from falls.³ Factors that determine the nature and severity of electrical trauma include voltage, resistance to current flow, type of current (direct or alternating), duration of contact with the current source, current path through the body, and the magnitude of energy delivered.⁴ When the chest is situated along the path that connects the entrance and exit points, the heart is often affected and can lead to complications like arrhythmias and myocardial tissue injuries. In most of the cases, patients who had myocardial infarction after electric shock have been reported to have normal coronary arteries and in the case of ST elevation MI; the aetiology is considered to be vasospasm.⁵ Due to the proximity of the right coronary artery to the chest wall, it is the most frequently involved artery in electrical injuries. Therefore, ST elevations in inferior leads are more frequently observed.⁶ But in our case, the ST elevations were present in the anterior leads which is reported rarely and caused the diagnostic challenge. Multiple mechanisms are proposed for these ECG changes which include coronary artery spasm, Direct thrombogenic effect on coronary arteries, direct thermal effect on myocardium, and ischemia secondary to arrhythmia-induced hypotension.⁷ Due to the persistent elevations after resuscitation in anterior leads of ECG and regional wall motion abnormality in the same territory, the patient was administered a loading dose of aspirin and clopidogrel through the nasogastric tube. No heparin or thrombolysis was given considering the diagnostic uncertainty between occlusive and non-occlusive myocardial infarction. The patient improved with just ventilator support and conservative management. Therefore, this case signifies the importance of constant patient monitoring, including his vitals, ECG changes, echocardiographic abnormalities, and serial troponin levels after resuscitation from post-electro-

cution cardiac arrest in deciding the further course of management and the need for coronary interventions in these patients.

Conclusion

Myocardial infarctions after electrical injuries are rare and most commonly occur due to non-occlusive causes. Most of the ST segment changes occur in the inferior leads but involvement of anterior territory is also a possibility as described here in this case. Thrombolysis in these conditions is rarely necessary and only coronary angiogram can be used to differentiate between occlusive and non-occlusive conditions. Primarily managing the airway, breathing, circulation, and disability with good resuscitation efforts in these cases are the mainstay of treatment.

Declarations

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Author contributions

Conceptualization, A.K.R. and A.K.M.; Methodology, A.S.; Software, R.G.S.; Validation, A.K.R., M.S.R. and A.S.; Formal Analysis, A.K.R.; Investigation, A.K.M.; Resources, R.G.S.; Data Curation, A.K.R.; Writing – Original Draft Preparation, A.K.R.; Writing – Review & Editing, A.S.; Visualization, R.G.S.; Supervision, M.S.R.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Data availability

The data that support the findings of this study are available on request from the corresponding author.

Ethics approval

Written informed consent for publication was obtained from the patient. We complied with the policy of the journal on ethical consent.

References


- Spies C, Trohman RG. Narrative review: Electrocution and life-threatening electrical injuries. *Ann Intern Med.* 2006;145(7):531-537. doi: 10.7326/0003-4819-145-7-200610030-00011
- Gentges J, Schieche C. Electrical injuries in the emergency department: an evidence-based review. *Emerg Med Pract.* 2018;20(11):1-20.
- Jaffe RH. Electropathology: a review of the pathologic changes produced by electric currents. *Arch Pathol.* 1928;5:839-869.

4. Waldmann V, Narayanan K, Combes N, Jost D, Jouven X, Marijon E. Electrical cardiac injuries: current concepts and management. *Eur Heart J*. 2018;39(16):1459-1465. doi: 10.1093/eurheartj/ehx142
5. Gursul E, Bayata S, Aksit E, Ugurlu B. Development of ST Elevation Myocardial Infarction and Atrial Fibrillation after an Electrical Injury. *Case Rep Emerg Med*. 2015;2015:953102. doi: 10.1155/2015/953102.
6. James TN, Riddick L, Embry JH. Cardiac abnormalities demonstrated postmortem in four cases of accidental electrocution and their potential significance relative to nonfatal electrical injuries of the heart. *Am Heart J*. 1990;120(1):143-157. doi: 10.1016/0002-8703(90)90171-s
7. Oltman CL, Clark CB, Kane NL, et al. Coronary vascular dysfunction associated with direct current shock injury. *Basic Res Cardiol*. 2003;98(6):406-415. doi: 10.1007/s00395-003-0428-5



