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ORIGINAL PAPER

Diana Muraviova [1*(DF)], Yuliia Kharchenko [2*(BC)], Kateryna Pierzynowska [3,4,5(EG)], Stefan Pierzynowski [4,5,6(F)], Jarek Wolinski [3(EG)], Olga Dyomshyna [1(D)], Volodymyr Zhyliuk [2(AC)], Galyna Ushakova [1(ACFH)]

The impact of ademetionine and ipidacrine/phenibut on the NCAM distribution and behavior in the rat model of drug-induced liver injury

[1] Oles Honchar Dnipro National University, Dnipro, Ukraine
[2] State Institution "Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine", Dnipro, Ukraine
[3] Department of Animal Physiology, The Kielanowski Institute of Animal Nutrition and Physiology Polish Academy of Sciences, Jabłonna, Poland
[4] Department of Biology, Lund University, Lund, Sweden
[5] Anara AB/SGPlus, Trelleborg, Sweden
[6] Department of Biology, Institute Rural Medicine, Lublin, Poland

ABSTRACT

Introduction. Recently, more attention is being paid to the drug-induced liver injury (DILI) as a consequence of the tuberculos is treatment and the need for new medicine is emphasized. The use of isoniazid and rifampicin has a potentiating effect, which increases the risk of substancial liver damage. In turn, systemic accumulation of toxic metabolites leads to negative changes in various organs, including the brain. It causes an imbalance in biochemical and neurophysiological processes in the brain, ultimately giving the onset to the development of hepatic encephalopathy.

Aim. The effects of rifampicin and isoniazid on the central nervous system have not been studied before and we aimed to evaluate the impact these two substances have on the neuronal cell adhesion molecules (NCAM) distribution and animal behavior in the rat model of DILI.

Material and methods. The 24 male Wistar rats, weighing 180-220 g were used for the experiment and divided to the groups (n=6): 1 – control; 2 – rats with experimental DILI; 3 – rats with DILI plus the intravenous infusion of S-adenosyl-L-methionine at a dose of 35 mg/kg; 4 – rats with DILI plus a fixed combination of ipidacrine hydrochloride at a dose 1 mg/kg body weight and phenibut at a dose 60 mg/kg body weight daily for the last 14 days of the experiment. All experimental procedures were carried out in the accordance with the principles outlined in the current Guide to the Care and Use of Experimental Animals. The locomotor and research activities were studied in the open field test. The activity of aspartate aminotransferase (AST, EC 2.6.1.1) and alanine aminotransferase (ALT, EC 2.6.1.2) in the serum of rats were tested to confirm the liver damage. The quantitative analyses of soluble and membrane forms of NCAM were performed with ELISA. The ANOVA followed by a Tukey post-hoc test was used to assess statistical differences between groups.

Corresponding author: Galyna Ushakova, e-mail: ushakovagalyna@gmail.com

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Results. Our investigation in the open field test revealed a significant decrease in the locomotor and research activity of rats after 28 days of rifampicin and isoniazid administration. The recovery of investigated parameters was observed in groups of animals treated with ademetionine (AD group) or combination of ipidacrine and phenibut (IP/PB group). We also observed that changes in rats' behavior were consistent with alterations of the NCAM levels in the thalamus and hippocampus. Thus, the level of membrane NCAM was significantly decreased under DILI in both investigated brain regions (thalamus and hippocampus), while both AD and IP/PB treatments restored membrane NCAM levels towards those observed in the control group at least in the hippocampus.
Conclusion. Obtained data suggests that both ademetionine and combinated drug containing ipidacrine and phenibut possesses neuroprotective properties and could prevent the decline in synaptic plasticity under antitubercular therapy.
Keywords. ademetionine, brain, ipidacrine/phenibut, isoniazid, liver disease, NCAM, rifampicin

Introduction

Drug-induced liver injury (DILI) accounts for up to 10 % of all adverse reactions associated with the use of drugs. According to World Health Organization (WHO), 50 out of 1000 patients are hospitalized due to the drug-induced complications.[1,2] Information provided by WEB-platform LiverTox (http://livertox.nlm.nih.gov) indicates that 353 (53 %) of the 671 drugs available for analysis provoke the hepatotoxicity. Moreover, isoniazid, pyrazinamide, and rifampicin are the most toxic liver agents. In particular, in studies published in the United States in 2015, based on the analysis of more than 600 cases in 12 clinical trials, 46 % of DILI cases were associated with antimicrobial drugs, such as antibiotics and antitubercular drugs.[2]

The simultaneous use of isoniazid and rifampicin causes a potentiating effect, which increases the risk of substancial liver damage.[3] The asymptomatic «subclinical» course of drug-induced hepatitis is dangerous, and further administration of these agents leads to the development of severe hepatitis, accompanied by jaundice and hepatic encephalopathy, which manifests as acognitive impairment.[4,5]

The main role in the development of these disorders be longs to the diminished detox function of the liver. Non-ionized ammonia easily penetrates the blood-brain barrier (BBB) and enters the astrocytes, where itismetabolized in the mitochondria in the presence of α-ketoglutarate to form of glutamine, a key component in the development of the astrocytic edema.[6] The active forms of oxygen and nitrogen are highly reactive molecules and are redox-active compounds, which, depending on the concentration, have both a positive (proliferation of cells) and negative effects (cell growth arrest, cell death) on nerve cells.[7,8] Oxidative and nitrosating stresses initiate neuro transmission disorders, mitochondrial dysfunction, and energy metabolism disorders in central nervous system (CNS).[9,10] The cognitive deficits observed in hepatic encephalopathy are also the result of the synaptic plasticity violations and changes in mediator transmission.[11] In particular, it is reported that hepatic encephalopathy is associated with highactivity of the GABA-ergic system of the brain due to increased γ-aminobutyric acid (GABA) concentration, expression of GABA receptors, and production of neurotrophic steroids, specifically aloprengonone.[12] At the same time, there is a decrease in glutamatergic neurotransmission characteristic for the chronic liver disorders, and observed violations in learning and memory may be associated with the inhibition of the glutamate nitrogen oxide-cGMP regulatory effect in the hippocampus which appearsas a response to hyperammonemia or increased levels of dopamine which result form the impaired liver function.[13]

Our study aimed to investigate neuronal cell adhesion molecules (NCAM) in various areas of the brain after the long-term administration of rifampicin and isoniazidin rats. NCAMs play an important roles in the regulation of neuronal differentiation and migration by interacting with growth factors and their receptors, as well as in the mechanisms of membrane potential regulation, determining the excitability of neurons.[14-16] Also, NCAMs in fluence the synaptic plasticity and cognitive processes of the mature brain, the short-term plasticity of existing synapses, and long-lasting plasticity associated with the elimination of old synapses and the formation of new ones. According to the contemporary notions about the functional role of NCAM, the blocked function of these proteins can lead to cognitive and emotional declines, such as changes in the perception of odor, memory, hearing, anxiety and space orientation.[17]

A lot of information on the effects of antimicrobials on the CNS has been collected over the last decade. However, the effect of rifampicin and isoniazid on the CNS could be felt no tonly by their expressive hepatotoxicity after prolonged use bu talso by the ability to cause a disturbance in the balance of the intestinal microflora and the development of dysbiosis, which potentially have negative impactas on the CNS it self as on the progression of toxic liver injury induced encephalopathy.[18] Moreover, the membrane-bound proteins, including NCAM are recognized as the primar target for the endotoxins'negative effects on CNS.[19] Therefore, the study of neuronal plasticity in the DILI model, as well as the possible ways of their pharmacological correction, is very relevant and could reveal new findings on the pathogenesis of cognitive impairmentin DILI.

As a correction of pathological conditions, when using antitubercular therapy, various substances and preparations are tested. They have various mechanisms of action (direct and indirect) that are scantily studied. In our study,

the drug Heptral was used, the active substance of which was S-adenosyl-L-methionine and the drug Kognifen, which is a combination of ipidacrine and phenibut.

Ademetionine (S-adenosyl-L-methionine) is a naturalaminoacid – a derivative of methionine and ispresent in all tissues. Ademetionine can penetrate through the BBB and its transmethylation process is key in the formation of such CNS neurotransmitters as catecholamines (dopamine, norepinephrine, adrenaline), serotonin, melatonin and histamine.[20] Neuroprotective effects of ademetionine may be mediated via the inhibition of oxidative stress and neuroinflammation by increasing the levels of endogenous glutathione and enhancing the activity of enzymes of the antioxidant defense system (superoxidismutease and glutathionetransferase), as well as improving energy metabolism in cells.[21-23]

Kognifen is a balanced combination of ipidacrine and phenibut. One of the two constitutive substances is phenibut (hydrochloride β-phenyl-γ-aminobutyric acid) – a phenyl analog of GABA. The nootropic activity of the drug is based on anti-hypoxic effects, an increasein energy metabolism, and synthetic processes in neurons.[24]

Phenibut has a direct effect on GABAergic receptors and facilitates GABA-mediated transmission of nerve impulses to the CNS.[25] It easily penetrates into all body tissues and through the BBB. Considering that GABA is the major inhibitory neurotransmitter in the CNS and as many as one-third of CNS neurons in the brain use GABA as their primary neurotransmitter, phenibut has a significant effect on the state of the central nervous system.[26]

Aim

The purpose of this work was to study the effects of ademetionine and combined drug ipidacrine/phenibut on the level of NCAMs in different brain areas in the rats with DILI provoked by the prolonged administration of rifampicin and isoniazid.

Material and methods

Animals

There search was carried out on 24 male Wistar rats, weighing 180-220 g which were housed in standard cages (48×27×20 cm) with free access to food and tap water (2–6 rats per cage). Animals were kept in a temperature-controlled room (22±2 °C), under a constant 12:12-h light/dark cycle (lights on at 06:00 hours). The experiment was conducted in the animal house of the State Establishment «Dnipropetrovsk Medical Academy of Health of the Ministry of Ukraine».All experimental procedures were carried out in the accordance with the principles outlined in the current Guide to the Care and Use of Experimental Animals and were approved by local Ethics Committee on Animal Experimentation of the State Institution "Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine" (Approval No.7, 2019).

Experimental Design

Animals were divided into four groups. The first group (C, n=6) of healthy rats, served as a control group. Control rats received administered with LAUROPAN T/80 Polysorbate (Industria Chimica Panzeri, Orio al Serio, Italy) and distilled water as a vehicle of in comparable volumes with experimental groups according to body weight daily during 28 days. The second group (DILI, n=6) included rats with DILI, an experimental which was reproduced by chronic intragastric administration of rifampicin at a dose of 86 mg/kg (PJSC SIC «Borshchahivskiy CPP», Kiev, Ukraine) and isoniazid in a dose of 50 mg/kg (PJSC «LUGAL», Kiev, Ukraine) using a standard solvent LAUROPAN T/80 Polysorbate (Industria Chimica Panzeri, Orio al Serio, Italy) and distilled water as a vehicle daily during 28 days[27]. Third group (AD, n=6) consisted of rats with DILI and received the intravenous infusion ofS-adenosyl-L-methionine (ademetionine) ("Geptral", Abbott Lababoratories GmbH, Hannover, Germany) at a dose of 35 mg/kg daily during the last 14 days of the experiment. Fourth group (IP/PB, n=6) consisted of rats with DILI which received a fixed combination of ipidacrine hydrochloride at a dose 1 mg/kg body weight and phenibut at a dose 60 mg/kg body weight (Kognifen®, Olainfarm, Olaineatvia). Rats were euthanized by cervical dislocation 24 hours after the last administration of drugs.

Open field test

For the assessment of locomotor and research activity, an open field test was used.[27,28] On the last (28th) day of the study, a 3 min open field session in the testing arena (100x100 cm, 30cm high walls, made of white plast) was performed for each animal. The testing arena contained 16 holes, each with a diameter of 6 cm that were located equidistantly from each other and the walls on the floor plane of its installation. For the test, each animal was placed at the center of the arena and its behavior was observed for 3 min, after that the animal was returned to its home cage, and the device was washed and sterilized with 70% ethanol to remove any trace of odor that could cause distractions. An assessment was made on the number of crossed squares (horizontal activity), vertical elevations (vertical activity) and holesvisits (research activity).

Protein extraction and determination

The hippocampus and thalamus were isolated from the brain and used subsequently for extraction of cytosolic and membrane protein fractions by differential ultracentrifugation. Homogenization of the brain was carried out in buffer A, which contained 25 mM tris - HCl (pH 7.4), 1 mM ethylenediaminetetraacetic acid (EDTA), 0.01 % sodium azide (NaN_3), 0.2 mM phenylmethylsulfonyl fluoride (FMSF). During successive centrifugation

stages (stage I – centrifugation for 60 minutes at 20,000 g, stage II – incubation of the precipitate 24 hours after the first centrifugation in buffer A, which additionally contained Triton X-100 – 2%, and centrifugation for 60 minutes at 20 000 g) fractions containing soluble NCAM (soluble – sNCAM isolated in stage I centrifugation) and membrane NCAM proteins (membrane – mNCAM isolated in stage II centrifugation) were isolated. All reagents were purchased from Sigma, St. Louis, Missouri, USA.

The quantitative determination of NCAM was performed using an ELISA, with primary rabbit monospecific polyclonal antibodies against NCAM (Abcam, Cambridge, UK), secondary anti-rabbit antibodies labeled with horseradish peroxidase (Abcam, Cambridge, UK), and purified NCAM proteinas a standard (R&D Systems, USA, Minneapolis, Canada) using a competitive solid-phase immunoassay analysis. Results obtained were printed outusing an Anthos-2010 absorbance reader (Anthos Labtec Instruments GmbH, Wals-Siezenheim, Austria).

Blood collection and analysis

Blood samples were taken immediately after midline thoracotomy from the right ventricle of heart of rats in terminal anesthesia using a 5 ml syringe with 25-gauge needle on the last day of the study period. Serum was obtained by placing whole blood in an empty tube and allowed the blood to clot. After that, the samples were centrifuged for 15 min at 3000 rpm. Serum was removed and the samples were stored at -20°C until further analysis.

The activity of aspartate aminotransferase (AST, EC 2.6.1.1), alanine aminotransferase (ALT, EC 2.6.1.2) in the serum of rats to confirm liver damage using reagent kits for clinical biochemistry manufactured by High Technology Inc. (North Attleborough, MA, USA) on HTI BioChem SA biochemical analyzer manufactured by High Technology Inc. (North Attleborough, MA, USA), according to the recommended methodology.[29] The De Ritis ratio was determined standardly using the ratio of serum activity of AST and ALT (AST/ALT ratio).[30]

Statistical alanalysis

An ANOVA, followed by a Tukey post-hoc test was used to assess statistical differences between groups. To assess data distribution, Shapiro-Wilk normality test was performed. Statistical processing of data was carried out using GraphPad Prism, v 8.1.0 software (GraphPad Software, Inc, San Diego, CA, USA). Data are represented as mean value (M) and the standard error of the mean (SEM). In all statistical analyses $p<0.05$ was considered significant.

Results

The results of the current study indicate that under rifampicin and isoniazid administration, the activity of both AlAT and AsAT in rat serum significantly ($p<0.001$) increased (1.5-fold increase for AlAT (from 44.45±2.72 to 64.60±2.81 U/l) and 3-fold increase for AsAT (from 36.64±2.13 to 104.52±5.86 U/l)), the De Ritis ratio was 1.61.

Results obtained from the open field test revealed that levels of horizontal and vertical activity in rats from the DILI group were decreased by 27.8% and 35.43% ($p<0.05$), respectively, when compared to those observed in C group rats (Fig. 1 A). Also, a significant ($p<0.05$) 52.16% decrease in the level of research activity when compared to the control animals from group C, was found in the DILI group (Fig. 1 A).

Horizontal activity values noted in AD group didn't differ significantly from those observed in the group C animals, however, the AD group animals demonstrated significantly ($p<0.05$) higher horizontal activity (by 31%) when compared to DILI rats (Figure 1 A). Horizontal activity of animals from the IP/PB group didn't differ significantly either from the such one observed in the C or DILI groups (Figure 1 A). The vertical activity of rats in both AD and IP/PB groups remained at the level of the control group (Figure 1 B).

The significant ($p<0.05$) decrease in research activity of 36% and 16.7% was noted for the animals from the AD and IP/PB groups, respectively, when compared to the control animals from group C (Figure 1 C). In the same time, the values of research activity in both AD and IP/PB groups, were significantly ($p<0.05$) higher, by 25% and 42.6%, respectively, than in DILI group. IP/PB group animals demonstrated significantly ($p<0.05$) higher research activity than the AD group rats (Figure 1 C).

C – the control group of healthy rats, administered with the vehicle, n=6; DILI – group of rats with drug-induced liver injury (DILI), n=6; AD – group of rats with DILI receiving ademetionine, n=6; IP/PB – group of rats with DILI receiving a fixed combination of ipidacrine hydrochloride and phenibut, n=6. Small letters given with result bars mean significant differences when $p<0.05$.

The content of the total protein in the soluble fraction obtained from the thalamus of rats from the DILI group was significantly ($p<0.05$) decreased by 17% compared to the group C (Figure 2 A). Values observed in the both AD and IP/PB groups were significantly ($p<0.05$) higher (by 38.6% and 63.5%, respectively) than those noted in the DILI group, and even higher than values seen in the group C (14.6% and 35% difference, respectively, $p<0.05$). The level of cytosolic protein in the IP/PB group was 18% higher than in the AD group ($p<0.05$) (Figure 2A).

The levels of total cytosolic and water-soluble protein in the hippocampus of DILI group rats didn't sig-

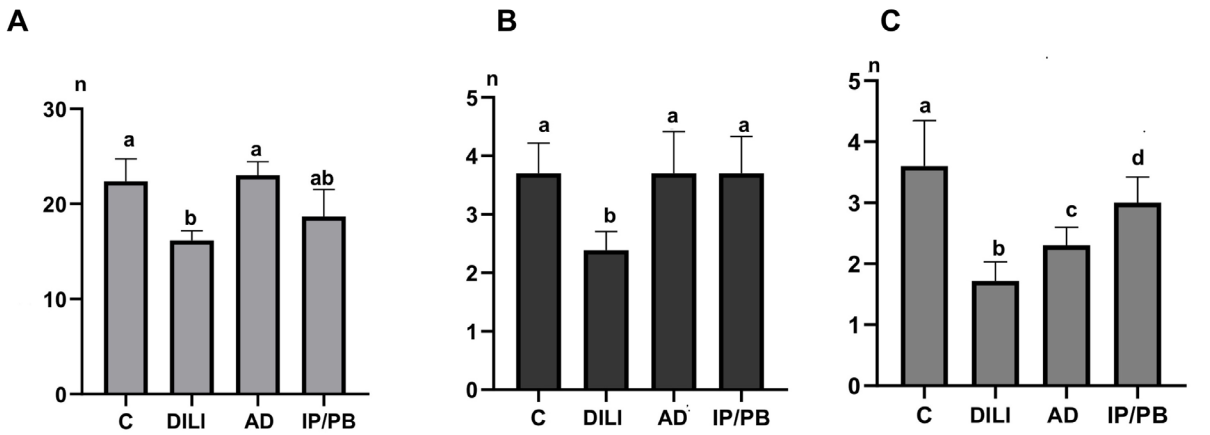

Fig. 1. A-C. The behavior of rats in the open field test on the last study day. A – Horizontal activity; B – Vertical activity; C – Research activity

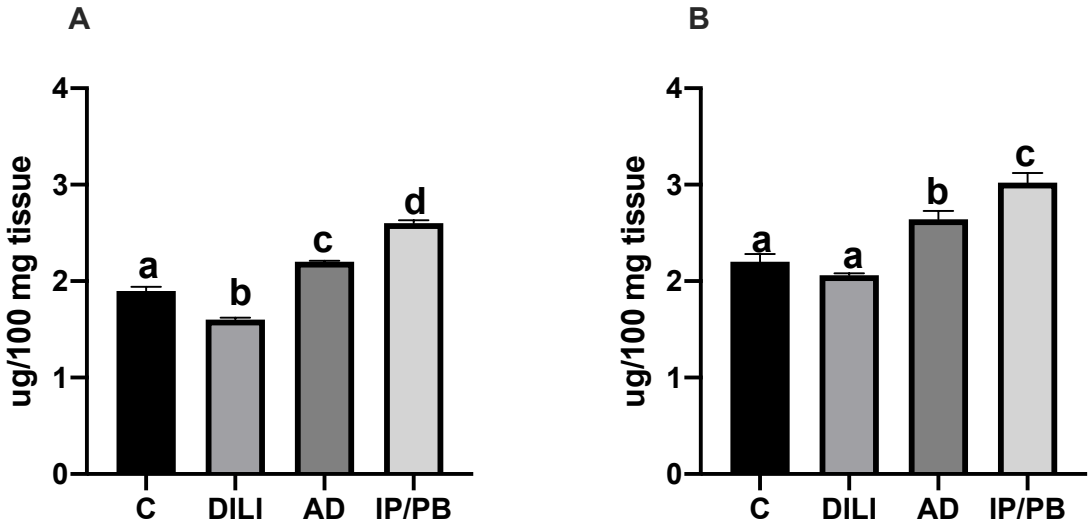

Fig. 2. A, B. The content of the total cytosolic and water-soluble protein extracted from the thalamus (A) and hippocampus (B) of rats. C – the control group of healthy rats, administered with the vehicle, n=6; DILI – group of rats with drug-induced liver injury (DILI), n=6; AD – group of rats with DILI receiving ademetionine, n=6; IP/PB – group of rats with DILI receiving a fixed combination of ipidacrine hydrochloride and phenibut, n=6. Small letters given with result bars mean significant differences when $p<0.05$

nificantly differ from those observed in the group C, while a significant ($p<0.05$) increase (by 20% and 37.3%, respectively), was seen in the AD and IP/PB groups (Figure 2 B). Total protein levels observed in the AD and IP/PB groups were significantly ($p<0.05$) higher (by 28% and 46%, respectively) when compared to the DILI group. The level of cytosolic protein in the IP/PB group was 14.4% higher than in the AD group, $p<0.05$ (Figure 2 B).

The content of the membrane fraction of total protein in the rats' thalamus significantly ($p<0.05$) decreased by 23.5%, 24% and 14% in the DILI, AD and IP/PB groups, respectively, when compared to the group C (Figure 3 A).

The content of the membrane fraction of total protein in the rats' hippocampus significantly ($p<0.05$) decreased by 10.7% in the DILI group compared to the group C (Figure 3 B). The levels of the membrane fraction of the total protein in the AD group didn't differ significantly from the values noted in the DILI group, however, values in the IP/BP group significantly ($p<0.05$) increased by 16.5% and 30.4% compared with C and DILI groups respectively.

The content of the soluble NCAM (sNCAM) fraction in the thalamus of animals from the DILI and IP/PB groups didn't differ significantly from that one observed in the group C. In the same time, values noted in the AD group, were significantly ($p<0.05$) lower (by ca 20%) when compared with those seen in the groups C and IB/PB (Figure 4 A).

The level of the sNCAM in the hippocampus of rats from the both AD and DILI groups didn't differ significantly from that one seen in the group C, while IP/PB treatmeant led to the significant ($p<0.05$) increase

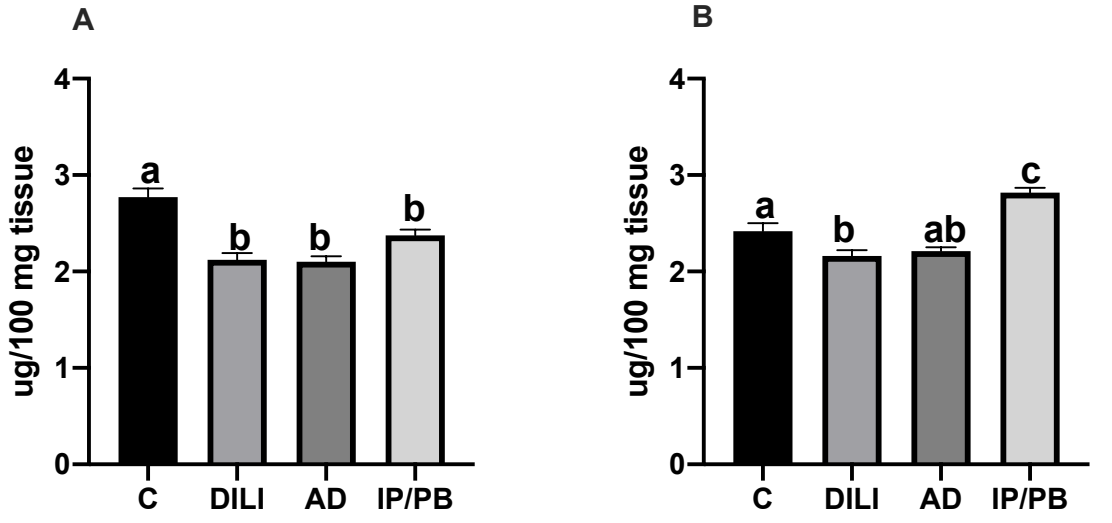

Fig. 3. A, B. The content of the total membrane protein in the thalamus (A) and hippocampus (B) of rats. C – the control group of healthy rats, administered with the vehicle, n=6; DILI – group of rats with drug-induced liver injury (DILI), n=6; AD – group of rats with DILI receiving ademetionine, n=6; IP/PB – group of rats with DILI receiving a fixed combination of ipidacrine hydrochloride and phenibut, n=6. Small letters given with result bars mean significant differences when $p<0.05$

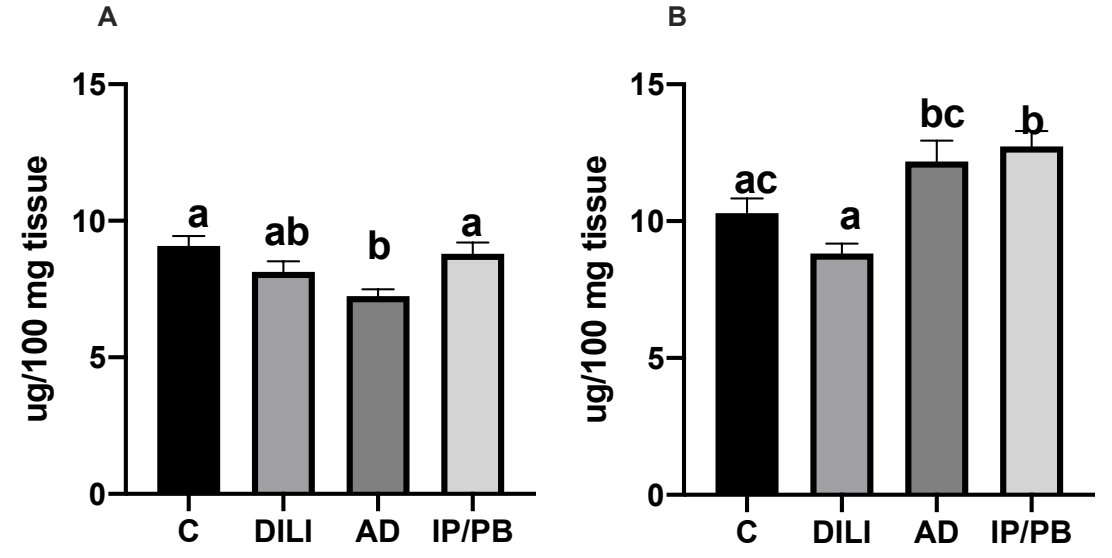

Fig. 4. A, B. The content of the soluble NCAM in the thalamus (A) and hippocampus (B) of rats C – the control group of healthy rats, administered with the vehicle, n=6; DILI – group of rats with drug-induced liver injury (DILI), n=6; AD – group of rats with DILI receiving ademetionine, n=6; IP/PB – group of rats with DILI receiving a fixed combination of ipidacrine hydrochloride and phenibut, n=6. Small letters given with result bars mean significant differences when $p<0.05$

of sNCAM content when compared to the C group values. The sNCAM levels observed in animals from both the AD and IP/PB groups, were significantly ($p<0.05$) higher (40.8% and 30%, respectively), when compared to those noted in the group DILI (Figure 4 B).

With regards to the membrane NCAM (mNCAM) fraction, in the thalamus of the DILI group rats it was significantly ($p<0.05$) decreased by 11% when compared to the group C. The values obtained in the AD and IP/PB groups were significantly ($p<0.05$) decreased by 19.2% and 19.3%, respectively, when compared to the C group. Values, observed in the AD group were significantly ($p<0.05$) decreased in comparison with those observed in the DILI group, while in IP/PB group mNCAM content didn't differ from that one, observed in DILI group (Figure 5 A).

The contents of the membrane NCAM fraction in the hippocampus in the DILI group was significantly ($p<0.05$) decreased by 9.5% when compared to the C group. In the same time, mNCAM content in AD and

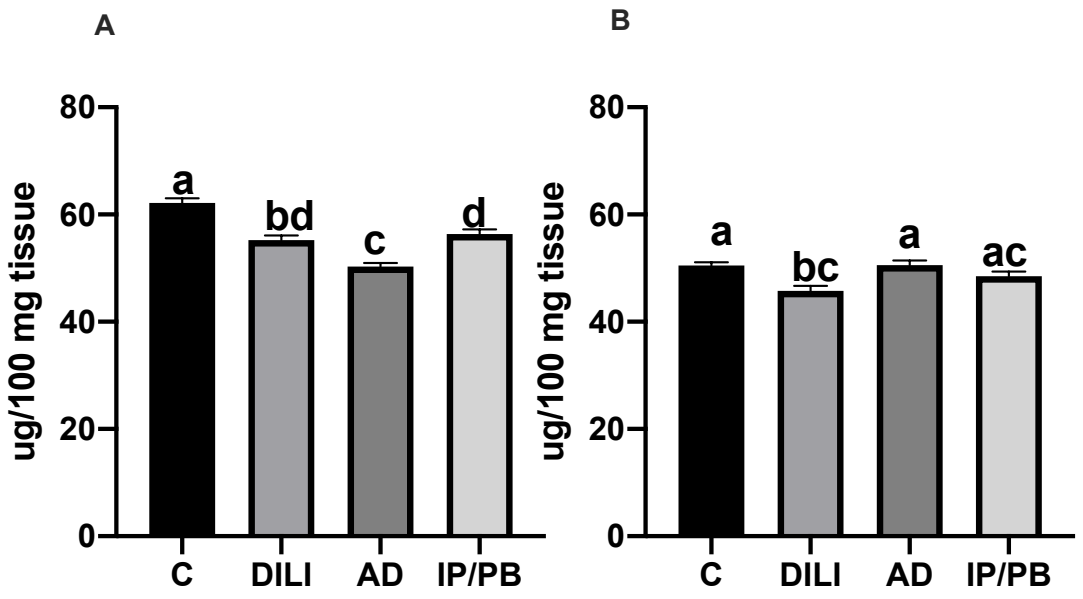

Fig. 5. A, B. The content of the membrane NCAM in the thalamus (A) and hippocampus (B) of rats. C – the control group of healthy rats, administered with the vehicle, n=6; DILI – group of rats with drug-induced liver injury (DILI), n=6; AD – group of rats with DILI receiving ademetionine, n=6; IP/PB – group of rats with DILI receiving a fixed combination of ipidacrine hydrochloride and phenibut, n=6. Small letters given with result bars mean significant differences when $p<0.05$

IP/PB groups remained at the level of the values of the C group. Compared with the DILI group, the mNCAM levels in the AD group was significantly ($p <0.05$) increased by 10.5% (Figure 5 B).

Discussion

The long-term use of antitubercular drugs leads primarily to the liver disorders, affecting the multiple organs of the experimental animals and leaving substancial influence on certain organs, including the brain. In case of liver homeostasis disruption, the increased permeability of BBB and following transfer of toxic products into the brain were observed previously.[31] In the present study we investigated the effects of ademetionine and combined drug IP/PB on the NCAM distribution in the brain in the rat model of DILI induced by the long-term administration of rifampicin and isoniazidum.

The obtained data of elevated activity of transaminases (AST and ALT) in the serum of the experimental animals was indicative for the injury caused to the liver, namely, to the mitochondria of hepatocytes, which results in the mitochondrial isoform of AST entering the bloodstream. Our results confirmed the data obtained by Awodele et al. showing the stimulating effect of rifampicin on the liver enzymes AST and ALT activity in serum.[32]

Previously it was concluded that the use of ademetionine as a drug with high protective and therapeutic effects of liver injury is promising. Lee and Ko showed the hepatoprotective effect of ademethionine in experimental liver injury.[33] Rats from the pre-treated with S-adenosylmethionine group showed a significant restoration of the ALT and AST levels in serum, compared with the experimental group.The result of the correction of hepatotoxicity by the hepatoprotective drug restored the value of biochemical parameters to the control level.

When studying the behavior of rats in the open field test, rats from the DILI group showed a significant decrease in locomotor and research activities, as well as in parameters of mnemonic functions, compared with the group C. Horizontal and vertical locomotor activity of rats from group with AD was restored to level of control animals. The partial recovery of horizontal locomotor activity and full recovery of vertical locomotor activity was observed in IP/PB group.

The main function of the soluble NCAM is to regulate extracellular signaling, intercellular adhesion andmigration of neurons.[34] Transmembrane adhesive molecules are not only mediators in the process of recognition between cells, but they can also convert signals with in the cell and, thus, cause a cellular response that regulates ontogenesis and synaptic plasticity (including learning and memory).[14,17] The redistribution of NCAM between two forms (soluble and membrane) under long-term effect of rifampicin and isoniazid was noted. The balanced content of transmembrane and soluble isoforms of this protein is of great importance for the normal development and functioning of the brain.[35,36]

The target of the negative effect of endotoxins in the brain is primarily membrane-bound proteins, including NCAM, which was manifested by a significant decrease in the concentration of these molecules ($p<0.05$)

in the PI / PB group in the fraction isolated from the hippocampus. In parallel with this, a significant increase ($p<0.05$) was observed in the hippocampus relative to the control of the content of the soluble form of NCAM due to enzymatic cleavage of membrane-bound NCAM, "cutting" of these molecules from the cell membrane. Therefore, as a result of the redistribution of NCAM between fractions during an experimental drug-induced liver injury, when an increase in the number of soluble and a decrease in membrane molecules was observed in the hippocampus, the normal functioning of both sNCAM and mNCAM is disrupted.

A number of drugs tend to penetrate the BBB. Rifampicin is no exception.[31,37] In studies of Shobo et al., drug penetration was visualized and its exact distribution in the rat brain was shown. And even with the sligh test concentrations of rifampicin, it penetrates the BBB and enters the brain tissue.[38] In DeMarco studies, after a single intravenous injection, rifampicin is rapidly appearingin the liver, blood and brain tissues. In the liver, the absorption index is the highest and its increase was observed within 60 minutes of the test. In the blood in the first 10 minutes, the results were maximum and decreased by the 60th minute. Also, rifampicin concentrations in the brain were found to around 15% of the levels found in blood.[39] Similar results were demonstrated in the article by Awodele et al., where authors presented histopathological data showing that rifampicin is able to penetrate the BBB and cause congestion of the meninges.[32]

Our own results obtained in the present study demonstrate the decrease in total protein content both in the soluble and membrane fractions of thalamus in the DILI group, when compared to the group C. In the hippocampus the same tendency was noted for membrane proteins, however, the total level of cytosolic/water-soluble proteins was increased. Obtained data demonstrates that rifampicin may affect protein synthesis in the brain.

In the same time, the total protein content in the soluble fraction of both hippocampus and thalamus in the AD and IP/PB groups was significantly increased, and even exceeded the values observed in the group C. The level of total protein in the membrane fraction of the thalamus and hippocampus of the AD group remained at the level of DILI animals. In the IP/PB group, the total protein level in the membrane fraction of both parts of the brain exceeded the DILI and AD groups. And in the hippocampus, these indicators were significantly increased and exceeded the values observed in group C.

The results shown in Figures 4–5, demonstrate a significant decrease in membrane NCAM content in both thalamus and hippocampus of animals from the DILI group. Taking in to account the central role of the thalamus in maintaining consciousness and attention, the data of behavior in the open field test confirm the obtained results (Fig. 1) with reducing the research activity in DILI animals. Moreover, the results showed a sufficient decrease in the content of soluble NCAM in the hippocampus, which is compar able to the decrease in the concentration of attention in rats from DILI group.[17,40] A significant reduction of the NCAM content observed in thalamus under the AD treatment compared to the DILI group, indicated a decrease in NCAM adhesive properties and inhibition of NCAM synthesis.[41] The effect of the drug IP/PB, is more positive because, compared with AD animals, the results are significantly restored to the level of Control group.

In the hippocampus an increase in the NCAM levels in the soluble fraction was observed in both AD and IP/PB groups compared to the Control and DILI animals. It can be assumed that the restoration of the soluble form of NCAM occurs due to enzymatic dissolution of membrane-bound proteins.[42] After all, the cytosolic form of NCAM reacts quickly even to minor changes in the body's sustainability by releasing the NCAM pool, which restores the strength of the contacts between the cells.[43]

Both in animal experiments and clinical studies it was suggested that S-adenosylmethionine can be used for the treatment of nervous system diseases, since it can pass through the BBB. Also, recently, curative effects of S-adenosylmethionine on depression, drug addiction, and cognitive dysfunction have been reported.[20] However, there is no direct evidence of the effect of both of the used drugs (AD and IP/PB).

In studies of Vavers et al., the positive results are presented indicating the neuroprotective activity of R-phenibut. Treatment with R-Phenibut at a dose of 50 mg/kg significantly alleviated reduction of brain volume in damaged hemisphere.[44] The results obtained after the correction of toxic drug-induced liver injury with AD or IP/PB indicate a positive effect of these drugs on the content the total protein and NCAM in the soluble and membrane fraction in the thalamus and hippocampus of rats. But the administration of drugs was carried out for 14 days. During this period, combination drug of ipidacrine/phenibut, having a directed effect on the nervous system. What can be observed by the results of the IP/PB group in the soluble NCAM fraction, which were increased and exceeded the values of the control group. And the results in the NCAM membrane fraction were restored to the level of Control animals. Ademetionin demonstrated a positive effect on the content of NCAM, but in our results of the content of NCAM in the AD group in the thalamus of both fractions, results remained at the DILI group level. Based on the experimental data, we can assume that its main target was the liver, and therefore the effect on the brain is mediated and that in order to improve brain performance, a longer period of administration of ademetionin is needed.

Conclusion

The long-term effect of isoniazid and rifampicin leads to decrease oflocomotor, exploratory activity and emotional reactivity, as well as parameters of mnemonic functions, which is confirmed by changes in the membrane NCAM content both in the thalamus and hippocampus. It should be noted that correcting treatment (hepatoprotective drug ademetionine and the nootropic combinated drug ipidacrine/phenibut) had a positive effect on NCAM level in the brain, compared to the results open field tests of behavior under effect of isoniazid and rifampicin in DILI group. Our investigation revealed that the combinated drug containing IP/PB which possesses neuroprotective properties could prevent the decline in synaptic plasticity under drug-induced liver injury.