CASUISTIC PAPER

Benign endotracheal tumor (hamartoma) mimicking bronchial asthma

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ABSTRACT

Introduction and aim. The most common benign tumor of the lung is hamartoma. In many cases, it is a spherical tumor, located peripherally, often without clinical symptoms. Predominantly it is found accidentally during radiological examination. In some cases the tumor reaches a significant size in the lung parenchyma or in the lumen of the bronchi or trachea. Then, symptoms such as cough, dyspnea, wheezing, less commonly hemoptysis, and chest pain may occur. In addition, tumors located endobronchial or endotracheal may cause recurrent pneumonia or mimic obstructive diseases of the lower respiratory tract such as chronic obstructive pulmonary disease, or bronchial asthma. We present the case of a patient with an endotracheal tumor mimicking bronchial asthma.

Description of the case. A 53-year-old male was taking bronchodilators and inhaled steroids for several months. The baseline chest radiograph showed no abnormalities. Spirometry suggested an obstruction of respiratory flow in the central or upper airways. The lack of improvement after asthma treatment required an extension of the diagnosis. Computed tomography allowed accurate visualization of the tumor lesion of the trachea, which was significantly obstructing its lumen, and resection was carried out.

Conclusion. Our case demonstrates that tracheal tumors can present symptoms similar to respiratory tract diseases. In unresolved cases, spirometry and computed tomography are helpful in proper diagnosis.

Keywords. benign endotracheal splinter tumor (hamartoma), benign endotracheal tumor, endotracheal resection of tumor

Introduction

Hamartoma is one of the most common benign tumor of the respiratory system. The incidence of the tumor in population is about 0.2%. It is 2–3 times more frequently found in men, and usually has character of a peripherally located lung tumor. In 10% of cases it may involve the bronchi, or trachea.¹ It accounts for approximately 8% of all lung tumors, 77% of which are benign.² The lesion may be composed of all mesenchymal tissue of lungs and airways, such as hyaline cartilage, adipose tissue, connective

tissue, and smooth muscle.³ If the lesions are peripheral, and small in size they do not cause complaints and are usually detected accidentally during imaging. However, if they reach a significant size, they may present with symptoms caused by compression of adjacent parts of the lungs, and bronchi such as coughing or hemoptysis. In case of endobronchial or endotracheal localization additional symptoms related to obstruction, such as dyspnea, wheezing, chest pain, or recurrent pneumonia may occur. On chest X-ray imaging, the lesion usually presents

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as a fairly well-defined, peripherally located, near circular or oval shadowing with uneven saturation, often with the presence of calcifications.

In some cases, calcifications in the lesion give a characteristic popcorn-like appearance. Usually the lesion is solitary, but less often multiple lesions are present. On chest computed tomography, the lesion is usually a tumor less than 2.5 cm in size with smooth or lobulated margins, with density characteristic of adipose tissue or calcifications.⁴

The prognosis of pulmonary hamartoma is good. Malignant changes have not been observed. The most common increase in lesion size is roughly 1–10 mm per year.² Treatment usually consists of removal of the lesion, lobectomy, or in extreme cases pneumonectomy. Endoscopic removal of the endotracheal or endobronchial lesion is also possible, together with treatment of pneumonia. In other cases, conservative treatment with observation of the lesion is done.

The primary symptoms of the bronchial asthma or chronic obstructive pulmonary disease are often non-specific and can be considered as a variety of respiratory illnesses. This symptomatic resemblance can lead to diagnostic ambiguity, finally resulting in misdiagnoses or delayed diagnoses.

Spirometry can be used to assess lung functions, mon-

itor the disease progression and response to treatment. Proper determination of the obstruction upper airways indicators in spirometry, can detect the changes suggesting larynx or trachea disorders. The findings in the mediastinum, including those in trachea, which are invisible in X-ray, are precisely evaluated by computer tomography.⁵

Aim

The presented article indicates that spirometry and computed tomography are helpful in the diagnosis of lesions located in the trachea.

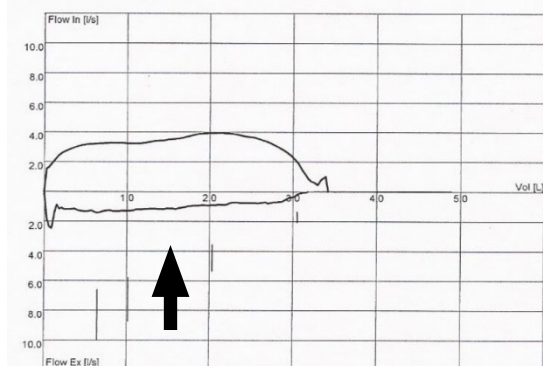
Description of the case

A 53-year-old patient, non-smoker, was admitted to the department of pulmonology and allergology for extended diagnosis of dyspnea. He had been treated for 9 months for bronchial asthma without effect. Bronchodilators used included long-acting β mimetic in combination with an inhaled steroids and cholinolytics.

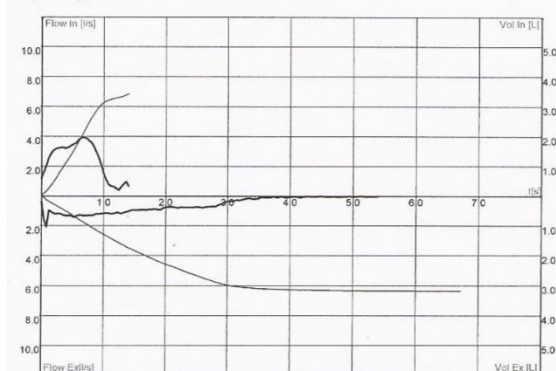
An anterior to posterior chest X-ray taken 10 months earlier showed an insignificantly enhanced bronchovascular pattern of the lungs, otherwise the image showed age-appropriate lungs and hilum, and free costophrenic angles. On admission to the clinic, the patient reported a feeling of dyspnea and wheezing on slight exertion, including when bending down and after

BADANIE SPIROMETRYCZNE DYNAMICZNE

Krzywa przepływ-objętość



Krzywa przepływ-czas Krzywa objętość-czas



Parametr	Jedn.	WN	WZ	%WN	LSR	P
FVC	l	4.07	3.19	78.4	-1.44	7.6
FIVC	l	4.07	3.44	84.3	-1.05	15.1
AT	l		0.24			
AT/FIVC			0.07			
FEV 0.5	l	2.64	0.66	24.9	-2.88	1.0
FEV 1	l	3.28	1.29	39.3	-3.91	1.0
FEV 2	l	3.65	2.28	62.4	-1.32	9.6
FEV 3	l		2.97			
FEV 6	l		3.17			
FEV1/FVC	l/l	0.78	0.40	52.0	-5.20	1.0
FEV1/FIVC	l/l	0.78	0.38	48.3	-5.60	1.0
FEV1/FVCMAX	l/l	0.78	0.38	48.3		
FEV1%FEV3	%		43.44			
FEV1%FEV6	%		40.75			
MEF 75	l/s	7.28	1.25	17.2	-3.52	1.0
MEF 50	l/s	4.45	1.16	26.1	-2.49	1.0
MEF 25	l/s	1.72	0.76	44.2	-1.23	11.4
MEF 25/75	l/s	3.72	1.04	27.9	-2.58	1.0
MEF 75/85	l/s		1.33			
PEF	l/s	8.31	2.54	30.6	-4.76	1.0
PEF/MEF75		1.14	2.03	177.5		
PIF	l/s	7.88	3.95	50.2		
PEF/PIF		1.05	0.64	61.0		
MIF 50	l/s		3.65			
MEF50/MIF50			0.32			
FIV 1	l		3.07			
FIV1/FIVC			0.89			
TFVC	s		3.39			
TFIVC	s		1.41			
TFVC/TFIVC			2.41			
AEX	l ² /s	18.13	3.26	18.0		
AIN	l ² /s		11.56			
AEX/AIN			0.28			
MVV	l/min	131.32	51.60	39.3		
Ilość pom. zgodnych ERS ATS			1			
Plateau	T/N	TAK	TAK			
FET	s	6.00	6.70			
TPEF	s	0.13	0.05			
EV	l	0.16	0.02			
FVCQ	D					
FEV1Q	D					
FIVCQ	D					