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ORIGINAL PAPER

Abdullah Osman Kocak [1(ABCDEFGH)], Sinem Dogruyol [2(ABCDE)], Ilker Akbas [3(BCDEF)], Bugra Kerget [4(CDEFG)], Sultan Tuna Akgol Gur [5(DEFGH)], Zeynep Cakir [1(AEFGH)]

The Impact of 'Stay At Home' Orders on Emergency Room Admissions

[1] Department of Emergency Medicine, Faculty of Medicine, Ataturk University, Erzurum, Turkey
[2] Department of Emergency Medicine, Manisa Merkez Efendi State Hospital, Manisa, Turkey
[3] Department of Emergency Medicine, Bingol State Hospital, Bingol, Turkey
[4] Department of Pulmonary Diseases, Faculty of Medicine, Ataturk University, Erzurum, Turkey
[5] Department of Emergency Medicine, Faculty of Medicine, Ataturk University, Erzurum, Turkey

ABSTRACT

Introduction. The 2019-novel-coronavirus (2019-nCoV) outbreak has become a common problem for the whole world.

Aim. To investigate the impact of the 2019-nCoV pandemic period in our country on emergency room admissions.

Materials and methods. The study was designed as a retrospective cohort. The first case of pneumonia infected with nCoV in our country was diagnosed on March 11, 2020. Considering the date of March 11, 2020, emergency room admissions for two periods of 7 days were investigated, pre-COVID-19 and COVID19. Demographic data, admission diagnosis, vital findings, stay times in emergency room, terminations and emergency department mortality examined. A group of 'geriatric' patient populations were created to examine the admission characteristics of patients aged-65 and over.

Results. The 3466 patients included in the study. The average number of daily admissions was significantly higher in the pre-COVID-19 period (350.4 ± 54.5), compared to the COVID-19 period (144.7 ± 20.2, p=0001). While the proportion of cardiac-caused admissions increased during the COVID period, the proportion of gastrointestinal-induced admissions decreased (p<0001). Hospitalization rates for both adult and geriatric patients increased during the COVID period (p<0001).

Conclusion. Despite all the negativity caused by the outbreak, this period has been one in which the public is aware of unnecessary emergency room which has been subsequently lessened.

Keywords. Covid-19, emergency visits, geriatric patients

Corresponding author: Abdullah Osman Kocak, e-mail: abdullahmrym86@gmail.com

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Introduction

The first case of pneumonia caused by the 2019 novel coronavirus (2019-nCoV), which has affected the world, was detected in Wuhan, China in December 2019.[1] The most frequent onset symptoms in this clinical picture of coronavirus–infected pneumonia caused by this viral factor are fever, cough and dyspnea.[2] In the clinical course of the disease, the clinical picture of pneumonia can become severe and result in organ dysfunction (e.g. shock, acute respiratory distress syndrome [ARDS], acute cardiac injury, and acute kidney injury) and even death.[3] The virus has shown a rapid spread in China. As of January 2020, cases infected with 2019-nCoV have started to be detected in countries other than China, with the first case in Thailand.[4] The first case of pneumonia infected with 2019-nCoV in Turkey was diagnosed on March 11, 2020. On the same day, the World Health Organization announced '2019-nCoV pandemic' and it was stated that this was the first pandemic due to coronavirus.[5]

Since the detection of the first 2019-nCoV case in Turkey, strict measures have been taken to prevent the spread of the virus. The Turkish Ministry of Health used internet and media outlets to inform the public about the epidemic and ways of transmission. Warnings were made in order to reduce unnecessary admissions to health institutions. In the first stage, 'stay at home' calls were made to people with comorbid diseases and to people 65 years and older. As of March 21, 2020, a formal curfew has been imposed for people aged 65 and over. Patients in the risk population were notified to call the hotline before reaching the health institutions, and the public was informed about making referrals by ambulance.[6]

Emergency services continue to serve as the most important step of the health system during the 2019-nCoV pandemic process, as with all mass incidents. Although there are significant changes in other patient care units, emergency services are battling the 2019-nCoV pandemic, while on the other hand they continue to function routinely.

Aim

In this study, we aimed to investigate the effect of the process after the first definitive 2019-nCoV case detected in our country on patient admissions to our emergency medical clinic. We examined the changes in emergency room admissions after the 'stay at home' calls by the Turkish Republic Ministry of Health.

Materials and methods

This study was planned as a retrospective cohort study. Based on the date of 11 March 2020, when the 2019-nCoV case was first confirmed in Turkey; subsequent 7-day patient admissions were examined.

Patient data evaluated in Erzurum, Turkey were obtained from system records of patients aged 18 and over who applied to the emergency department of a 3rd Grade university hospital. The cases examined during this period were grouped as COVID-19 period. As a check period, patient admissions on this date and on the 7-day period before it were examined. The cases examined during this period were grouped as pre-COVID-19 period.

Demographic data of patients, diagnosis at admission (International Classification of Diseases, version 10), vital findings, stay times in the emergency room (minutes), terminations (hospitalization or discharge) and emergency department mortality were examined. Admission complaints for each patient were first recorded separately. Then complaints were categorized as cardiovascular (chest pain, palpitations), respiratory (shortness of breath), neurological (loss of strength, sudden loss of consciousness, seizure), environmental (trauma, traffic accident, assault, intoxication, allergic reaction, burn), gastrointestinal (abdominal pain, nausea/vomiting, diarrhea, stomach pain), nonspecific (headache, dizziness, weakness, myalgia) and other (ear nose, eye, genitourinary system). In addition, a group of 'geriatric' patients was formed to examine the admission characteristics of patients aged 65 and over.

Only data from the first admission of the patients were included in the study. The ethics committee approval for the study has been made by the institution where the work was carried out.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Normal distribution was tested with the Kolmogorov-Smirnoff test. Percentages and frequencies for categorical variables and mean (± standard deviation) values for continuous variables were determined. The Student's *t*-test was used for two continuous group comparisons. The Pearson's $\chi 2$-test was used for categorical variables. A P value of 0.05 was considered significant.

Results

The total number of patients included in the study was 3466, and the gender distribution was 1666 (48.1%) female, and 1800 (51.9%) male. The average age was 47.1 ± 18.8. There were 1013 admissions in the COVID-19 period and 2453 in the pre-COVID-19 period. For these two periods of 7 days, the average number of daily admissions was significantly higher in the pre-COVID-19 period (350.4 ± 54.5), compared to the COVID-19 period (144.7 ± 20.2) ($p<0.001$). There was no significant difference between patients admitted in two periods in terms of average age and gender distribution ($p>0.05$).

Demographic characteristics and distributions of vital findings according to the admission period are specified in Table 1.

Table 1. Demographics, Vitals and Laboratory Findings of the Patients According to the Application Periods

Characteristics	Pre-COVID-19	COVID-19	
Sex, n (%)			
-Male	1279 (52.1%)	521 (51.4%)	p>0.050
-Female	1174 (47.9%)	492 (48.6%)	
Age (years), mean	44.9±18.5	52.5.3±18.4	p>0.0001
Vital signs			
-SBP(mmHg), mean	127.2 (70-250)	127.0(82-200)	
-DBP(mmHg), mean	78.2 (45-160)	77.1 (60-125)	
-HR (beat/min), mean	87.1 (50-145)	86.2 (75-135)	
-O_2 Saturation (%), mean	93.6 (60-99)	94.1 (70-99)	p=0.040
-Body temperature (°C), mean	36.0 (36-39)	36.6 (36-39)	
ED Outcomes			
-Length of stay(min), mean	152.4 ±101.3	123.4±90.6	p=0.018
-ED Mortality, n (%)	4 (57.1%)	3 (42.9%)	p>0.050

Values expressed as number(%) or mean ± standard deviation

DBP: Diastolic blood pressure; ED: Emergency department; HR: Heart rate; SBP: Systolic blood pressure

When the average stay times of the patients in the emergency room was examined, it was observed that it was 152.4 ±101.3 minutes during the pre-COVID period and 123.4±90.6 minutes during the COVID period. The difference was statistically significant (p=0.018).

When both periods are examined together, the most common causes of admission are chest pain with 392/3466 patients (11.3%) and abdominal pain in 346/3466 patients (10%). Significant changes were not observed (p>0.05) between the admissions caused by chest pain in the pre-COVID (10.8%) and in the COVID period (12.5%). During COVID period (8%), admissions for abdominal pain significantly reduced (p=0.012) compared to pre-COVID period (10.8%).

When examined from the perspective of categorized admission complaints, cardiac-led admissions were numerically 290/2453 (11.8%) in the pre-COVID period and 166/103 (16.4%) in the COVID period. The distribution of neurological-caused admissions was 89/2453 (3.6%) in the pre-COVID period and 79/1013 (7.8%) in the COVID period. Both of these proportional increases were statistically significant (p<0.001). Admissions for gastrointestinal reasons were 290/2453 (25.2%) in the pre-COVID period and 166/1013 (17.4%) in the COVID period. This numerical and proportional reduction in the number of admissions was statistically significant. Distribution of admission complaints in categories for all patients was specified in Figure 1.

The rate was 10.3% when at the hospitalization status of patients for all periods is considered. Hospitalization rates were 7.9% in the pre-COVID period, and 15.9% in the COVID period and the increase was found to be significant (p<0.001). While the average age of the patients who were hospitalized during pre-COVID period was 52.1±19.2, it was 45.7±17.3 in the COVID period (the mean difference: 6.37, 95% CI: 2.57-10.2; p=0.001). From the point of view of vital findings, a significant difference was detected only in oxygen saturations. While the average oxygen saturation of pa-

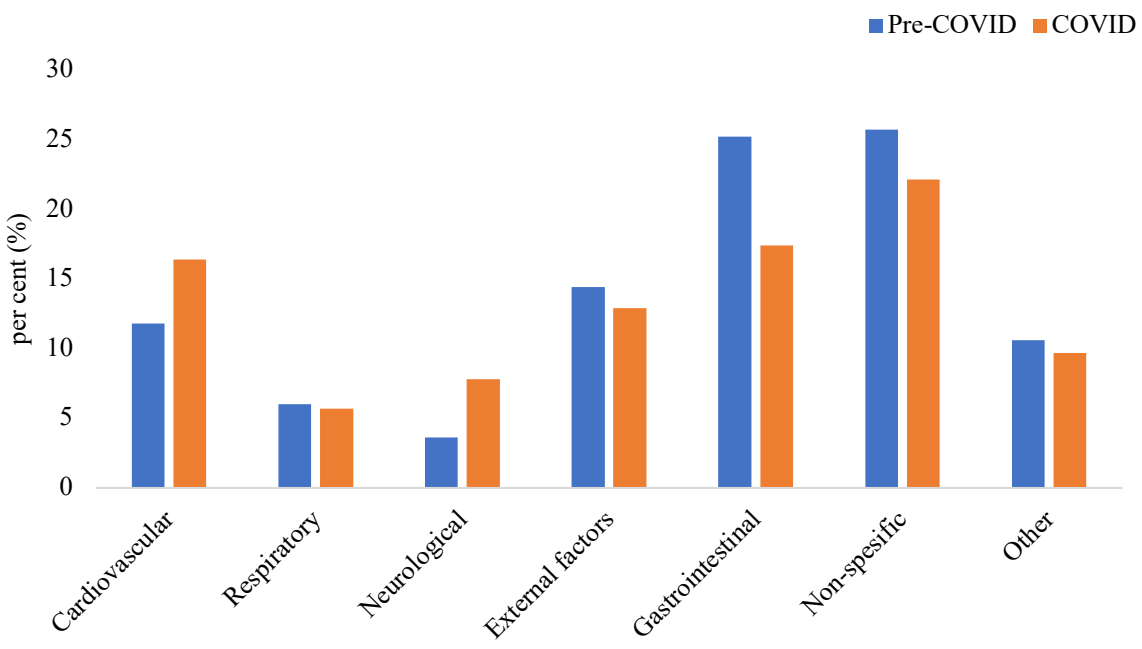

Fig. 1. Categorical distribution of application diagnoses during both pre-COVID and COVID periods

tients hospitalized during the pre-COVID period was 92.5 ±4.8, it was 94.2±2.8 during COVID period (the mean difference: 1.83, 95% CI: 2.64-1.02; p<0.001). The reasons for the admission of the hospitalized patients were examined according to the periods. A significant increase was detected only in the frequency of patients admitted with sore throat complaints. While there were no patients admitted with sore throat complaints, in the Pre-COVID period, the ratio was 6.2% (p<0.001) in the COVID period.

Proportion of patients aged 65 and over to all patients was 863/3466 (24.9%). 507 Geriatric patients (58.7%) applied in the pre-COVID period and 356 (41.3%) in the COVID period. The number of geriatric patient admissions decreased during the COVID period. However, the proportion of geriatric admissions to all admissions was 20.7% in the pre-COVID period and 35.1% in the COVID period. This difference between the admission rates was statistically significant (p<0.001). Chest pain was the most common causes of admissionfor all periods in the geriatric population (14.9%) shortness of breath (11.8%) in terms of pre-COVID and COVID periods, no significant changes were seen in these admission complaints. The rate of hospitalization in the geriatric population was 11.4% in the pre-COVID period, compared to 16.3% during the COVID period. This increase in hospitalization rates was statistically significant (p=0.040). The most common reasons for admission for all periods in the geriatric population were chest pain (14.9%) and shortness of breath (11.8%). When examined in terms of pre-COVID and COVID periods, there was no significant change in these admission complaints. Hospitalization rate in geriatric population in the pre-COVID period was 11.4% and 16.3% in the COVID period. This increase in hospitalization rates was statistically significant (p=0.040).

Discussion

In this study, we found that the call to 'stay at home' since the date of the first 2019-nCoV case in our country caused a significant decrease in the number of patients admitted to the emergency room. We also observed significant changes in the number of admissions and hospitalization rates. In our study, we examined the changes in the health care system through COVID pandemics from an emergency room perspective. Despite all its negativity, we found that this process gave useful results in public awareness and preventing unnecessary emergency room use. In our study, even during the COVID period, we found a reduction of about 50% in the number of patients admitted to the emergency department daily. Guo H et al. found a 38% reduction in dental emergency room admissions during the epidemic in China in their study.[6,7] We think this is mostly about people staying at home and avoiding going to health care institutions that are carry a high risk of infection during the pandemic process. In addition, during the COVID period, patient stays in the emergency room was significantly shortened. We think that the main reason for this situation is that in crowded units where the risk of transmission is high, such as emergency services, there is an effort to shorten the wait time both in the hospitalization and discharge processes.

The emergency room admission diagnoses are divided into two according to the seriousness as emergent and non-emergent. Admissions with emergent diagnoses make up about 40% of total admissions.[8] Cardiac-caused admissions, especially chest pain, are the first among emergent emergency room admissions and account for 5% of all emergency admissions.[9,10] On the other hand, when non-emergent admissions are considered, the most common diagnoses are gastrointestinal system related conditions, especially abdominal pain. In our study, there was no significant change in chest pain-related admissions compared to pre-COVID period during COVID. When we categorically examined the reasons for the admissions, we did not see a numerically significant change in cardiac-related admissions. However, the proportion of cardiac-related admissions for all admissions increased significantly during the COVID period.

In the COVID period, we found a significant numerical and proportional reduction in gastrointestinal system related admissions. This showed us that not only the number of patients during the COVID period, but also non-emergent admissions decreased. However, it did not happen as we had feared during the COVID period, and the rates of emergency service admissions for patients with emergent emergencies were routinely continuing. We believe that the proportional increase in the number of these patients is due to a decrease in other admissions.

In a study examining patients admitted to emergency departments, it was noted that hospitalization rates decreased by years, but were around 6% to 9%.[11] In our study, hospitalization rates during the pre-COVID period were in line with the literature. However, during the COVID period, we found that hospitalization rates was double the normal rates. We believe this is associated with a decrease in non-emergent admissions. We also found changes in some of the characteristics of patients hospitalized in COVID period. We found that in these patients there was a decrease in the average age and increase in average oxygen saturations. The number of patients who were hospitalized with a non-emergent admission diagnosis such as sore throat had increased. We believe that this is due to the effect of the current pandemic on hospitalization criteria even in the early stages.

Approximately 20% of emergency room admissions are made up of the patient group who are 65 years and older. Admissions in this patient population are quite common and are often associated with more se-

rious medical conditions.[12] Older adults are most frequently admitted to the emergency department due to complaints related to cardiac conditions.[13] Again, hospitalization rates are high for this patient population and are 2.5-4.6 times as much as normal.[14] In our study, the pre-COVID period was consistent with the literature in terms of the frequency of patient applicants aged 65 years and older. There was no increase in the number of geriatric patients admitted during COVID period. However, the rate of geriatric patients for all patient admissions increased significantly during the COVID period. In both periods, the most common cause of admission was chest pain, and hospitalization rates increased during COVID period. In our country, there was no reduction in the admission rates of geriatric patients during the pandemic period with real urgent complaints, and patients who applied were often hospitalized in the services. This indicates that; in terms of the geriatric population who are thought to be affected by the pandemic both directly and indirectly there was no deterioration in the functioning of the emergency department at the early stage.

Limitations

In our study, a total of 14 days of patient data for pre-COVID and COVID period were retrospectively examined. The short time frame covered by our study is one of the most fundamental limitations. However, the large number of patients admitted during this period has enabled us to achieve statistically significant results. In addition, the shortness of this process creates limitations in terms of discharge and mortality data. We believe that these limitations can be resolved by planning a similar study that examines data for admissions over a wider period of time.

Conclusion

As a result, the 2019-nCoV pandemic has caused significant changes in emergency room admissions, both numerically and in terms of quality, since the day of the first case in our country. One of the most important factors affecting this process of change is raising public awareness about the concept of 'isolation at home'. In this way, unnecessary emergency room admissions were prevented and real emergency patient care continued without disruption despite the pandemic.

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ORIGINAL PAPER

Maryam Muhammad Zakari [1(ABCDEFG)], Aliyu Yabagi Isah [1(ABCDEFG)],
Richards Offiong [1(ABCFG)], Thairu Yunusa [2(BCFG)], Idris Nasir Abdullahi [3(BCFG)]

Seroprevalence of Toxoplasmosis among Human Immunodeficiency Virus infected pregnant women in Abuja Teaching Hospital, Nigeria

[1] Department of Obstetrics and Gynecology, University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria
[2] Department of Medical Microbiology and Parasitology, University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria
[3] Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Ahmadu Bello University, Zaria, Nigeria

ABSTRACT

Introduction. Toxoplasmosis is a neglected parasitic infection that has economic and epidemiological significance. Data on toxoplasmosis seroprevalence among Human Immunodeficiency Virus (HIV) infected pregnant women may be of obstetric and neonatal concern.

Aim. The study was designed to determine the seroprevalence of Toxoplasmosis and associated risk factors in HIV-positive pregnant women attending the University of Abuja Teaching Hospital, Abuja, Northcentral Nigeria.

Material and methods. This was a hospital-based cross-sectional study. A total of 160 HIV seropositive pregnant women were recruited. Blood samples were collected and tested for anti-*T. gondii* IgM and IgG using Enzyme Linked Immunosorbent Assay (ELISA). Structured questionnaires were used to collate the sociodemographic variables of participants.

Results. Out of the 160 of HIV seropositive pregnant women, the seroprevalence anti-T. gondii IgG and IgM were 29.4% and 4.4%, respectively. There was no significant association between anti-*T. gondii* and all sociodemographic variables studied ($p>0.05$).

Conclusion. The overall result of this study revealed that the majority of pregnant women were exposed to toxoplasmosis much earlier in life. Hence, these findings will assist obstetricians and gynecologists in the early diagnosis and management of *Toxoplasma gondii* infection in pregnant women, especially HIV coinfected ones with IgM seropositivity.