Fig. 1. Flow-volume curve shows significant expiration flattening – left upper part (black arrow), volume-time curve – left lower part, spirometry protocol – on the right

eating. He denied coughing, hemoptysis or chest pain.

On physical examination, inspiratory and expiratory wheezes were noted. Functional tests showed: in spirometry, significant obstructive-type ventilation abnormalities (FEV_1 1.29 l – 39.3% of the predicted value 3.28 liters, FVC 3.19 l – 78.4% of the predicted value 4.07 liters, FEV_1/FVC ratio: 0.40 – 52% of the predicted value 0.78, positive reversibility test – increase in FEV_1 by 300 ml (9%), FVC by 620 ml (15.1%). FEV_1/PEF ratio 0.70 (0.63 after reversibility test) or FEV_1/PEF 8.46 ml/l/min (FEV_1 in ml, PEF in l/min) – indicates narrowing of the central or upper respiratory tract (Fig.1).

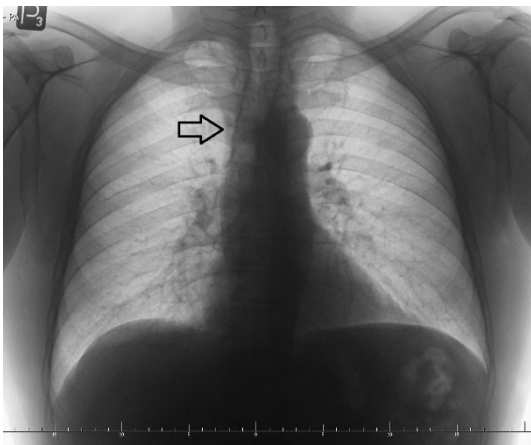
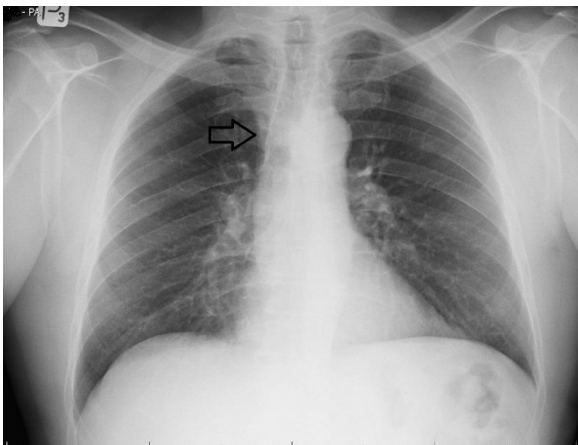


Fig. 2. Chest radiograph in antero-posterior projection, arrows point to a shadow in the distal 1/3 of the trachea

Body plethysmography volumetric parameters did not deviate from normal: TLC 94% of the predicted value, RV 97% of the predicted value. In contrast, a significant increase in respiratory resistance values was observed. Due to persistent inspiratory and expiratory wheezing on physical examination, suspected laryngeal stridor, the patient was consulted by otorhinolaryngologists, where no pathology was found in the larynx or the upper tracheal segment.

Chest radiograph in anterior to posterior projection showed no focal changes in either lung field, normal hilum was visualized, non-dilated mediastinal shadow,

and free costophrenic angles. In the tracheal projection at the level of the aortic arch a near oval shadow was noted. A computed tomography scan showed a tumor 18 mm in diameter in the tracheal lumen, located 25 mm above the main branch, emerging from the lateral wall on the left side, smoothly circumscribed, homogeneous in structure and low in density corresponding to adipose tissue (approximately 115 IU). The lesion significantly constricted the tracheal lumen leaving 4 mm wide space around the tumor (Fig. 2 and Fig. 3). The patient was transferred to the Department of Thoracic Surgery, where endoscopic electro resection of the tracheal tumor with a metal loop was performed using a rigid bronchoscope. Subsequently, argon coagulation of the tracheal wall at the site of the severed pedicle was performed under bronchofiberscope guidance, achieving full hemostasis. Two months after the procedure, a follow-up bronchofiberscopy was performed, during which no recurrence of the tracheal tumor was noted.

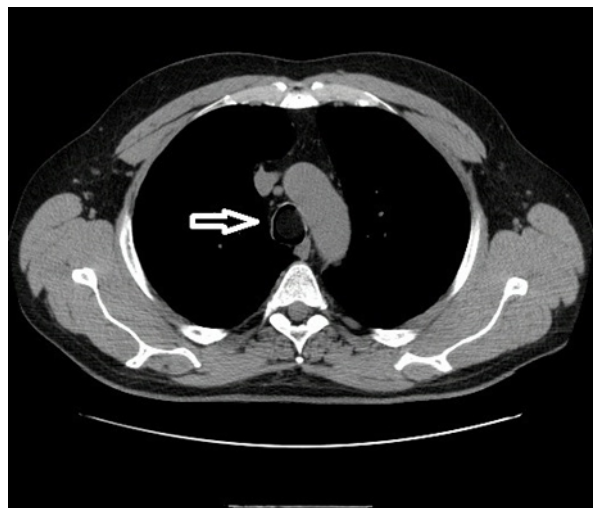
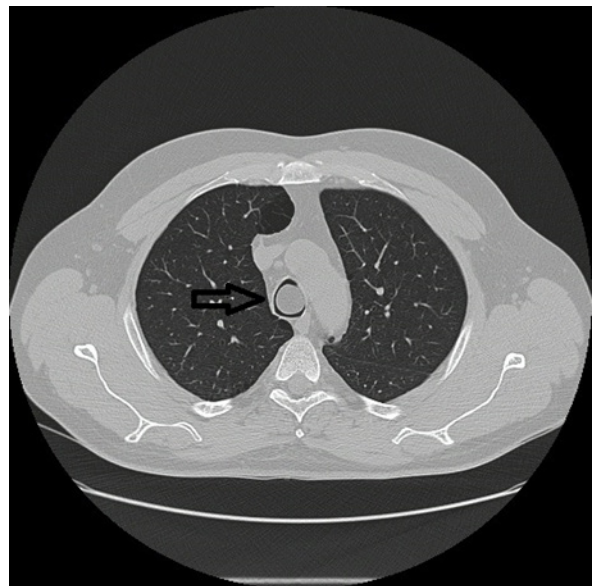


Fig. 3. CT scan of the thorax at the level of aortic arch: on the left – lung window, on the right – mediastinal window,

the arrows indicate a lesion in the tracheal lumen

Macroscopically, the tracheal tumor presented as a partially encapsulated lesion measuring 20x19x20 mm with a base of excision of 14x12 mm, solid in cross-section, pale yellowish in color (Fig. 4).