Keywords. HIV coinfections, Nigeria, pregnant women, toxoplasmosis

Corresponding author: Idris Nasir Abdullahi, e-mail: eedris888@yahoo.com, inabdullahi@au.edu.ng

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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Introduction

Toxoplasma gondii (T.gondii) is regarded as one of the causes of opportunistic parasitic diseases amongst HIV infected persons, especially pregnant women. Severe morbidities can occur to both mother and fetus.[1] Cell-mediated immunity, which typically develops after acute infection with *T. gondii,* does not eradicate the disease. The expression of IgM and IgG antibodies in sera is indicative of recent or primary and past exposure to *T. gondii*, respectively.[1]

Primary toxoplasmosis in pregnant women can have serious consequences for the mother and fetus.[1] Although the mortality rate of this parasitic infection in adults appears very low, it causes devastating effects including blindness, neurological impairment, and mental retardation in children when infected in utero with worse consequences in children of immuno-compromised mothers.[1,2]

In Brazil, a recent report shows that 63% of pregnant women were positive for IgG and 5.3% for IgM against *T. gondii*.[3] Tanzania, Ethiopia, and Ghana have reported rates of 44.5%, 83.6%, and 92.5%, respectively, among the studied pregnant population.[4-6] Prevalence of IgG and IgM specific antibodies among pregnant women in Egypt was 38.3% and 18.3%, while a rate of 39.9% and 2.5% was reported in Turkey, respectively.[7,8] A report from Sokoto-Nigeria showed that variations across trimesters with 30.5%, 22.5%, and 30.7% in the first, second, and third trimesters of pregnancy respectively.[9]

In immuno-competent mothers, exposure to *T. gondii* before pregnancy carries virtually no risk of fetal infection; this predominantly occurs in primary infections acquired while pregnant.[10] The immuno-compromised state as seen in HIV positive pregnant women, however, tends to facilitate in-utero vertical transmission. This is mostly as a consequence of latent infection or reactivation.[11-13] In patients with HIV/AIDS, reactivation can occur with CD4+ T cell count of <200 cells/μL. [14] When the CD4+ T cell count is less than 100 cells/μL, the clinical and symptomatic toxoplasmosis becomes very likely.[14,15] Reactivation typically manifests as central nervous system involvement.[15]

The disease severity, however, decreases with gestational age with first-trimester infection resulting in major sequelae or pregnancy loss and mild or no involvement apparent at birth.[16] Secondary prevention is by serological screening to identify those that acquire an infection during pregnancy, and if the fetal infection is detected, therapeutic options including termination of pregnancy and antibiotic treatment to the fetus in utero should be discussed.[17] Despite the relatively high seroprevalence of HIV infection and increased risk of toxoplasmsosis in women, there is a paucity of toxoplasmosis studies in HIV infected pregnant women in Northern Nigeria.

Aim

Hence, this study was designed to determine the seroprevalence of Toxoplasmosis and associated risk factors in HIV-positive pregnant women attending the University of Abuja Teaching Hospital, Abuja, Northcentral Nigeria.

Material and methods

Study Design

This was a hospital-based cross-sectional study conducted from July 2013 to August 2014.

Study Area

The study was conducted at the Departments of Obstetrics and Gynaecology and Immunology, University of Abuja Teaching Hospital, Abuja. Women were enrolled at ante-natal clinics of the University of Abuja Teaching Hospital (UATH), Gwagwalada, Abuja, Nigeria. The hospital provides health care services to the inhabitants of Abuja and neighboring states including Niger, Kaduna, Kogi, and Nassarawa states. The Hospital has an average of 3,000 deliveries annually.

Study Population

This included consecutively enrolled 160 HIV-positive pregnant women who provided signed informed consent prior to enrolment. After signing informed consent, each participant completed a structured questionnaire on sociodemographic characteristics.

Inclusion Criteria

HIV-infected pregnant women between the ages 15year to 45 years attending the UATH.

Exclusion Criteria

1. Persons who did not consent to be part of the study.
2. Pregnant women less than 15 years.
3. Non-pregnant women
4. Those not on antiretroviral therapy

Study Sample Size

Earlier studies in the geo-political zone of the study location found that the seroprevalence of toxoplasma IgG antibodies in pregnant women was 2.4%. [18] Therefore, the minimum sample size at 95% level of confidence interval was calculated using Fischer's formula for cross-sectional studies. The calculated minimum sample size was 40. However, this was increased by 4 folds to 160 to enhance the statistical credence of the study.

Ethical Approval

The ethical clearance for this study was obtained from the Research Ethics Committee of the University of Abuja Teaching Hospital (Approval Number: FCT/UATH/HREC/PR/416). Written informed consent and

accent (as the case may be) were sought from all participants before enrollment into the study. All data were treated with utmost confidentiality and anonymized throughout the study.

Sampling Method and Data Collection

Subjects were enrolled randomly. Interviewer-administered, structured questionnaires were used to collate sociodemographic data of subjects. The questions outlined in the data forms were explained to the subjects and then completed with the required information which included biodemographic data.

Each client that consented was requested to sit on a chair comfortably and was informed that she might experience a little discomfort during the venepuncture. The site intended for the venepuncture at the forearm was cleansed with an alcohol swab, and a selected vein from the forearm was pricked with a sterile needle attached to a Vacutainer bottle and 5 ml of blood was drawn. The needle was gently withdrawn and dry cotton was applied on to the site with a gentle pressure applied to achieve hemostasis. The entire procedure was aimed to be of minimal risk to the clients. Each needle was used only once and properly discarded after use into a sharp container. This procedure was done by the researcher and two research assistants and dispensed into a labeled 10ml plain bottle. These were put in racks and transported to the laboratory. The serum was separated by centrifugation at 10000xg for 10 minutes at 18^0C. After centrifugation, the separated sera were refrigerated (2-8˚C) until analysis was done within 24 hours of sample collection. The serum was carefully removed using a fine bore pipette to avoid extracting red cells. The samples were analyzed for the presence of immunoglobulin G or M (IgG/IgM) class antibodies to T. gondii Enzyme-Linked Immunosorbent Assay (ELISA) using Toxo IgG and IgM ELISA kit from Fortress Diagnostics Limited, (North Ireland, UK)

The fortress diagnostics ® (TOXO IgG/IgM) ELISA kits are qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *T. gondii*. The sensitivity and specificity of the Toxoplasma IgG and IgM ELISA kits were both 99.9% on plasma and sera. The test was done and the results interpreted following kits manufacturer's instructions. Multiskan ™ FC Microplate Photometer (Thermofischer Scientifc Inc., Massachusetts, United States) was used to measure the absorbance of the final reaction products of the enzyme immunoassay.

Statistical Analysis

All generated data were analyzed using Statistical Package for Social Science (SPSS) (California Inc, USA) version 24. Association between the seroprevalence of *T. gondii* antibodies and sociodemographic variables of pregnant women was determined by two-tailed Chi-square test. *P* values <0.05 at 95% confidence interval were reported as statistically significant.

Results

This study was carried out among 160 HIV seropositive pregnant women between the ages of fifteen years and forty-five years and none withdrew after consenting to the study. The mean age of HIV seropositive pregnant women was 30.4±2.2 with the highest proportion within the age range of 20-39 years accounting for 55.7% of the pregnant women enrolled and the lowest proportion being 40-45 years group accounting for 20.0%. However, this distribution was not statistically significant (p>0.05, Table 1). The mean gestational age and mean parity of the total study population were 28.7±3.1 and 3.4±1.3 years, respectively.

Out of the 160 HIV seropositive pregnant women whose blood was examined for the presence of *T. gondii* antibodies, 18 of these subjects were positive for anti-Toxoplasma antibodies with the overall seroprevalence of T. gondii antibodies was 33.8%. The seroprevalence of anti- *T. gondii* IgG and igM were 29.4% and 4.4%, respectively.

Anti-*T. gondii* IgG was predominantly obtained among 20-39 years age group, representing 95.7% of the total IgG anti-Toxoplasma antibodies. None was obtained from the age group <19 years. From the 20-39 years age group, 7 blood samples analyzed were positive for IgM anti-Toxoplasma antibodies, representing 100% of the total IgM anti-Toxoplasma seropositive in the study. The distribution of IgG and IgM anti-*T. gondii* antibodies among HIV-positive pregnant women was not statistically significant (p=0.778 and 0.804 for IgG and IgM, respectively) (Table 1).

From the 160 HIV seropositive pregnant women, 56 women were nulliparous, 54 with parity between 1-4, and 50 women with parity of five and above. 22 (46.8%) anti-*T. gondii* IgG was obtained among women with 1-4 parity and 19 women representing 40.4% with anti-*T. gondii* IgG were obtained from women with >5 parity. However, anti-*T. gondii* IgM was predominantly obtained among pregnant women with parity of 1-4, representing 57.1% of the total anti-*T. gondii* IgM. The distribution of IgG and IgM *anti-T. gondii* antibodies regarding parity of the pregnant women was not statistically significant (p=0.642 and 0.909 for IgG and IgM respectively, Table 1).

Out of the 160 of HIV seropositive pregnant women, anti-*T. gondii* IgG were predominantly obtained among pregnant women in the third trimester with 48.9% of the total anti-*T. gondii* IgG positive and 44.3% of those with anti-*T. gondii* IgG negative results (Table 1). Anti-*T. gondii* IgM was predominantly obtained among pregnant women in the third trimester with

Table 1. Sociodemographic characteristics and *Toxoplasma gondii* antibodies among HIV seropositive pregnant women*

Variable	IgG		*P* value	IgM		*P* value
	Positive (%)	Negative (%)		Positive (%)	Negative (%)	
Age (years)						
≤ 19	0(0.0)	5(4.4)		0(0.0)	5(3.3)	
20–39	45(95.7)	98(86.7)	0.778	7(100.0)	136(88.9)	0.804
≥ 40	2(4.3)	10(8.9)		0(0.0)	12(7.8)	
Total	47(29.4)	113(70.6)		7(4.4)	153(95.6)	
Place of residence						
Urban	43(91.5)	84(74.3)	0.360	7(100.0)	120(78.4)	0.790
Rural	4(8.5)	29(25.7)		0(0.0)	33(21.6)	
Total	47(29.4)	113(70.6)		7(4.4)	153(95.6)	
Educational status						
No formal education	3(6.4)	25(70.6)		0(0.0)	28(18.3)	
Primary	14(29.8)	9(8.0)	0.061	2(28.6)	21(13.7)	0.248
Secondary	10(21.3)	38(33.6)		0(0.0)	48(31.4)	
Tertiary	20(42.6)	41(36.3)		5(71.4)	56(36.6)	
Total	47(29.4)	113(70.6)		7(4.4)	153(95.6)	
Parity						
Nulliparous	6(12.8)	50(44.3)		1(14.3)	55(35.9)	
Para 1-4	22(46.8)	32(28.3)	0.642	4(57.1)	50(32.7)	0.919
≥ Para 5	19(40.4)	31(27.4)		2(28.6)	48(31.4)	
Total	47(29.4)	113(70.6)		7(4.4)	153(95.6)	
Gestational age						
1st Trimester	9(19.2)	25(22.1)		1(14.2)	33(21.6)	
2nd Trimester	15(31.9)	38(33.6)	0.606	3(42.9)	50(32.7)	0.119
3rd Trimester	23(48.9)	50(44.3)		3(42.9)	70(45.7)	
Total	47(29.4)	113(70.6)		7(4.4)	153(95.6)	

**Significant association determined by two-tailed Chi-square test*

48.9% of the total anti-*T. gondii* IgG positive and 44.3% of those with anti-*T. gondii* IgG negative results from 20-39 years age group, 7 blood samples analyzed were positive for anti-*T. gondii* IgM. Subjects between 20-39 year age group represented 95.7% of the total anti-*T. gondii* IgG seropositives. None was obtained from the age group <19 years. For subjects within the 20-39 years age group, 7 of the blood samples analyzed were anti-*T. gondii* IgG seropositive.

Discussion

In this study, the seroprevalence of anti- *T. gondii* IgG and IgM were 29.4% and 4.4%, respectively, with an overall seroprevalence of 33.8%. This is closely comparable with 27.4% and 34% recorded from similar studies reported at Ibadan and Kano cities of Nigeria, respectively.[18,19] The relatively high prevalence recorded in this study indicates that pregnant women living with HIV/AIDS may be susceptible to repeated exposure or reactivation of chronic *T. gondii* infection in our setting. The overall prevalence of *T. gondii* antibodies in our study was higher than 29.9% recorded in Zaria but lower than others carried out in Lagos and Maiduguri where 40.2% and 48.9% were recorded respectively.[1,20,21] Lagos is a bustling riverine area where outdoor activities thrive while Maiduguri dwellers have been ravaged by insecurity that has grossly affected their standard of living including access to potable water, hygienic meats, and vegetables.

Studies reported within and outside Africa have recorded very high seroprevalence of toxoplasmosis of 83.6%, 92.5%, 48.0%, and 63.0% among pregnant women in Ethiopia, Ghana, India, and Brazil, respectively.[3,5,6,22] Perhaps, geographic and hot climatic conditions in these countries that favor sporulation would have accounted for these wide margins in prevalence.[10,14,23-25] The climatic condition of our study area may not be as favorable as those listed above for oocysts' survival. Conversely, much lower rates (less than 10%) have been reported in the USA and UK.[26,27] It is expected that these high-income nations had good waste disposal systems, potable water, and high standards of living, in addition to a temperate climate that will not favor the thriving of *T. gondii* oocytes.

In this study, there were no significant associations among the socio-demographic characteristics. Hence, this is a negative result. However increasing age, tertiary education, and urban settlement appear to facilitate infection.[28] Age as a factor may be an indicator of high susceptibility of exposure to many risk factors for primary *T. gondii* infection during their lives than younger individuals.[29] Such findings have also been observed by Ogoina *et al* and Al-Harthi *et al* in Zaria and Saudi Arabia respectively.[30,31] Gwagwalada, a suburb in the federal capital of Nigeria, has also accommodated an increasing number of urban dwellers from various educational and social backgrounds which may have contributed to these socio-demographics. These findings are also in agreement with reports from most studies around the world.[1,5,21,31]

Conclusion

The overall result of this study revealed that the majority of pregnant women were exposed to toxoplasmosis much earlier in life. Hence, these findings will assist obstetricians and gynecologists in the early diagnosis and management of *Toxoplasma gondii* infection in pregnant women, especially HIV coinfected ones with IgM seropositivity.

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ORIGINAL PAPER

Oyediran Emmanuel Oyewole (ABCDEFG), Christiana Mautin Todowede (ABCDEG), Isaac Oluwafemi Dipeolu (DEFG)

Knowledge, perception and child care practices among adolescent mothers in Ibadan Metropolis, Nigeria

Department of Health Promotion and Education, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Nigeria

ABSTRACT

Introduction. There is little information regarding childcare practices among adolescent mothers in the study areas.

Aim. This study was aimed at investigating knowledge, perception and childcare practices among adolescent mothers.

Material and methods. A descriptive cross-sectional survey was conducted on randomly select 382 adolescent mothers. A validated semi-structured questionnaire was used to collect data, which were analysed using, descriptive and multivariate analyses with p-value set at 0.05. Age of respondents was 18.5±0.7 years.

Results. Majority (80.6%) had poor knowledge of when to start ante-natal care. Also, 70.0% of the respondents could not perceive growth monitoring as a necessary strategy for child survival and 86.4% perceived diarrhoea as normal for children during the teething period. Many (58.4%) did not practise exclusive breastfeeding. Respondents with secondary education were less likely to have poor knowledge than those with primary education (OR: 0.2, CI: 0.6-0.9, 95%). Respondents, who received supervision from older women during childcare, were less likely to have poor childcare practice than those who did not (OR: 0.2, CI: 0.4-0.7, 95%).

Conclusion. Respondents had poor knowledge of childcare practices when childcare survival strategies were used as the yardstick for evaluation. Involvement of older women is suggested to assist adolescent mothers improve their knowledge and practices of childcare.

Keywords. adolescent mothers, child survival strategies, childcare practices

Introduction

Mothers play essential roles in the life of children; an experienced mother with good observation skills can quickly identify many problems in the early stage of life of the child especially where childcare is in the right perspective. Starting from birth, early bonding between mothers and their babies has been observed to contribute to mental health development of children.[1] Childcare has also been considered from the perspectives of one-on-one interactions with infants and having good knowledge of child feeding practices as well as playing activities; done more often between children or with

Corresponding author: Oyediran Emmanuel Oyewole, e-mail: diranoyewole@gmail.com, oyewole2002@yahoo.com

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other caregivers such as siblings or grandparents. The study posited that community members considered that caring for children from 0–2 years is a woman's domain as this was acknowledged by men and women.[2] Ang and Tabu described care as "the provision (in the household and the community) of time, attention, and support to meet the physical, mental and social needs of the growing child in an educational environment with parental support".[3]Some studies revealed that poor childcare practices from caregivers are factors contributing to child mortality.[4,5] Things are changing today as the number of adolescent mothers in Nigeria is increasing steadily and this has significant health and social implications for both adolescent mothers and child.[6]

Teenagers who become parents are likely to experience more educational, health, social and economic difficulties than their counterpart who are not yet parents.[7] Consequently, their children may be exposed to more significant social deprivation and disadvantage. These outcomes have been demonstrated to be more adverse still in the case of looked-after children who become parents. This is because this group is more likely than others to be unemployed, have more emotional health problems, be expected to be independent and have little support.[8] The majority of adolescent mothers have little knowledge and competence for childcare and many are not capable of providing their infants with basic needs due to their low socio-economic status.[8] Mangeli et al., also noted that adolescent mothers require support on several issues such as childcare, education, financial problems, and varying needs of their own and that of their children.[8] Infants of teenage mothers are prone to low birth weight, prematurity, developmental disabilities, and poorer developmental outcomes than the infants of older mothers. Deficits in cognitive and social development in the children of adolescent mothers may persist into adolescence.[9] The adolescents who become parents are known to experience more educational, health, social and economic difficulties than young people who are not parents. Consequently, their children may be exposed to more enormous social deprivations and disadvantages.[6]

Mothers are the primary caregivers, and they must have the required maturity and skills necessary for giving infant care. It has been shown that teenage pregnancy is of significant health concern because of its association with higher morbidity and mortality for both the mother and child.[6] Howbeit, few studies have documented the knowledge, perception and practices related to childcare among adolescent mothers.

According to Qayyum et al., childcare practices should focus on feeding, sleeping, toileting, among other things. Childcare practices require enough resources for the caregiver to be able to put knowledge into practice.[10] It is essential to document the constraints to good childcare practices among adolescent mothers to design appropriate intervention strategies to reduce likely adverse health and social outcomes. This will go a long way to achieve Goal 3 of the Sustainable Development Goals.

Aim

This study was, therefore, designed to investigate the knowledge, perception and practices related to childcare among adolescent mothers in Ibadan metropolis.

Material and methods

The study was a descriptive cross-sectional survey conducted in Ibadan metropolis. Ibadan is the capital of Oyo State and located in South West of Nigeria. The metropolis is divided into five Local Government Areas (LGAs) namely Ibadan North West, Ibadan North East, Ibadan North, Ibadan South West and Ibadan South East. Residents of the city are mostly of Yoruba ethnic group, which is the dominant ethnic group in the city. Most residents are in the low and middle socioeconomic status.

Sampling, Instrument and Procedure for Data Collection

The study population were all consenting adolescent mothers aged 15-19 years (any female within the age range who gave birth or had her first pregnancy) in the selected communities in Ibadan metropolis. A four-stage sampling technique adopted to select 382 adolescent mothers through the assistance of community health care workers and community women leaders during the period of the data collection. Assenting and consenting respondents were provided with detailed information about the objectives of the study, and after adequate understanding, they gave their assent/consent and indicated willingness to participate in the study by signing the informed consent form.

Interviewers, comprising community women and health workers were trained on interpersonal communication skills, interviewing techniques, and ethical considerations. After the training, there were practical sessions through demonstration and return-demonstration of the new skills acquired. They also completed and signed confidentiality forms before the commencement of the study. A validated interviewer-administered semi-structured questionnaire (both English and Yoruba versions) was used for data collection. The questionnaire consisted of five sections viz respondents' demographic characteristics, assessment on the level of knowledge of adolescent mothers on childcare, perceptions of teenage mothers on childcare, childcare practices among adolescent mothers and the constraints to childcare practices among adolescent mothers. Respondents' knowledge of childcare was assessed on a 24-point knowledge scale; perception of childcare was assessed on a 16-point perception scale while practice was measured using a 36-point practice scale.

Table 1. Respondents socio-demographic characteristics (N=382)

Demographic characteristics	№	%
Age (in years)		
15	3	0.8
16	5	1.3
17	11	2.8
18	142	37.2
19	221	57.9
Marital status		
Married	349	91.4
Single	33	8.6
Working status		
Working	317	83.0
Not working	65	17.0
Religion		
Christianity	145	37.9
Islam	236	61.8
Traditional	1	0.3
Parity		
More than one child	183	47.9
One child	199	52.1
Pregnancy intentions		
Intentional pregnancy	281	73.6
Unintentional Pregnancy	101	26.4

With the assistance of Primary Health Care workers in the selected communities (based on their level of rapport with community members), respondents in the selected political wards and communities were visited in their homes and interviewed. The selection of the respondents was purposive due to the nature of the inclusion criteria (adolescent mothers aged 15-19 years). Data collection process lasted for about four months.

Measures and Data Management

Each questionnaire was checked in the field for completeness and later sorted, cleaned, coded and entered into a computer; analysis was performed using the IBM/ Statistical Package for Social Sciences (IBM/SPSS) version 22 software. The analysis consisted of descriptive and inferential statistics (Chi-square test and logistic regression) with the level of the significance set at $p \leq 0.05$.

Scores ≤12 points and >12 were categorised as poor and good knowledge of childcare, respectively. Similarly, perception of respondents towards childcare was rated as scores ≤8 and >8 categorised as wrong and right perception of childcare, respectively. Respondents' practice of childcare was assessed with scores ≤18 and >18 categorised as poor and good childcare practice, respectively.

Ethical Considerations

Ethics approval was obtained from the Oyo State Ministry of Health Research Ethical Review Committee, Ibadan, Nigeria with Ref. No. AD 13/479/309. Written informed consent was obtained from each respondent after explaining the objectives of the study, the procedures involved, assurance of confidentiality and that participation is voluntary.

Results

Socio-demographic Characteristics of Respondents

Respondents' age ranged between 15 to 19 years, with a mean age of 18.5 ± 0.7 years, the highest level of education being secondary school (65.7%). Islam (61.8%) topped the list of the religions practised by the respondents, while trading (40.8%) and crafts/artisans (30.6%) were the common occupations of the respondents. The majority of the respondents (91.1%) were not living with parents (Table 1).

Knowledge of childcare practices among adolescent mothers

Finding from the study showed that most respondents (80.6%) did not know the time when a pregnant woman should begin antenatal class. Almost all of the respondents (94.5%) said breast milk should be introduced to a baby immediately after delivery, while (5.5%) said it should be introduced some days after delivery and (0.3%) did not know. However, 43.7% of the respondents said that a mother could adopt a suitable family planning method after six weeks of delivery; while 30.4% did not know, 12.0% said some months after delivery; 11.3% said immediately after child delivery, 2.4% said when a woman no longer wants to give birth again and 0.3% said when menstruation starts. Moreover, 25.9% of the respondents did not know when an infant should be fully immunised, 48.4% reported at nine months, while 18.3% said at one year, 5.0% said after one year and 2.4% said before nine months. Also, 48.4% of the respondents said that oral rehydration therapy is used for diarrhoea, while 38.4% did not know, 12.6% said it is used for sick children, and 0.5% said it is for teething. The majority, (80.6%) of the respondents did not know the average weight of a baby at birth, 13.1% said above 2.5kg, 4.2% said 2.5kg and 2.1% said below 2.5kg. The majority of respondents (81.2%) had poor knowledge of childcare practices (See Table 2).

Perception of childcare practices among adolescent mothers

Ninety-four per cent did not perceive attending antenatal care as a waste of time, 3.7% agreed that it is a waste of time, while 2.4% were not sure. Fifty-five per cent of the respondents disagreed that water should be given to a baby from birth because water quenches thirst, 41.1% agreed to the statement, while 3.9% were

Table 2. Knowledge of childcare among adolescent mothers (N=382)

Knowledge Variables	№	%
The time when a pregnant woman should to attend antenatal care clinic		
I don't know	308	80.6
When she is aware of her pregnancy	74	19.4
The time when water should be introduced to a baby		
At birth	81	21.2
Before six months post natal	97	25.4
At six months post natal	196	51.3
I don't know	8	2.1
A nursing mother cannot get pregnant if she practices exclusive breastfeeding		
No	268	70.2
I don't know	65	17.0
Yes	49	12.8
The time when a baby should have first immunisation		
At birth	99	25.9
Before the 8 days of naming ceremony	129	33.8
After the 8 days of naming ceremony	126	33
I don't know	28	7.3
Playing with a toy can be a source of infection to babies		
No	232	60.7
Yes	116	30.4
I don't know	34	8.9
Rating	**№**	**%**
Poor knowledge	310	81.2
Good knowledge	72	18.8
Total	382	100.0

Mean knowledge score = 11.642 SD = 2. 432

Table 3. Perception of childcare among adolescent mothers (N=382)

Perception Variables	№	%
I believe the first breast milk discharged by a mother should not be given to a baby		
Not sure	14	3.7
Agree	33	8.6
Disagree	335	87.7
I feel vaccines injected in well-nourished children can cause illness in them		
Not sure	14	3.7
Agree	15	3.9
Disagree	353	92.4
I believe adopting a suitable family planning method does not have a positive effect on a child's health		
Not sure	63	16.5
Agree	69	18.1
Disagree	250	65.4
I suppose playing toys are provided for children only to stop them from disturbing the adults and not for any health benefit		
Not sure	118	30.9
Agree	225	58.9
Disagree	39	10.2
Rating	**№**	**%**
Poor perception	204	53.4
Good perception	178	46.6
Total	382	100.0

Mean perception score = 7.389 SD = 0.924

not sure. A majority (80.9%) agreed that diarrhoea is normal for children during teething period, 13.6% disagreed with the statement, and 5.5% were not sure. Also, 52.9% were not sure if growth monitoring was a necessary strategy to monitor child's growth, 30.1% agreed to the statement, while 17.0% disagreed. The summary of respondents' perception of childcare practices showed that many (53.4%) had it wrong (Table 3).

Childcare practices among adolescent mothers

A majority (84.6%) of the respondents had never used a family planning method before while (15.4%) had used. The sources of the respondents' children drinking water were bottled water (51.3%), tap water (29.3%), not taken water yet because the baby was less than 6 months old (13.4%), sachet water (3.7%), well (1.6%) and rainwater (0.8%). The majority (63.1%) of the respondents did not treat child's drinking water, 23.6% treated child's drinking water and 13.4% were not applicable. Few (23.6%) of the respondents boiled children's drinking water, and 76.4% did not respond. Some, (42.7%) of the respondents' children were first immunised after the naming ceremony, 40.8% were immunised before the naming ceremony, 9.9% were immunised at birth, while 5.0% were immunised months after delivery and 1.6% did not know. The majority, (75.7%) of the respondents did not have a first aid box at home. Most, (94.2%) of the respondents' children were weighed last at birth, 2.4% were weighed some months before the survey; 1.6% were weighed few days before the survey, and 1.6% did not know. The majority, (67.3%) disposed their children's excreta in a waste bin, 20.9% used pit latrine, 6.3% flushed in the toilet, 3.9 dropped it in the drainage, 1.0 threw into the bush and 0.5% burned it. Also, 65.7% of the respondents cleaned up after disposing children's excreta using soap and water, 27.0% used water only while 7.3% used disinfectant, soap and water. Few, (29.1%) of the respondents had older women that supervised them during childcare, and 70.9% did not have such assistance. Moreover, 62.3% of the respondents' children played with toys and 51.8% of

the respondents did not sanitise children's toys before allowing them to play with the toys. Assessment of childcare practices among the respondents showed that most (91.6%) of the teenage mothers had poor childcare practice (Table 4).

Table 4. Childcare practices among adolescent mothers (N=382)

Practice item	№	%
Received vaccination during pregnancy		
Yes	332	86.9
No	50	13.1
When breastfeeding was initiated after birth		
At birth	355	92.9
Some days after birth	27	7.1
When water was first given to the baby after birth		
Before six months	131	34.3
Six months	108	28.3
At birth	92	24.0
Not yet	51	13.4
Child's vaccination status		
Not up to date	344	90.0
Up to date	30	7.9
Don't know	8	2.1
Preparation of oral rehydration therapy		
Don't know	254	66.5
Dissolve ORS in a bottle of water	91	23.8
Put salt and water into warm water and allow to cool	34	8.9
Dissolve ten cubes of sugar and one teaspoon of salt into one bottle of water	3	0.8
Rating	**№**	**%**
Poor practice	350	91.6
Good practice	32	8.4
Total	382	100.0

Mean practice score = 17.752 SD = 3.562

Constraints to childcare practices among adolescent mothers

Almost all the respondents (98.7%) did not have any health condition that affects their childcare practices. Few (26.2%) of the respondents thought they should not have had a child when they did Table 5).

There was a significant relationship between the level of education of adolescent mothers and knowledge of childcare practices (Table 6). Knowledge of childcare practices was higher among respondents with secondary education. Furthermore, there was a significant relationship between adolescent mothers' knowledge and their perception of childcare (Table 8). A significant relationship was also found between the knowledge of adolescent mothers and opinion on childcare practices (Table 9). There was a significant relationship between the knowledge of childcare and teenage mothers' practices (Table 10).

Table 5. Constraints to childcare practices among adolescent mothers (N=382)

Variables	№	%
Receive any health education lesson on childcare practices	**No**	**%**
No	41	10.7
Yes	341	89.3
Receive any health education lesson on childcare practices after delivery		
No	34	8.9
Yes	348	91.1
Work/job hinders from caring for one's child properly		
Yes	17	4.5
No	365	95.5
Dependence on spouse/parents affect one's childcare practices		
Yes	11	2.9
No	371	97.1
Inadequate finances affect one's child-care practice		
Yes	101	26.4
No	281	73.6
Location of health facility affect child-care practices		
Yes	142	37.2
No	240	62.8

Table 6. Comparing level of education and knowledge of adolescent mothers

	Knowledge of adolescent mothers		
Level of education	Poor	Good	Total
	№ (%)	№ (%)	№ (%)
Primary	127 (45.2)	154 (54.8)	281 (100)
Secondary	76 (75.2)	25 (24.8)	101 (100)

X^2= 26.945 df =1 P = 0.003

Table 7. Comparing perception and knowledge of adolescent mothers

	Knowledge of adolescent mothers		
Perception	Poor	Good	Total
	№ (%)	№ (%)	№ (%)
Poor	188 (94.5%)	11 (5.5%)	199 (100%)
Good	144 (78.7%)	39 (21.3%)	183 (100%)

X^2= 20.878 df =1 P = 0.000

Table 8. Comparing childcare practices and knowledge of adolescent mothers

	Knowledge of adolescent mothers		
Childcare practices	Poor	Good	Total
	№ (%)	№ (%)	№ (%)
Poor	76 (75.2)	25 (24.8)	101 (100)
Good	127 (45.2)	154 (54.8)	281 (100)
X^2= 26.945	df =1		P = 0.001

Multivariate Analysis

Findings from further analysis on respondents' socio-demographic and knowledge show that only respondents with secondary education were less likely to have poor knowledge than those with primary education (OR: 0.231, 95% CI: 0.624 – 0.943, p-value <0.05) (Table 9).

Table 9. Predictors of knowledge on respondents' child care practice

Variable	Odds ratio	95% CI	p-value
Marital status			
Single	1.000		
Married	0.436	0.120–1.591	0.209
Educational Status			
No formal/Primary	1.000		
Secondary	0.231	0.624–0.943	0.003
Religion			
Islam	1.000		
Christian	1.017	0.213–4.857	0.984
Traditional	0.980	0.202–4.755	0.980
Pregnancy intention			
Intentional	1.000		
Accidental	2.675	0.329–1.741	0.143
Parity			
More than one child	1.000		
Only one child	0.234	0.862–1.331	0.432
Supervision from older women			
Supervised	1.000		
Non supervised	1.159	0.650–2.067	0.618

Also, findings from further analysis on respondents' socio-demographic and practice show that respondents who received supervision from older women during childcare were less likely to have poor childcare practice than those who received no supervision (OR:0.257, 95%CI: 0.424–0.734, p-value<0.05) (Table 10).

Discussion

In comparison with the NIGERIA Demographic Health Survey of 2018; teenage mothers are more likely to experience adverse pregnancy outcomes and put to the lowest socioeconomic status.[6]Today, it is difficult for the teenage mother who was forced out of school by pregnancy to return to school after delivery because they must care for the child. Both the school and community will not openly welcome their return to school for the fear that the adolescent mother will become a bad influence in school. If she manages to get back to school, she may have to put up with a lot of ridicule from her colleagues. Barmao-Kiptanui and colleagues found that teenage mothers dropped out of school were generally worse off with a *per capita* income half of that of older mothers.[11] Bihoun and colleagues also pointed out that repeat pregnancy and births in teenage mothers have been linked to decreased educational achievement, increased dependence on governmental support by the adolescent mother, increased infant mortality, and low birth weight.[9,12] According to Bihoun et al., these adverse outcomes result in increased societal expense and contribute to the continuation of the adolescent pregnancy cycle.[9]

Table 10. Predictors of childcare practice

Variables	Odds ratio	95% CI	p-value
Marital status			
Single	1.000		
Married	3.431	0.220–1.693	0.509
Educational Status			
No formal/Primary	1.000		
Secondary	1.348	0.176–1.816	0.421
Religion			
Islam	1.000		
Christian	2.517	0.363–3.658	0.487
Traditional	1.654	0.557–1.047	0.3182
Pregnancy intention			
Intentional	1.000		
Accidental	2.675	0.329–1.741	0.143
Parity			
More than one child	1.000		
Only one child	0.331	0.563–2.431	0.722
Supervision from older women			
Non-supervised	1.000		
Supervised	0.257	0.424–0.734	0.001

Findings also showed that about a quarter of the respondents had unintended pregnancies. This finding was consistent with that of Yarber and colleagues, where they observed that most teen pregnancies are unwanted while about 22% are planned.[13] Yarber et al. noted that one-third of pregnant teens received inadequate parental care.[13] Thus, babies born to young mothers are more likely to have childhood health problems and hence may have more frequent hospital visits compared to those born to older mothers.

Overall, childcare-related knowledge among teenage mothers was poor among the respondents, and this

reflected in their knowledge of oral rehydration therapy (ORT), exclusive breastfeeding and immunisation. Less than half of the respondents were able to link ORT with diarrhoea. This finding is similar to that of Sanusi and Gbadamosi where they found that adequate knowledge of child survival was low among mothers less than 20 years and they had the least knowledge score about ORT.[5]

A majority of the respondents perceived diarrhoea as normal for children during the teething period, which is similar to other studies in Nigeria and Ethiopia, where it was reported that mother perceived that teething period must come with diarrhoea.[14,15] This perception is a common misconception in other parts of the world, which has led to poor management with serious health outcomes.

A majority of the respondents in the present study had never used any form of family planning methods before, which means that there is a possibility of them getting pregnant within short interval. Templeman and colleagues investigated postpartum contraceptive use among adolescent mothers in the United States, where 70.0% reported sexual activity by age 19 and each year, 8-10% becomes pregnant. Of those adolescents who gave birth, 17-35% will become pregnant again within a year of delivery.[16] The finding is, however, contrary to that of Agbor, and Adonis et al., where they found that less than half of teenage mothers in their research in Cameroon had been to a family planning centre.[17,18] A majority of their respondents initiated breastfeeding after birth which is inconsistent with the findings of a study among adolescent mothers in Bangladesh where only 44.6% of new-borns were breastfed within 1 hour of birth.[4] Also, a few respondents had the first immunisation at birth for their children which accounts for the respondents' children incomplete vaccination status. This finding corroborates the result of a study among adolescent mothers in Bangladesh where the proportion of the new-borns that received postnatal care within 24 hours of birth was 9%.[4]

Growth Monitoring and Promotion (GMP) is vital for the early detection of malnutrition and illnesses in children. However, a few respondents in this present study practised growth monitoring. This finding is in line with the result of Sanusi and Gbadamosi, where growth monitoring was practised by only 7.5% of the mothers studied.[5] The low practice of GMP may be due to inadequate knowledge in reading the growth chart teenage mothers and its relevance to child nutrition and survival.[5,19]

Although, more than a quarter of the respondents had older women who assisted them with childcare; there was a significant association between adolescent mothers who had older women who helped with childcare and their childcare practices. The older women compensated for the inexperience of the adolescents and served as caregivers, which improved childcare practice among adolescent mothers who had such assistance. The finding is similar with the result of a study which reported that "women acquire their knowledge about natural medicine through information transmitted from older women to younger ones, and such knowledge is exclusively composed by effective practices".[20]

The constraints to childcare practices mentioned by the respondents include inadequate finance to pay bills and daily upkeep, location of health facility, not ready for childbearing, among many others. These constraints are some of the consequences of teenage pregnancies, which were identified by other studies. For example, Kulwa and colleagues found that income and unavailability of household resources were the major constraints to good childcare practice among teenage mothers.[21] Atimati and Adams submitted that educational status, standard of health facility where ante-natal care was received and the age of the mother have great influence on exclusive breastfeeding, which is one the important components of childcare practices.[22] Tomereli and Marcon also found that adolescent mothers are inexperienced and not capable of taking care of children effectively.[19]

Conclusion

The implication of being forced out of school as a result teenage pregnancy portends great danger for the future development of such teenager. Her ability to compete favourably with her peers in the future economic space is fully mortgaged. She may never come of out the poverty cycle of life and the future of the child she has given birth to may also be negatively affected; creating a nugget of generational disadvantaged population. Practically, this calls for stronger parental/care-giver guidance and also for schools to provide more information on prevention of teenage pregnancy among young girls.

Childcare-related knowledge among adolescent mothers was poor. Besides, there were some wrong perceptions and poor child care practices, which have potentials for compromising the health of their babies. The implication of poor knowledge of ort is that there may be the likelihood of increased child morbidity and mortality among teenage mothers. In practical terms, there is need for special education on ort during post-natal care among teenage mothers.