Fig. 4. Macroscopic image of the lesion

Histopathological examination revealed that the tumor composed predominantly of mature adipose tissue, fibro myxoid tissue, and pseudo glandular structures, arranged in disorganized manner. In some fields a lobular structure with the presence of clefts from the respiratory epithelium was present. On the lumen side of the bronchus, the tumor was covered by benign respiratory epithelium undergoing squamous metaplasia. Beneath the epithelium, a focal, chronic inflammatory infiltrate was visible. No cartilage elements or other tissues of mesenchymal origin were found. The tumor was removed in its entirety.

Microphotographs show mature adipose and fibro myxoid tissue overlying the respiratory epithelium. No cartilaginous tissue was visualized. The slice is from the endobronchial surface of the tumour. Slightly deeper, islands of benign bronchial glands with seromucous structure were found (Fig. 5–7).

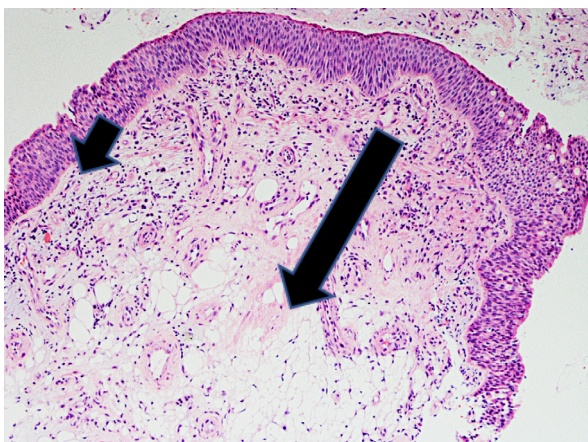


Fig. 5. Hamartoma composed of mature adipose tissue (large arrow) and fibro-myxoid tissue (small arrow) containing blood vessels with thickened walls, the nodule is covered by a benign, slightly proliferated squamous epithelium undergoing squamous metaplasia, beneath the epithelium, a chronic inflammatory infiltrate is visible (H&E

stain, 200X)



Fig. 6. Epithelial elements in the hamartoma tissue, forming pseudo glandular structures (arrows), fibro-myxoid tissue and islands of mature adipose tissue in the background (H&E stain, 100X)

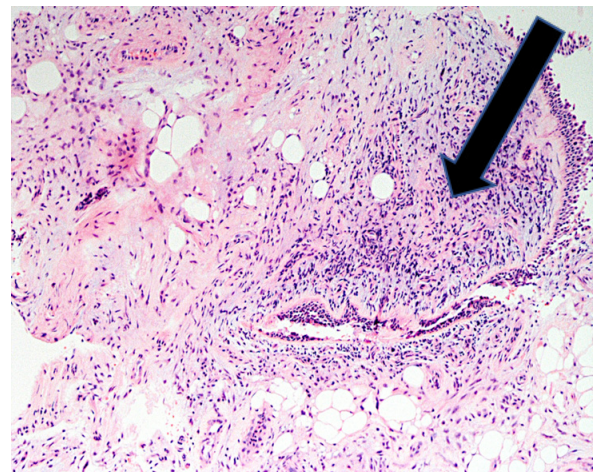


Fig. 7. Respiratory epithelial clefts separating the hamartoma tissue into lobules composed of mixed mesenchymal tissue (H&E stain, 100X)

Discussion

Hamartomas of the respiratory tract are mainly found in the lung parenchyma, and are usually clinically silent. Small lesions do not require invasive treatment, and instead should be monitored for growth. When large, they may compress the adjacent lung tissue and bronchi causing obstruction. If the tumor grows inside the lumen of trachea or bronchi, the patient's complaints may mimic respiratory diseases such as bronchial asthma, chronic obstructive pulmonary disease, or recurrent pneumonia.⁶⁻⁸ If they are small in size, the lesions may not be visible on a standard chest X-ray.

In the presented case the baseline chest X-ray did not describe pathology. The current thorough chest X-ray analysis indicated a discrete shading in the tracheal projection. Audible wheezing during auscultation

of the patient lungs should take into account the possibility of central or upper airway obstruction. Entering the above information on the referral to the radiologist has a significant impact on a more accurate assessment of the trachea in X-ray.