Many constraints identified in the present study may not be peculiar to teenage mothers alone. However, if they had delayed pregnancy a little for them to be mature, get some measures of education and a stable job to enhance their socioeconomic status, the constraint to childcare practices among adolescent mothers could have been prevented. Teenage

motherhood should not be encouraged or celebrated in any society, as it contributes to some of the indices of under-development, high morbidity and mortality rates, especially in many developing countries. There are many possible negative implications of teenage motherhood, especially in the developing world, where opportunities to regain life's dreams are limited after delivery. A teenage mother will need all the available social supports to survive. If these are not available, survival instincts will show up. These may lead to infanticide, child abuse by neglecting to care for the baby, outright selling of the baby to the willing buyers or the ritualists, abandoning the child on the roadside/dunghill, among many other anti-social vices. Many of these adolescent mothers are young individuals with great potentials that can be harnessed for their personal development and the nation, if adequate interventions to prevent early sexual exposure have been instituted and promoted at the family, community and governmental levels. The need for schools and community-based sex and sexuality education is of essence. Faith-based approach can also compliment what the schools and communities should do. The parent/givers should ensure proper care of their teenagers to prevent early pregnancy by monitoring and cordially relate with them with good inter-personal communication. In case the adolescent is already pregnant, older women close to the adolescent in the community should be encouraged to provide all the necessary support in childcare. It is important to state that adolescent mothers are usually confused and sometimes depressed because of guilt feelings and possible social discrimination. However, this should be the time the older adults, especially their mothers or close members of the family should be of good support by assisting and teaching them basic child survival strategies and coping methods to avoid further mistakes in child care, future plans and counseling against another pregnancy, which can jeopardise their future the more. They should be encouraged to know the opportunities that they still have in life, either by returning to school in a new location or enrol them into any vocation of their choice. Registering for vocational study as an entrepreneur can also be initiated three months post-natal. This is necessary for economic empowerment, which has a great potential for shielding them against another pregnancy once they are economically empowered to meet the basic financial needs. Some local non-governmental or governmental organisations including faith-based societies can establish centres, where these adolescent mothers can be assisted to get back on life track to success.

Overall, the implication of the findings from this study established the fact that teenage motherhood should be prevented using all available and appropriate health promotion and education approaches. However, when teenage motherhood has resulted, older mother or experienced women/care-giver should provide support and basic child survival strategies training for such a teenage mother to assist in caring for the baby and possibly provide advice on how to prevent another pregnancy too soon. Information on accessing family planning services can also be provided to the teenage mothers.

Practically, teenage pregnancy can be controlled when the family, the schools and the larger society consider this as a problem, which will affect the development of the entire society. Sex education should be encouraged and promoted to prevent the occurrence of teenage pregnancy. However, if it occurs, the teenage mother must be supported to nurture the child and at the same time, encouraged to prevent a re-occurrence and ensure that the teenager's future is brought back on track either through school re-enrolment or entering for a vocational study.

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ORIGINAL PAPER

Wojciech Domka [1(ABDFG)], Łukasz Ożóg [2 (ABDFG)], Dorota Bartusik-Aebisher [3 (ABDFG)], David Aebisher [2 (ABDFG)]

The larynx cancer in vitro study by MRI relaxtion time of water

[1] Department of Otolaryngology, Medical College of Rzeszów University, Rzeszów, Poland
[2] Department of Photomedicine and Physical Chemistry, Medical College of Rzeszów University, Rzeszów, Poland
[3] Department of Biochemistry and General Chemistry, Medical College of Rzeszów University, Rzeszów, Poland

ABSTRACT

Introduction. Squamous cell carcinoma (SCC) of the larynx accounts for a significant percentage of all head and neck cancers.
Aim. In this paper we determine the differences in magnetic resonance relaxation time (MRI) of water in cancerous and healthy larynx tissues.
Material and methods. This study is aimed on T_2 MRI modalities for monitoring morphology of larynx tissue.
Results. Our results showed that T_2 MRI relaxation time measured in larynx tissue can be used to assess early cancer condition of larynx tissues. The changes of T_2 MRI correspond to tumor growth within normal tissue.
Conclusion. The study showed potential of MRI for the non-invasive monitoring of larynx condition.
Keywords. larynx tissue, magnetic resonance imaging, T_2 mapping, T_2 relaxation time

Introduction

The use of MRI to assess and characterize pathology and normal tissue has been extensively described in the literature. By using the differences in tissue relaxation behavior, we are able to show differences between pathological tissue and normal tissue.[1,2] However, this requires proper preparation of both the equipment (appropriate calibration) and the sequences themselves (optimization of the test protocol) so that the results are reliable.[3,4] An important role in the characterization of tissues is played by tissue heterogeneity, especially those pathological. The use of T_1 and T_2 relaxation times and mapping techniques available in MRI systems gives the opportunity to evaluate tissues on the basis of their relaxation properties.

One of the more interesting MRI imaging techniques that uses differences in tissue relaxation is the T2 mapping technique. T_2 mapping sequence and processing is technique acquires multiple echoes at different echo times (TE) at each slice location that represent different T_2 weighting. Data obtained using this technique can be processed to produce T_2 color maps which demonstrate more subtle changes in tissues structure that are not visible on gray scale MR images. The changes in T_2 values correlate with the variations in water and oxygen content. T_2 is a tissue-specific time parameter

Corresponding author: David Aebisher, e-mail: daebisher@ur.edu.pl

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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that differs between tissues. There is no precise value for the specific tissue but is constant for a given magnetic field strength. Abnormal tissues, on the other hand, tends to have a higher T_2-value than normal tissue. The value of T_2 depends on the tissue type, the structure of the environment, and the mobility of protons.[5,6]

Aim

This study aimed to presents the results of MRI mapping in larynx tissue.

Material and methods

Larynx Tissue

Freshly excised samples (N=11) of normal and cancerous laryngeal tissue and normal and cancerous thyroid tissue were obtained from the Frederic Chopin Clinical Regional Hospital No. 1 in Rzeszów, Poland. The human tissue studies were approved by the Bioethical Commission of the District Medical Chamber in Rzeszów (Resolution number 105/B/2017). Once received, the tissues were stored in 15 mL polypropylene graduated conical test tubes fitted with a screw tight cap (Kartell Labware, Milano, Italy) at 5°C. The average size of the excised tissues was 10 mm×4 mm×5 mm, respectively.

T_2 Mapping

These experiments were performed using Magnetic Resonance Imaging (MRI) 1.5 Tesla field. The laryngeal tissues were taken to the MR imaging plant to determine the T_2 time. A total of 6 larynx cancer tissues and 5 normal larynx tissues were treated and imaged in this study. Immediately after surgery to remove the tumor, high-resolution MR images were acquired from each tissue to determine T_2 relaxation times and T_2 maps. The tissues MR images were acquired using a 1.5 Tesla field MR scanner (Optima MR360 Advance, General Electric Healthcare, USA). A 3 inch surface coil was used for the image acquisitions. Images with varying echo times (TEs) were then obtained using a commercial T_2 MAPS sequence to enable T_2 calculation. MR images were obtained at eight different echo-times (9.2, 18.4, 27.6, 36.9, 46.0, 55.2, 64.4 and 73.6 milliseconds) in one single acquisition (TR=650 milliseconds, field of view 5.00 cm×5.00 cm, matrix size 224×224, slice thickness 2.0 mm, receiver bandwidth 31.25 kHz, NEX = 3). Typically, one coronal slice was acquired to cover all tissue through the middle. The total scan time to simultaneously acquire the eight T_2-weighted images was 7 minutes 20 seconds. These MR parameters were used for all tissues.

Statistical Analysis

The data was analyzed using Statistica 13.1 software (StatSoft Polska Sp.z o.o., Krakow, Poland). The data were analyzed using the dependent samples *t-test* to check the differences in the T_2 time results between the individual steps of the experiment. Values were considered significantly different when the *p*-value was less than 0.05.

Results

We used the software package READY View on work station AV4.6 (General Electric Healthcare) to compute the T_2 maps. Second, we manually chose a layer that cuts the center of the tissue on which the T_2 maps were generated. On the T_2-weighted MR images, the tissues appeared as a bright region. One author manually drew the boundary of the tissue on the image and then saved the object map of the tissue. The T_2 value for each voxel was determined within the tissue region (and the average value for the area was calculated). We compared the mean T_2 values for the cancer tissues and normal tissues of larynx. MR relaxation times measurements *in vitro* is reproducible, completely stable and readily available. T_2 maps obtained during measurements are presented below. T_2 maps were generated by single exponential fitting from multiecho (0–90 ms) pulse sequences with intervals of 8.2 ms, a time repetition of 650 ms and a field of view of 5 cm over a 224×224 matrix (Figure 1).

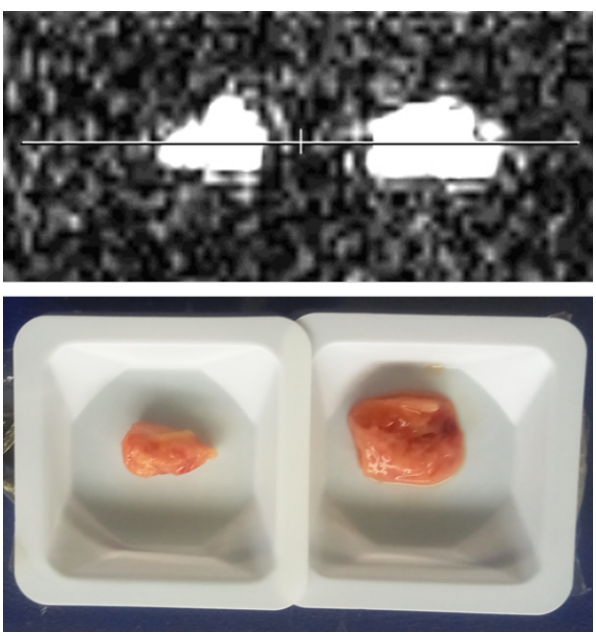

Fig. 1. The MR image of the calibration sequence presenting the method of planning the examination and the selection of the scanning layer (layer thickness 2mm) and the same cancer tissue and health tissue of larynx on real photo

Measured and then determined T_2 values of cancer tissues (mean=102±7 ms; n=6) were significantly higher (p=0.031; p<0.05) than normal tissues (mean=90±9,6 ms; n=5). The central rectangle shows the first quartile to the third quartile (interquartile range - IQR).

Table 1. T2 values for cancerous (C1-C6) and healthy (H1-H5) tissues

	C1	C2	C3	C4	C5	C6
T_2 (ms)	93 ± 4	98 ± 5	100 ± 5	104± 5	102 ± 5	114 ± 6
	H1	**H2**	**H3**	**H4**	**H5**	
	79 ± 4	80 ± 4	92 ± 5	102 ± 5	92 ± 5	

A segment inside the rectangle (horizontal line) shows the median and "whiskers" above and below the box show the locations of the minimum and maximum measured T_2 time. This result confirms that the T_2 maps technique makes it possible to distinguish between normal and cancerous tissue.[7-11]

Discussion

The method to study tissue condition is one of the most important aspects in individual treatment. MRI can offer very sophisticated analysis of diseased and healthy larynx tissues. Squamous cell carcinoma (SCC) of the larynx showed decrease in water content in *in vitro* samples. Thus, MR parameters such as T2 relaxation time measured *in vitro* is useful as a basis for correlation with clinical noninvasive measurement. Additionally, MR relaxation times measured in cancer cell cultures can be a predictor of cellular changes during treatment. In MRI, the signal is strongly depending on the change of TE and TR parameters; choosing these parameters on the basis of the obtained data we are able to plot relaxation curves and determine times T_2 (Table 1).

Conclusion

Quantitative T_2 relaxation times allows to distinguish between healthy and cancerous tissue. T_2 mapping allows to monitor changes in water concentration *in vitro*, and thus allows to characterized tissue condition. The measurements of healthy tissue show lower values of T_2 than cancerous tissue. MRI noninvasive and repetitive measurements is very attractive tool in the pre- and clinical context in otolaryngology.

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ORIGINAL PAPER

Ashiyat Kehinde Akodu [1(ACDFG)], Thompson Adewale Ogunbiyi [1(ABCGH)], Oluwaseun Akinleye Fapojuwo [1(ACDE)]

Cognitive behavioural therapy and core stabilization exercise on pain-related disability and psychological status in patients with non-specific chronic low back pain

[1] Department of Physiotherapy, College of Medicine, University of Lagos, Yaba, Lagos, Nigeria
Clinical Trial Registry number: PACTR201910791448143

ABSTRACT

Introduction. Exercises have been shown to relieve symptoms in non-specific chronic low back pain (NSCLBP) patients.

Aim. This study compared the effects of cognitive behavioural therapy (CBT) and core stabilization exercises (CSE) on pain-related disability, psychological status and sleep disturbance in patients with NSCLBP.

Material and methods. This randomized controlled trial involved a total of thirty-seven (37) participants. They were randomly allotted into three groups [CBT (11), CSE (14) and control (12)]. The intervention was done once per week for duration of 60 minutes for the CBT group, 30 minutes for CSE group and 10 minutes for the control group twice per week for 8 consecutive weeks. Assessment of outcome was done at baseline, 4 weeks and 8 weeks. Data were analyzed using statistical package for social science version 25 at alpha level of less than 0.05.

Results. The results of this study showed that there was significant improvement in the level of pain-related disability ($p= 0.001$), level of anxiety ($p =0.001$), depression ($p = 0.01$, $p = 0.001$, $p =0.001$) and sleep disturbance ($p = 0.001$) in all the groups (CBT, CSE, control) post treatment.

Conclusion. CBT and CSE are both effective in the treatment of pain-related disability, sleep disturbance, and psychological status of NSCLBP patients.

Keywords. chronic low back pain, cognitive behavioural therapy, disability, exercises, patient

Corresponding author: Ashiyat Kehinde Akodu, e-mail: akoduashiyat@gmail.com, aakodu@unilag.edu.ng

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Introduction

Low back pain (LBP) imposes a significant burden on individuals and society at large and it is one of the commonest reasons for seeking health care.[1] The self-limiting and challenging nature of chronic low back pain (CLBP) has forced the victims to be more and more doubtful about the variety of management techniques commonly promoted as the universal remedy to their ailments.[2] An increase in the body of public health research has suggested physical activity and an array of psychological risk factors as being relevant to the origin of CLBP.[3]

Cognitive behavioural therapy (CBT) is a form of psychotherapy that treats problems and boosts happiness by modifying dysfunctional emotions, behaviours, and thoughts.[4] Cognitive behavioural therapy has been found to be effective for a number of chronic pain conditions affecting children and older adult.[5]

Core stabilization exercises (CSE) are aimed at improving the neuromuscular control, strength, and endurance of the muscles that are central to maintaining the dynamic spinal and trunk stability.[6]

Back care education is another therapy used in the management of patients with low back pain. It entails health education on how to maintain proper posture while performing activities of daily living and behavioural modifications for the prevention of back pain.[7] Back care education has been found to be effective in treating low back pain in different population.[8]

Studies about the relative efficacy of CSE and CBT alone for alleviation of NSCLBP have been well reported.[9-11] However, it appears there is dearth of empirical data establishing the more effective of the two interventions (CBT and CSE) on individuals with NSCLBP.

Aim

This study compared the efficacy of CBT, CSE and back care (BC) with stretching on pain-related disability, psychological status and sleep disturbance in patients with NSCLBP.

Material and methods

This study is a single blinded randomized controlled trial, registered with the Pan African Clinical Trial Registry (PACTR201910791448143). Thirty-seven (37) patients with NSCLBP participated in this study. Sample size was calculated using the sample size determination for comparing proportions.[12] By assuming α value of 1.96, β value of 0.84 and prevalence of 0.85.[13] They were volunteers from a tertiary healthcare facility in Lagos, Nigeria. Participants with history of non-specific chronic LBP with or without pain radiating to one or both lower limbs, Participants who scored between 24-30 on mini mental scale.[14] were included into the study. Participants with previous spinal surgeries and participants with history of trauma to the back were excluded from this study.

Health Research and Ethics Committee of College of Medicine, University of Lagos (CMUL) gave approval for this study with approval number (CMUL/HREC/06/19/535). Informed consent was gotten from the participants before including them in the study. Socio-demographic variables (age, sex, height, and weight) of the participants were taken. Pre-intervention assessment of pain related disability, psychological status (depression and anxiety), insomnia were done with Pain disability Index (PDI), Hospital Anxiety and Depression Scale (HADS) and insomnia severity index.

Fifty-three participants volunteered to be part of the study, eight were ineligible based on the exclusion criteria. Forty five qualified participants were randomly assigned into 3separate groups (CBT, CSE, BC) through a computer generated random number sequence, which was created prior to meeting each participant. This allowed them to be distributed into any of the three groups according to their mode of presentation. Fifteen participants were allocated into CBT group; fifteen participants into CSE group while 15 participants into Back care (BC) group. But 8 participants dropped off in the course of the study. Participants in CBT group were treated for a duration of 1-hour with a frequency of one session per week for 8 weeks.[10] Participants in CSE group were treated for a duration of 30 minutes with a frequency of two treatment sessions per week for 8 consecutive weeks, while participants in BC group which is the control were treated with back care advice and stretching exercises of lower limbs for 15 to 20 seconds duration on each group of muscles with a frequency of two treatment sessions per week for 8 consecutive weeks.[7,9,15]

Though only 37 participants completed this study, 4 participants did not receive allocated intervention while another from the study and 4 did not complete the study due to different reasons ranging from illness, and movement to another state (Figure 1). These exercises were done twice weekly for 2 months. Assessment of pain related disability, psychological status (depression and anxiety) and insomnia was done at baseline, end of 4th and 8th weeks.

Protocol for Cognitive behavioural therapy (CBT)

CBT intervention consists of eight weekly 1-hour sessions that provide:

1. Education about the role of maladaptive automatic thoughts (e.g., catastrophizing) and beliefs (e.g., one's ability to control pain, hurt equals harm) in chronic pain, depression, and anxiety.

2. Instruction and practice in identifying and challenging negative thoughts, thought- stopping techniques, use of positive coping self-statements,

goal-setting, relaxation techniques, and coping with pain flare-ups.

3. Education about activity pacing and scheduling, and about relapse prevention and maintenance of gains.[10]

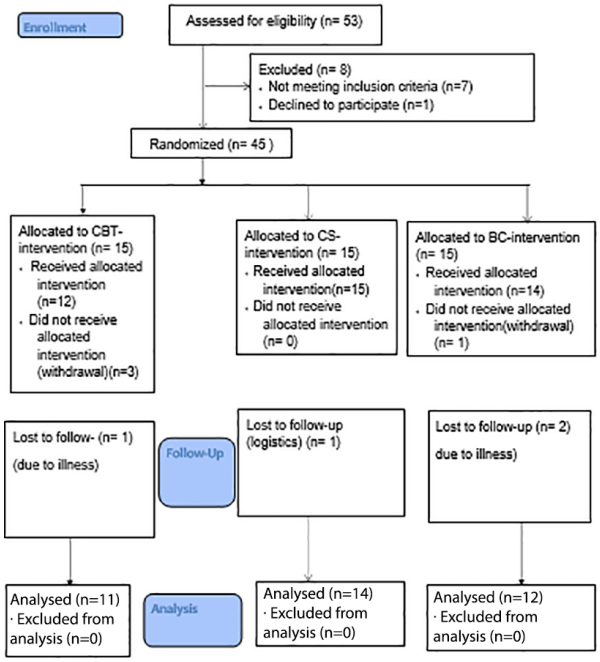

Fig. 1. Flow chart for the study

Protocol for Core stabilization exercises (CSE)

This comprise of abdominal bracing, Heel slides while bracing the abdomen, Leg Lift with abdominal bracing, Bridging with abdominal bracing, Bridging and leg lift with abdominal bracing, abdominal bracing in standing position, Arm lift with bracing in quadruped position, Leg lift with bracing in quadruped position, Alternate arm and leg lift with bracing in quadruped position.[9]

Protocol for Back care (BC) Advice

It was educational package comprising of instructions and diagrams showing proper safe lifting and carrying techniques, maintaining good posture while standing, avoiding prolonged sitting, bending, stooping and squatting and proper sweeping technique.[7]

Protocol for Stretching Exercises to the Lower Extremities

Lying Quadriceps Stretch, Sitting Hamstring Stretch, Calf Muscles stretch, Hip Adductors, Hip Abductors, Hip Flexors/Extensors stretch, Gluteal muscle stretch.[15]

Statistical analysis

Statistical package for Social Sciences (SPSS Inc., Armonk, New York, USA) 25.0 version for windows package program was used to perform data analysis. Mean ± standard deviation was used in summarizing demographic data. Friedman test was used to compare baseline, end of 4th and 8th week post treatment changes in outcome variables in each group. Least significant difference post hoc analysis was used to determine where the significant lies across the weeks. Kruskal-Wallis test was used for across group comparison. Mann Whitney U test was used to compare the outcome measure between CBT and CSE groups. All statistical tests were performed at 0.05 level of significance (i.e. $p<0.05$).