It may be helpful to mark the indicators: FEV_1/PEF (obstruction >0.48) or FEV_1/PEF ml/l/min (obstruction >8 ml/l/min), which suggest narrowing of the central or upper respiratory tract such as the main bronchi, trachea or larynx.⁸ Chronic complaints such as cough, breathlessness, wheezing, stridor, hemoptysis, or recurrent pneumonia are a lead based on which the diagnosis should be expanded to include CT scan and/or bronchoscopy, which can detect even smaller lesions.⁹

In the presented case, the symptoms persisted for 10 months despite anti-asthmatic treatment. It is considered that the occurrence of symptoms for more than 2 months with optimal treatment of bronchial asthma should require an extension of the diagnosis, including, above all, computed tomography.

The prognosis of such finding is favorable, and usually involves endoscopic removal of the lesion. Resection of a benign lesion from the lung parenchyma or from the lumen of the airways is always advantageous, as it excludes the possibility for the lesion to become malignant. Patients with an unspecified lesion in the lung parenchyma or airways, who cannot be treated surgically, should have the lesion evaluated using positron emission tomography scan and a computed tomography for potential malignancy.¹⁰

Apart from causing an obstruction within the respiratory tract itself, hamartomas sprouting from the lung tissue can potentially cause issues in different organ systems, such as cardiovascular where the tumor can compress arteries or put pressure on the heart itself.¹¹ This case study is a good example of how important it is to not ignore recurrent clinical findings or chronic illnesses as they can have curable underlying causes.

Conclusion

In the presented case there was a significant narrowing of the tracheal lumen. Inappropriate or delayed diagnosis could have led to serious complications and even death of the patient. Initially diagnosed with bronchial asthma, the patient was taking bronchodilators and inhaled steroids for several months.

Lack of improvement after the previous treatment, characteristic auscultatory changes in the form of inspiratory and expiratory wheezing and obstruction of the airways, especially the upper ones, require a revision of the current diagnosis. The use of the FEV_1/PEF index may indicate central or upper airway obstruction. Computed tomography allows proper assessment of the lungs and mediastinum. Invisible or poorly visible changes in chest X-ray should also be confirmed by it,

as shown by the presented case.

Declarations

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Author contributions

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Conflicts of interest

The authors have no conflict of interest.

Data availability

Not applicable.

Ethics approval

The patient signed informed consent regarding publishing his data.

References

- Umashankar T, Devadas AK, Ravichandra G, Yaranal PJ. Pulmonary hamartoma: Cytological study of a case and literature review. *J Cytol.* 2012;29(4):261-263. doi: 10.4103/0970-9371.103948
- Guo W, Zhao YP, Jiang YG, Wang RW, Ma Z. Surgical treatment and outcome of pulmonary hamartoma: a retrospective study of 20-year experience. *J Exp Clin Cancer Res.* 2008;27(1):8. doi: 10.1186/1756-9966-27-8
- Stevic R, Milenkovic B. Tracheobronchial tumors. *J Thorac Dis.* 2016;8(11):3401-3413. doi: 10.21037/jtd.2016.11.24
- Yuan L, Wang S, Wei J, Yang K, Mao Y. Mesenchymal cystic hamartoma of the lung: A case report. *Medicine (Baltimore).* 2022;101(1):e28242. doi: 10.1097/MD.00000000000028242
- Radosavljevic V, Gardijan V, Brajkovic M, Andric Z. Lung hamartoma--diagnosis and treatment. *Med Arch.* 2012;66(4):281-282. doi: 10.5455/medarh.2012.66.281-282
- Hona C, O'Harab C, Litlec V. Endotracheal hamartoma case report: Two contrasting clinical presentations of a rare entity. *Int J Surg Case Rep.* 2017;38:98-101. doi: 10.1016/j.ijscr.2017.07.023
- Sarioglu N, Susur A, Goksel T, Paksoy S, Erel F. An Unexpected Cause of Hemoptysis: Endobronchial Lipomatous Hamartoma. *Med Arh.* 2014;68(1):65-66.
- Odak M, AlAzzawi M, Alshami A, Alsaoudi G, Cosentino J. Endobronchial Hamartoma Presenting as Recurrent Pneumonia and Chronic Cough. *Cureus* 2021;13(3):e13717. doi: 10.7759/cureus.13717
- Cetinkaya E, Gunluoglu G, Eyhan S, Zeki Gunluoglu M, Ibrahim Dincer S. A Hamartoma Located in the Tra-