Results

Forty-one participants with NSCLBP participated in this study. However, thirty-seven completed the study; with 11 (29.7%) participants in CBT group, 14 (37.8%) participants in CSE group and 12 (32.4%) participants in the control group. The distribution of physical characteristics of the participants is shown in table 1.

The mean age of the participants in all the groups is 52.30±9.07 years. Twenty-three (62.2%) of the participants were females and 14 (37.8%) were males.

The mean body mass index (BMI) of the participants in all the groups is 27.05± 2.58 Kg/m^2. The groups did not differ significantly in age and BMI (Table 1).

Table 2 shows a detailed comparison of mean within group using Friedman test. At 8th week post-intervention there was significant difference in pain-related disability (p=0.001), psychological status (anxiety and depression p=0.001), and sleep disturbance (p=0.001) within each group. Least significant difference post hoc analysis revealed that the significant ($p<0.05$) lies between baseline and 8th week in all the outcome parameters assessed in all the three groups.

The result showed that there was no statistically significant difference in pain-related disability (p=0.16), psychological status (anxiety, p=0.24; depression p=0.14) and sleep disturbance (p=0.13) across the three groups post-intervention (Table 3).

The Mann Whitney U test showed that there was no statistically significant difference in pain-related disability, (p=0.15, 0.14], psychological status [anxiety; p=0.06, 0.13; depression; p=0.14, 0.08) and sleep disturbance; (p=0.11, 0.07] between CBT group [Median (Interquartile range) = 16.0 (24.0), 12.0 (20.0) ; 8.0 (10.0), 5.0(9.0); 7.0(9.0), 4.0(6.0);10.0(10.0), 6.0 (13.0)] and CSE group [13.0(14.0), 4.0(13.5); 2 (7.5), 1(7.5);1.5 (12.0), 1.0(5.5); 3.5(8.5), 1.0(4.8)] for pain-related disability, anxiety, depression and sleep disturbance at the end of 4th and 8th week.

Discussion

The aim of this study was to compare the efficacy of CBT and CSE on pain-related disability, sleep disturbance, and psychological status in patients with NSCLBP.

In this randomized controlled study, there was marked improvement in clinical outcomes (pain-related disability, sleep disturbance, and psychological status) in

Table 1. Physical characteristics of the participants*

Variables	All Groups	CBT Group Mean ±SD n=11	CSE Group Mean ±SD n=14	Control Group Mean ±SD n=12	f-value	p-value
Age (years)	52.30±9.07	48.90± 11.59	54.36 ± 5.65	53.00 ± 9.60	1.18	0.32
Weight (Kg)	78.95±7.20	75.46± 8.35	80.57 ± 6.17	80.25 ± 6.65	1.94	0.16
Height (m)	1.71±0.04	1.70± 0.04	1.72 ± 0.04	1.70 ± 0.03	0.46	0.64
BMI (Kg/m²)	27.05±2.58	26.07± 3.25	27.41 ± 2.58	27.51 ± 1.71	1.14	0.33

* significant at p<0.05, BMI: Body Mass Index, CBT Group: Cognitive Behavioural Therapy group, CSE Group: Core Stabilization Exercise group, Control Group: Back Care and Stretching group, F: Analysis of Variance

Table 2. Friedman results of outcome variables of participants in the three groups at baseline, end of 4th week and 8th week post-intervention*

	Baseline Median(IQR)	End of 4th week Median(IQR)	End of 8th week Median(IQR)	Friedman	P-value
CBT Grp					
PD	24.00 (18.00)	14.50 (16.00)	21.50 (13.50)	18.73	0.001*
Anxiety	12.00 (5.00)	4.00 (11.00)	8.50 (7.80)	15.21	0.001*
Depression	9.00 (10.00)	6.00 (11.30)	10.00 (8.00)	11.76	0.001*
SD	18.00 (10.00)	6.50 (6.50)	14.00 (10.50)	19.19	0.001*
CSE Grp					
PD	16.00 (24.00)	13.00 (14.00)	16.50 (8.80)	26.14	0.001*
Anxiety	8.00 (10.00)	2.00 (7.50)	5.00 (5.80)	21.14	0.001*
Depression	7.00 (9.00)	1.50 (12.00)	7.50 (7.00)	19.60	0.001*
SD	4.00 (6.00)	1.00 (5.50)	10.00 (8.80)	21.15	0.001*
Control Grp					
PD	12.00 (20.00)	4.00 (13.50)	11.00 (4.00)	23.17	0.001*
Anxiety	5.00 (9.00)	1.00 (7.50)	2.50 (2.50)	21.17	0.001*
Depression	4.00 (6.00)	1.00 (5.50)	4.00(4.00)	23.13	0.001*
SD	6.00 (13.00)	1.00 (4.80)	5.00(8.30)	23.13	0.001*

* PD: Pain-related Disability, SD: Sleep Disturbance, IQR: Interquartile range, CBT Grp: Cognitive Behavioural Therapy group, CSE Grp: Core Stabilization Exercise group, Control Grp: Back Care advice and Stretching group

Table 3. Kruskal-Wallis results of outcome variables of participants in the three groups at baseline, end of 4th week and 8th week post-intervention

Variables	CBT group Median (IQR)	CSE group Median (IQR)	Control group Median (IQR)	H-value	*p*-value
Baseline					
PD	24.00 (18.00)	14.50 (16.00)	21.50 (13.50)	2.22	0.33
Anxiety	12.00 (5.00)	4.00 (11.00)	8.50 (7.80)	3.12	0.21
Depression	9.00 (10.00)	6.00 (11.30)	10.00 (8.00)	2.54	0.28
SD	18.00 (10.00)	6.50 (6.50)	14.00 (10.50)	5.12	0.08
End of 4th week					
PD	16.00 (24.00)	13.00 (14.00)	16.50 (8.80)	1.85	0.39
Anxiety	8.00 (10.00)	2.00 (7.50)	5.00 (5.80)	4.58	0.10
Depression	7.00 (9.00)	1.50 (7.50)	7.50 (7.00)	3.14	0.21
SD	10.00 (10.00)	3.50 (8.50)	10.00 (8.80)	3.50	0.17
End of 8th week					
PD	12.00 (20.00)	4.00 (13.50)	11.00 (4.00)	3.62	0.16
Anxiety	5.00 (9.00)	1.00 (7.50)	2.50 (2.50)	2.89	0.24
Depression	4.00 (6.00)	1.00 (5.50)	4.00 (4.00)	3.88	0.14
SD	6.00 (13.00)	1.00 (4.80)	5.00 (8.30)	4.05	0.13

* significant at p<0.05, PD: Pain-related Disability, SD: Sleep Disturbance, IQR: Interquartile range, CBT Group: Cognitive Behavioural Therapy, CSE Group: Core Stabilization Exercise, Control Group: Back Care and Stretching, H: Kruskal-Wallis Test

the three groups (CBT, CSE groups, and the back care combined with stretching group).

The finding of this study revealed that CSE are efficacious in the management of pain-related disability in patients with NSCLBP. This was supported by previous studies.[16,17] Who in their own studies reported that CSE was effective in reducing pain and disability in patients with NSCLBP.

The reduction in pain can be attributed to muscular contraction during spinal stabilization exercises which provides sensory input to trigger different pain inhibitory mechanisms in the central nervous system. These lead to a rise in the plasma serotonin level, as a likely means of the spinal stabilization exercises-induced analgesia.[18]

The result of this study also revealed that CBT improved pain and disability in patients with NSCLBP. This finding is in line with previous study by Jalali et al., who reported that CBT was effective in reducing pain and disability level.[19] Best practices in biopsychosocial management of NSCLBP involve behavioural prescriptions for increasing activity and overcoming avoidance associated with fear or irrational cognitions.[20]

A systematic review by Hajihasani et al., reported that CBT is a beneficial treatment for NSCLBP, leading to improvements in pain and disability.[21] A study by O'Keeffe et al., reported that CBT did not lead to greater improvements in pain but with disability.[22]

In explaining the reduction in pain, Van Ryckeghem et al., described that we can point to the impressionability of the individual's cognitive evaluations in the area of bodily information, attention diversion from potentially threatening bodily information, increased battle against worrying bodily feedback, changes in explanation and interpretation of body sensations and thus, improved pain self-efficacy.[23] A study by Devan et al., also indicated that the pain-related thoughts and feelings played a very important role in pain self- management education and enhanced self-compassion in patients which might explain a reduction in pain-related disability in this individual.[24]

This study showed that back care plus stretching was effective in the reduction of pain which is in agreement with works done by Paolucci et al., and Garcia et al., that showed in their studies that back care was effective in improving pain and disability.[25,26] Pain relief can be as a consequence of improvement in lifting techniques, standing, sitting and sleeping postures.[27]

The result of this study revealed that CSE are effective in improving the psychological status (depression and anxiety) of patients with NSCLBP. This is in line with findings of Akodu and Akindutire, which reported that CSE are very useful in the management of depression and anxiety in NSCLBP patients.[9] This could be as a result of decline in the pain sensation of the participants' post-treatment.[9] This also supports the claim of Balasubramaniam et al.,[28] who reported that when there is a reduction in the level of perception of pain and disability the level of depression reduces.

The result of this study equally demonstrated an improvement in psychological status with CBT as supported by previous study.[29] The improvement could possibly be due to a bidirectional and potentially causative influence of pain and depression on one another.[28] A study by Wenzel et al., also postulated that depressed patients engaging in activities that give them a sense of pleasure and accomplishment help patients re-engage in their environment, become more active, and attend to the fact that they are engaging in pleasurable activities, all of which can be associated with a significant improvement in mood and depressive symptoms.[30]

This study also showed that back care plus stretching was effective in improving the psychological status (depression and anxiety) of patients with NSCLBP. This is in line with a study done by Paolucci et al., which concluded that back care has positive effects on the psychological status of patients with NSCLBP.[25] This improvement could be due to the reduction in pain and disability level of the participants.[28]

The result of this study revealed an improvement in sleep disturbance of patient with NSCLBP post treatment after CSE. This finding agreed with Akodu and Akindutire who investigated the effects of core stabilization exercises on sleep disturbance in patients with NSCLBP and concluded that CSE are effective in improving sleep disturbance.[7] The improvement could be as a result of decline in pain and disability which in turn improves their sleep quality.[7] Pain is correlated with sleep which in turn disturbs sleep. Sleep disturbance also increases pain intensity and reduces the ability to tolerate pain.[31] Evidence has shown that sleep disturbance is associated with the development of anxiety disorder.[32] A study by Lee et al., also reported that patients who had subjective sleep disturbance were more likely to develop moderate to severe depression.[33]

The outcome of this study revealed an improvement in the sleep disturbance of patient with NSCLBP post treatment after CBT. This is supported by the report of previous study who reported meaningful improvements in insomnia severity after treatment with CBT.[34] The improvement in sleep disturbance is probably due to the reduction in pain and practice of proper sleep hygiene and relaxation techniques that was acquired while undergoing the CBT program.[35]

The outcome of this study also showed that back care advice plus stretching was effective in improving sleep disturbance in patients with NSCLBP. A possible explanation might be the association between CLBP and sleep. Chronic low back pain has been found to be related to several dimensions of sleep including sleep disturbance.[31]

All the interventions (CBT, CSE, Back care advice plus stretching) have proven to be effective in the treat-

ment of patient with NSCLBP and one is not superior to the other. This may simply be due to the multimodal effects of exercise on symptoms of patients with NSCLBP. This finding shows the effectiveness of most modalities commonly used in the treatment of patients with NSCLBP in physiotherapy.[36]

The study was limited due to small sample size and participants were lost to follow up.

Conclusion

There were no significant differences found in outcomes across the three groups. So none of the 3 interventions is superior to the other. It is therefore worthy of note that physiotherapists can use any of the interventions in the treatment of patients with NSCLBP.

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ORIGINAL PAPER

Oyediran Emmanuel Oyewole (ABCDEFG), Ayodele Solabi (ABCDEG)

Knowledge of modifiable risk factors for cardiovascular diseases among university undergraduates in Ibadan, Nigeria

Department of Health Promotion and Education, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Nigeria

ABSTRACT

Introduction. Undergraduates in many institutions live a lifestyle that could predispose them to non-communicable diseases (NCDs) including cardiovascular-related. Previous studies on modifiable risk factors (MRFs) against NCDs had focused mainly on adults, whereas young people should be prime targets for prevention programmes.

Aim. This study was aimed at investigating knowledge of MRFs against cardiovascular diseases (CVDs) among university undergraduates in Ibadan, Nigeria.

Material and methods. A descriptive cross-sectional design was adopted, where 500 undergraduates participated. Data were collected using Focus Group Discussion (FGD) guide and validated questionnaire. Data analyses were conducted using thematic approach and bivariate methods at 5% levels of significance, respectively.

Results. Mean age was 22.8±3.0 years and 51.4% were females. The majority reported that their fathers (82.8%) and mothers (83.0%) had no hypertension history. The FGD revealed that students were knowledgeable of MRFs and preventive behaviours but still engaged in unhealthy lifestyle practices. The MRFs identified included excessive alcohol consumption (85.4%), unhealthy diet (77.6%), physical inactivity (75.2%) and smoking (70.2%). Respondents (56.4%) had good knowledge of MRFs against CVDs; 57.0% had fair lifestyle practices and 54.8% had good knowledge of preventive behaviour against CVDs.

Conclusion. Gender was significantly associated with knowledge of CVDs preventive behaviours. Institutional-based lifestyle modification programmes, using peer group education is suggested.

Keywords. cardiovascular diseases, knowledge, modifiable risk factors

Introduction

There has been a concern for the recent increase in incidence and prevalence of cardiovascular diseases (CVDs) among younger population in Nigeria as established in some of the recent surveys. Cardiovascular diseases have been considered mostly in the adult population in the previous studies of non-communicable diseases.[1] These diseases are associated with unhealthy lifestyle driven by modifiable risk factors. These factors include smoking, lack of physical activity, low fruit and vegetable intake, high fat, caffeine overuse, improper sleeping habits, salt intake, and excess alcohol intake.[2-4]

Corresponding author: Oyediran Emmanuel Oyewole, e-mail: diranoyewole@gmail.com, oyewole2002@yahoo.com

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In Nigeria, as in many other developing countries, CVDs have a higher mortality rate than in the developed countries.[5] The deaths resulting from CVDs are attributable to four common behavioural risk factors: low physical activity, tobacco use, the harmful use of alcohol and poor diet.[6] The continuing enormous burden of CVD in developed countries, the increasing trends in cardiovascular risk profiles of adolescents and adults, and the emerging increases in CVD in developing countries underscore the crucial need to redouble prevention and treatment efforts.[7] This is particularly important in Nigeria and by extension, Africa; where the healthcare expenditure per capita is 23 dollars (4.6% of total Gross Domestic Product).[7]

Although, CVDs are considered the diseases of the middle age or the elderly, evidence from previous studies have shown that the risk factors begin early in life.[8,9] Behaviours of students are considered a temporary part of college life; however, unhealthy habits picked up at this stage of their lives grow up with them to adult life.[10] University or college life is a crucial stage for individuals as at this time, and their behaviours are conducive to change. University and college arenas, therefore, represent an important opportunity for health education. Previous studies on knowledge of cardiovascular diseases risk factors have focused on older adults and patients at high risk of cardiovascular diseases.

Changes in lifestyle to modify cardiovascular disease (CVD) risk factors if taken early in life, helps to utilise the full prevention value of the change. Risk of CVD can be decreased by adherence to dietary and lifestyle modifications, which results in lower risk factor levels. Findings from this study can be used to design appropriate lifestyle modification programmes, which will help the young adult to adopt healthy behaviours while they are still young. In addition, findings may also be useful for policy dialogue on prevention of cardiovascular diseases, especially among the young adult generation, who will be the future leaders.

Aim

The aim of this study was to probe into the knowledge of modifiable risk factors of cardiovascular diseases among university undergraduates in Ibadan, Nigeria.

Material and method

The study was a descriptive cross-sectional survey conducted in a tertiary institution in an urban area. The protocol for the study was reviewed and approved by the University of Ibadan/University College Hospital Ethics Review Committee, Ibadan with assigned number: UI/EC/15/0159. This study was conducted at the University of Ibadan, Ibadan, Nigeria. The institution, occupying over 1,032 hectares of land, is located in Ibadan North Local Government Area. The University was initially established on 17 November 1948 as an external College of the University of London (then it was called the University College, Ibadan). The University became an autonomous University in 1962 and had a little over 2000 students. The site of the University was leased to the colonial authorities by Ibadan Chiefs for 999 years.[11] The University is a Federal Government institution, which runs undergraduate and postgraduate courses hence, the students are both undergraduate and postgraduate who are mainly young adults. The university is made of two campuses; the main campus and the College of Medicine campus, which is situated within the University College Hospital (UCH) premises – a teaching hospital for undergraduate and postgraduate medical students. The University has 12 faculties (there were only 12 faculties as at the time of this study. A new faculty was created from the faculty of the social sciences when this manuscript was been prepared), several centres and institutes. There are 13 halls of residence in the University; nine of these in the main campus are for the undergraduate students, while the only the one, Alexander Brown Hall (ABH) was located within the UCH premises mainly, for the medical students.

Sampling, Instrument and Procedure for Data Collection

Multistage sampling technique was adopted to select a sample size of 500 samples through a proportionate method from the selected halls of residence (male and female), students' hostel blocks and rooms were selected using systematic random sampling. The sampling interval for systematic sampling was determined by dividing the sample size by the total population of students in the halls. A sampling interval (k) = N/n; 500/125 = 4; therefore, the sampling interval determined was 4. A number was randomly picked by balloting from 1 to 4 to determine the first number to be picked from the list of students. Four was subsequently added to the first number picked and this continued until 500 students were recruited. Respondents were not recruited through the faculties and faculties did not have equal number of respondents. The respondents could not be recruited into the study from this medium because they were not all available for selection. Hence, halls of residence was used as the location for selection of the respondents because it was the best medium to reach out to them in their natural settings in their rooms. Other locations in the university including the faculties, departments and sport centres could not be used because respondents were not stable for the interviews due to lectures and other engagements. Halls of residence was the most suitable environment to make random selection of respondents that would represent the entire population of the university undergraduates. Based on the varying degrees of students' population from different faculties (selection using proportionate method), bivari-

ate statistical analysis to compare the fields of study with the knowledge of modifiable risk factors for cvd was not assessed.