- chea. *Ann Thorac Cardiovasc Surg*. 2011;17:504-506. doi: 10.5761/atcs.cr.10.01608
10. Capitanio S, Nordin AJ, Noraini AR, Rossetti C. PET/CT in nononcological lung diseases: current applications and future perspectives. *Eur Respir Rev*. 2016;25(141):247-258. doi: 10.1183/16000617.0051-2016
11. Ulas AB, Aydin Y, Eroglu A. Pulmonary Hamartomas: A Single-Center Analysis of 59 Cases. *Eurasian J Med*. 2022;54(3):270-273. doi: 10.5152/eurasianjmed.2022.21150



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— Article from a journal, number of authors from 1 to 6

Author AA, Author BB, Author CC. Title of article. *Accepted Abbreviated Journal Title*. Year;Volume(Issue):Page-Page. doi (if available)

Lee JC, Seo HG, Lee WH, Kim HC, Han TR, Oh BM. Computer-assisted detection of swallowing difficulty. *Comput Methods Programs Biomed*. 2016;134(2):72-78. doi: 10.1016/j.cmpb.2016.07.010

Morris A. New test for diabetes insipidus. *Nat Rev Endocrinol*. 2019;15(10):564-565. doi: 10.1038/s41574-019-0247-x

— Article from a journal, number of authors more than 6

Author AA, Author BB, Author CC, et al. Title of article. *Accepted Abbreviated Journal Title*. Year;Volume(Issue):Page-Page. doi (if available)

Gonzalez ME, Martin EE, Anwar T, et al. Mesenchymal stem cell-induced DDR2 mediates stromal-breast cancer interactions and metastasis growth. *Cell Rep*. 2017;18:1215-1228. doi: 10.1016/j.celrep.2016.12.079

Jordan J, Toplak H, Grassi G, et al. Joint statement of the European Association for the Study of Obesity and the European Society of Hypertension: obesity and heart failure. *J Hypertens*. 2016;34:1678-1688. doi: 10.1097/HJH.0000000000001013

— Websites

Author AA (if indicated). Webpage title. Name of Website. URL. Published or Updated date. Accessed date.

Cholera in Haiti. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/haiticholera/>. Published October 22, 2010. Updated January 9, 2012. Accessed February 1, 2012.

Address double burden of malnutrition: WHO. World Health Organization site. <http://www.searo.who.int/mediacentre/releases/2016/1636/en/>. Accessed February 2, 2017.

— Book

Author AA, Author BB. *Title of Work*. Location: Publisher; Year:Page-Page

Doane GH, Varcoe C. *Family Nursing as Relational Inquiry: Developing Health– Promoting Practice*. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:25-28.

London ML, Ladewig PW, Ball JW, et al. *Maternal & Child Nursing Care*. Upper Saddle River, NJ: Pearson Education; c2011:101-103.

— Chapter in a book

Chapter Author AA. Title of chapter. In: *Name of Book*. Edition Number. Editor AA, ed. Location: Name of Publisher; Year:Page-Page.

Grimsey E. An overview of the breast and breast cancer. In: *Breast Cancer Nursing Care and Management*. 2nd ed. Harmer V, ed. Chichester, UK: Wiley-Blackwell; 2011:35-42.

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