Measures

Mixed methods of data collection, which involved qualitative approach using Focus Group Discussion [FGD] guide, with ten open-ended questions and quantitative method, using questionnaire were used to collect data. The contents of the both instruments were based on the themes from the study objectives. These included open-ended questions on knowledge of modifiable Cardiovascular Diseases (CVD) risk factors, lifestyle practices, preventive behaviours and source of information about modifiable CVD risk factors among undergraduates for the qualitative. The quantitative instrument was a validated, self-administered semi-structured questionnaire. The questionnaire was divided into five sections, namely socio-demographic characteristics of respondents, knowledge of modifiable risk factors for cardiovascular diseases measured on a 26-point knowledge scale. The knowledge of preventive behaviours against cardiovascular diseases was measured with a 24-point knowledge scale, lifestyle practices associated with modifiable cardiovascular disease risk factors measured on a 24-point practice scale and in addition, sources of information available to respondents on modifiable risk factors for cardiovascular disease.

Procedure for data collection

Visits were made to all the undergraduates' halls of residence four research assistants (RAs) to establish rapport with hall wardens, porters and students and to intimate them with the study objectives before data collection. Four Focus Group Discussion (FGD) sessions were conducted among consented participants (each session comprising of eight participants) by four trained research assistants. The FGD sessions were held in a location devoid of interference within the halls of residence. The FGD participants were excluded from questionnaire interviews to avoid bias data. The quantitative aspect involved the administration of the questionnaire, which was done by the researcher and the four RAs. The questionnaire was self-administered, respondents were approached, and a brief introduction about the study was made. Written informed consent was obtained from the respondents who indicated their willingness to participate in the survey after detail information was provided. They were informed that the data would be used for research and publication alone, that participation was voluntary, and that data collected will be kept confidential. The questionnaire was completed within an hour, and the completed ones were checked immediately to ensure that no aspect of the instrument was omitted.

Data analysis

Results from the FGDs were analysed through the use of the thematic approach. Close and open-ended questions were coded, and the data were fed into the computer using the IBM/Statistical Package for Social Sciences (IBM/SPSS Version 20). The data were analysed using descriptive and inferential statistics with the p-value set at 0.05. The results were presented in tables and charts.

Results

Demographic characteristics of the respondents

More than half (51.4%) of the respondents were females, 96.2% were singles, and the mean age was 22.8 ± 3.0 years (Table 1). Most respondents, 24.8% and 24.2% were in 200 and 300 levels, respectively, and most (20.0%) were students from the Faculty of the Social Sciences (Figure 1). The majority pointed out that their fathers and mothers (82.8% and 83.0%, respectively) had no history of hypertension. Also, more than half (53.8%) indicated that none of their family members had history of hypertension (Table 1). It was also recorded that 7.6%, 8.4% and 26.2% of respondents stated that they did not know if their fathers, mothers and any members of their family, respectively had history of hypertension.

Table 1. Socio-demographic characteristics of the respondents (N=500)

Variable	№	%
Age		
<20 years	62	12.4
20–29 years old	423	84.6
≥30 years old	15	3.0
Sex		
Male	243	48.6
Females	257	51.4
Level of study		
100	109	21.8
200	124	24.8
300	121	24.2
400	58	11.6
500	28	5.6
Marital status		
Single	481	96.2
Married	19	3.8
Fathers' history of hypertension		
Yes	48	9.6
No	414	82.8
Don't know	38	7.6
Mothers' history of hypertension		
Yes	43	8.6
No	415	83.0
Don't know	42	8.4
Family members' history of hypertension		
Yes	100	20.0
No	269	53.8
Don't know	131	26.2

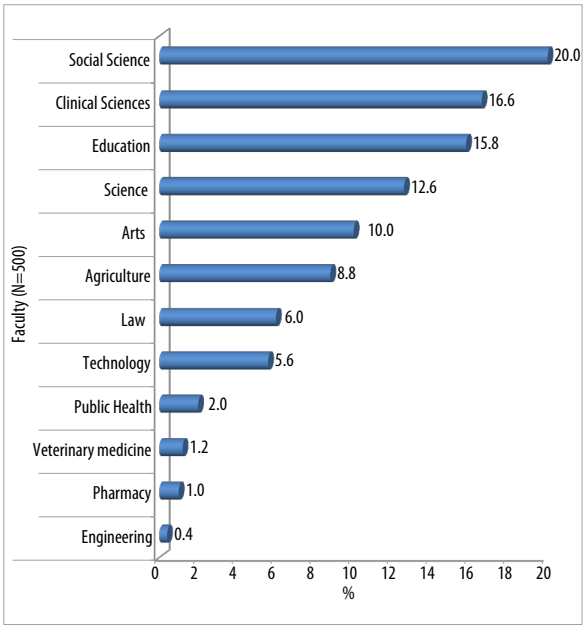

Fig. 1. Respondents' faculty of study

Knowledge of cardiovascular diseases (Heart diseases)

Participants' knowledge of the modifiable risk factors for cardiovascular diseases varies. Some stated it as diseases that affect the heart or causes failure to breathe. Moreover, most mentioned hypertension, heart failure, cardiac arrest and stroke as examples of cardiovascular diseases. Some the participants pointed out that heart diseases could affect parts of the body like the lower part of the heart, coronary vessels, heart muscles and blood vessels. According to one of the female participants,

"Heart diseases are directly called cardiovascular diseases; they are diseases that affect the heart and blood vessels" (Female A participant from Queen Idia Hall).

Other female participants noted:

"Heart diseases are diseases that affect the muscles of the heart and vessels of the heart, any structure of the heart" (Female A participant from Alexander Brown Hall)

"I would buy the idea of sickness or disease of the heart that will make the heart not to perform or function normally as it is supposed to" (Female G participant from Queen Idia Hall).

A male participant added that:

"Heart disease is when somebody has heart failure" (Male B participant from Sultan Bello Hall)

Other qualitative findings show a varying level of knowledge of modifiable risk factors that predispose people to cardiovascular diseases. These factors, as mentioned included smoking, alcohol intake, stress, fatty food intake, hereditary, lack of exercise, obesity, age, gender, race and diabetes. According to a male participant, *"Smoking, eating foods that are not well prepared, not well cooked"* (Male A participant from Sultan Bello Hall).

Participants from two female halls added that, *"They said too much of alcohol is not good; it is not good in the sense that it dries up the lungs and if the lungs are dried up, it would surely affect the heart and the kidney"* (Female B participant from Queen Elizabeth Hall).

"*Too much of stress can cause heart disease, and I think stress could lead to heart diseases"* (Female AA participant from Queen Idia Hall).

According to another male participant, *"Well, there are several factors; they could be modifiable or non-modifiable. The non-modifiable factors are the age factor, as you grow older; the vessels of the heart tend to reduce in size, so the volume of blood that passes through them reduces too. Then gender factor, it is common in the male gender, then family history, some families are more predisposed to heart disease, then the race, I think it is more in blacks than in whites"* (Male A participant from Kuti Hall).

Quantitative data based on the 26-point knowledge of modifiable risk factors for cardiovascular diseases rating; showed the knowledge score was 19.3±4.3, and most respondents, 56.4%, had good knowledge (Tables 2 and 3).

Table 2. Respondents' knowledge of modifiable risk factors for cardiovascular diseases (N=500)

Statement	True № (%)	False № (%)
Majority of heart diseases can be prevented	447 (89.4)*	53 (10.6)
The most commonly known risk factor for stroke is hypertension	428 (85.6)*	72 (14.4)
Excessive alcohol intake can increase the risk of heart disease	427 (85.4)*	73 (14.6)
Hypertension increases the risk of getting heart disease	410 (82.0)*	90 (18.0)
Being overweight or obese increases a person's risk of developing heart disease	390 (78.0)*	110 (22.0)
Diets high in animal fat predispose people to heart disease	388 (77.6)*	112 (22.4)
Physical inactivity increases the risk of developing heart disease	376 (75.2)*	124 (24.8)
Individuals with diabetes are more likely to have hypertension	296 (59.2)*	204 (40.8)
Young adults are not predisposed to having heart disease	179 (35.8)	321 (64.2)*
People always know when they have heart disease	178 (35.6)	322 (64.4)*
Stress is not a risk factor for heart disease	174 (34.8)	326 (65.2)*
Smoking is not a risk factor for heart disease	149 (29.8)	351 (70.2)*
There is no relationship between fatty food consumption and heart disease	134 (26.8)	366 (73.2)*

* Correct answer

Table 3. Knowledge score on modifiable risk factors for cardiovascular diseases (N=500)

Knowledge score	№	%
Poor knowledge	42	8.4
Fair knowledge	176	35.2
Good knowledge	282	56.4
Total	500	100.0

Knowledge of cardiovascular diseases preventive behaviours

There were similarities in the participants' responses to questions on the preventive practices against cardiovascular diseases. The majority pointed out that avoiding foods that contain high fat and cholesterol could reduce a person's vulnerability to cardiovascular diseases. According to some participants, *"We should minimise high-fat intakes like eating much of fried foods, hydrogenated fats like margarine, butter and other types of fats from animals, and we should amend how we take all these fatty foods"* (Male A participant from Bello Hall).

"All these chickens you buy outside, for example, from 'Tantalizers' (name of a local fast food eatery), they are not good for our health. For proper diet, eat a lot of vegetables. Vegetables should be half of your plate, and then the solid food should be small, 'amala' or any swallow food should be ¼ size of the plate and the meat (not too much). You should divide your plate into 4, ½ part should contain vegetable then small portion should contain the swallow then the meat and fruits. Then the kind of palm oil you use, palm oil that is so light don't use the type that is very thick and settles a lot at the bottom of the container those contains fats too much" (Female G participant from Alexander Brown Hall).

Findings also showed that participants pointed out that regular exercise is one of the ways to prevent cardiovascular diseases. A male participant stated that:

"I will say that we should take at least 30 minutes of exercises, but even though sometimes we don't have that time, I think we should walk, trek to replace daily exercise. For me I trek from my hostel to my department, from my department back to my hostel, then to market and church, I think that's a better way to exercise" (Male H participant from Independence Hall).

A few participants have a different view on the preventive behaviours against cardiovascular diseases; they believe that regular check-ups are a useful means of preventing cardiovascular diseases. A female participant stated that:

*"I think check-up is generally good for the body but for student or generally youth it's not easy for us to go to the hospital for a general check-up because we all know what we are to do. We have this regular schedule from class to home to fellowship, now going to the nearest hospital for a check-up is somehow, some people are even afraid of going for a check-up. If there is a body probably an NGO that can be going from one house to another for backup support to the Federal Government of Nigeria, doing the check-up free of charge for youth if not for any other group of people. It will be the best, so people can know the status of their heart and act fast if there's any problem"(*Female Q participant from Queen Elizabeth Hall).

Quitting smoking and alcohol was another strategy suggested by the participants, which can be adopted to lower the risk of developing cardiovascular diseases. One of the discussants remarked that:

"Smoking is the common avenue to heart problem, so to prevent the problem; one must not even near smokers let alone smoke. Smoking affects the CVS, it is going to affect the lungs of smokers definitely, and the major function of CVS is to pump blood, oxygenated blood to the body tissues, when the lungs are affected, the lungs can no longer exchange carbon dioxide for oxygen, then there is less oxygen in the blood circulation, if there is less oxygen in the blood circulation, the major function of CVS is to deliver oxygen to body tissues, it will affect the body tissues" (Male AY participant from Kuti Hall).

Some other participants noted:

"Yes, we should all avoid smoking (chorus answer)" (Female participants from Queen Hall)

Table 4. Respondents' knowledge of cardiovascular diseases preventive behaviours (N=500)

Statement	True № (%)	False № (%)
Checking one's blood pressure regularly to ensure it is within the normal range can reduce the risk of heart disease	466 (93.2)*	34 (6.8)
Eating foods high in animal fat cannot predispose one to heart disease	145 (29.0)	355 (71.0)*
A person who stops smoking will lower their risk of developing heart disease	414 (82.8)*	86 (17.2)
Engaging in regular physical activity will lower a person's risk of heart disease	412 (82.4)*	88 (17.6)
Only exercising at a gym or in an exercise class will lower a person's chance of developing heart disease	162 (32.4)	338 (67.6)*
Eating fruits and vegetables regularly is not good for the heart	118 (23.6)	382 (76.4)*
Eating a lot of red meat decreases heart disease risk	177 (35.4)	323 (64.6)*
Checking one's blood sugar level regularly to ensure it is within the normal range can reduce the risk of developing heart disease	430 (86.0)*	70 (14.0)
Cutting down salt intake can sometimes help to reduce hypertension	417 (83.4)*	83 (16.6)
Taking alcoholic drinks excessively increase the risk of heart disease	405 (81.0)*	95 (19.0)
Relaxing during your leisure time can help reduce stress	411 (82.2)*	89 (17.8)
Reducing weight, if overweight or obese will not help in reducing the risk of heart disease	205 (41.0)	295 (59.0)*

* Correct answer

Table 5. Overall knowledge scores on cardiovascular disease preventive behaviours

Knowledge score	№	%
Poor knowledge	58	11.6
Fair knowledge	168	33.6
Good knowledge	274	54.8
Total	500	100.0

Respondents' knowledge of cardiovascular diseases preventive behaviours were assessed on a 24-point knowledge scale (Table 4). The majority (93.2%) indicated that regular blood pressure check could reduce the risk of developing cardiovascular diseases while 71.0% opposed to the notion that eating foods high in animal fat cannot predispose one to develop cardiovascular diseases. A majority (82.8%) agreed with the idea that a person who quits smoking lowers his or her risk of developing cardiovascular diseases and 82.4% affirmed that engaging in regular physical activity reduces a person's risk of developing cardiovascular diseases. Most respondents indicated that eating fruits and vegetables regularly (76.4%) and reduction in eating lots of red meat (64.6%) are some of the means of reducing the risk of developing cardiovascular diseases. Also, the majority (86.0%) noted that regular checking of one's blood sugar level could reduce the risk of developing (Table 4).

The score for respondents' knowledge of cardiovascular disease preventive behaviours was 18.6±4.5, more than half, 54.8%, had good knowledge of cardiovascular disease preventive behaviours (Tables 4 and 5).

Lifestyle practices associated with modifiable risk factors for cardiovascular diseases

Findings on lifestyle practices related to modifiable risk factors for cardiovascular diseases showed that the majority of the female participants visited fast food centres than the male counterpart. The primary reason given was that they could not prepare their food themselves, especially whenever examination is approaching and when they just resumed session (when they still have much money on them). According to some participants, *"I eat some junks, and the kind of vegetable oil I use is this kind of oil they generally sell at the market with very high cholesterol. Then, exercise is not that adequate only the one we do every day we climb the third floor, go toward etc. that's what I do every day" (*Female FY participant from Alexander Brown Hall) *"I like fried eggs a lot, so the fat is not too good for me, and I am a bit lazy even though I am a girl I don't like jumping around, and my exercise is not that adequate I don't exercise frequently, but I tried to eat less so I try to balance like that" (*Female L participant from Alexander Brown Hall) *"I don't exercise, and I eat lots of chocolates and fatty foods……." (*Female B participant from Queen Elizabeth Hall)

Some discussants admitted that eating fatty foods or foods high in cholesterol could predispose someone to heart disease. According to some female participants:

"If I take too much of fatty food, it can lead to heart disease" (Female A participant from Queen Elizabeth Hall).

"It is this cholesterol issues o, because I eat lots of egg and I heard that egg contains a lot of cholesterol" (Female BB participant from Queen Idia Hall)

One participant expressed her opinion on the consumption of junks and foods that contained high fat which has become part of her lifestyle due to her body frame. According to her, *"Eating of fatty food, I always take too much of it without any fear because you can see me that I'm slim, I don't have any fear for it and fried food"* (Female S participant from Queen Idia Hall).

Justifying reasons for consuming food high in fat and cholesterol, some participants were of the view that living on high fat or cholesterol content food could not be avoided even though it is confirmed as a predisposing factor to heart disease. They expressed that, *"I don't prevent it at all, but I know I increase the measures because I know of taking a lot of butter, meats, etc. that has fat. But I only prevent it through exercise, which is trekking from Queen Elizabeth Hall to Faculty of Education, from Queen Elizabeth Hall to Bodija market etc. So, I make sure I eat what I like and enjoy my life. People that used to prevent heart disease will they not die? I 'kuku'(better) know that one day, anyhow one will 'kuku' die, something has to kill us, why don't we 'kuku' enjoy our life, this very life we are. I've seen some people not putting Maggi (common Nigerian food seasoning) into their soup, how will such soup taste, please eat enough Maggi, eat enough meat and whatever that pleases you, so after enjoying your life die and go*" (Female D participant from Queen Elizabeth Hall).

"I don't consider myself preventing any heart disease, as you can see, I'm slim, and I eat anything I feel like eating. Moreover, I exercise a lot, like trekking is what I do mostly, and I think it's very good exercise. Stress is another factor, but I don't stress myself at all, and if I should stress myself, I make sure I relax a lot and eat so well" (Female BBY participant from Queen Idia Hall).

Respondents' lifestyle practices associated with modifiable risk factors for cardiovascular diseases

Respondents' lifestyle practices related to modifiable risk factors for cardiovascular diseases were assessed on a 26-point scale. Most respondents (73.2%) indicated that they occasionally eat fast foods, and 59.4% sometimes choose to eat low-salt and low-fat meals. More than half, 55.2%, affirmed that they eat beef or fried foods and included vegetables in their meal occasionally. Those who included fruits in their daily meal and hardly exercise were 54.8% and 51.6%, respectively. Only 6.6% of respondents mentioned they smoked always but the frequency of smoking and the number of cigarettes smoked per day was not captured in this study. Most (78.6%) indicated that they never smoked nor exposed themselves to cigarette smoke, and 64.8% never took alcoholic drinks. Some respondents (59.4%)

attested that they always walked for at least 30 minutes daily to get to and from places and 51.4% never ate out. Occasionally, 53.4% of the respondents took soft drinks or sweetened beverages. The respondents who slept up to 8 hours daily and observed leisure time or engaged in recreational activities occasionally were 47.6% and 49.0%, respectively (Table 6). Respondents' score on lifestyle practices associated with modifiable risk factors for cardiovascular diseases was 16.5±2.7, and the majority, 82.2%, had fair lifestyle practices (Tables 6 an 7).

Table 6. Respondents' lifestyle practices associated with modifiable risk factors for cardiovascular diseases (N=500)

Statement	Always Nº (%)	Occasionally Nº (%)	Never Nº (%)
Consumption of fast food	120 (24.0)	366 (73.2)	14 (2.8)*
Choosing low-salt and low-fat meals	163 (32.6)*	297 (59.4)	40 (8.0)
Eating beef or fried foods	216 (43.2)	276 (55.2)	8 (1.6)*
Adding vegetables in daily meal	216 (43.2)*	275 (55.0)	9 (1.8)
Including fruits in the daily meal	208 (41.6)*	274 (54.8)	18 (3.6)
Exercising regularly	217 (43.4)*	258 (51.6)	25 (5.0)
Smoking or exposing oneself to cigarette smoke	33 (6.6)	74 (14.8)	393 (78.6)*
Walking for at least 30 minutes daily to get to and from places	297 (59.4)*	193 (38.6)	10 (2.0)
Eating out	257 (51.4)	200 (40.0)	43 (8.6)*
Consuming alcoholic drinks	43 (8.6)	133 (26.6)	324 (64.8)*
Taking soft drinks or sweetened beverages	226 (45.2)	267 (53.4)	7 (1.4)*
Sleeping for 8hrs daily	227 (45.4)*	238 (47.6)	35 (7.0)
Observing leisure time or engaging in recreational activities	238 (47.6)*	245 (49.0)	17 (3.4)

* Good lifestyle practice

Tab. 7. Lifestyle practices score (N=500)

Lifestyle practice score	Nº	%
Poor practice	30	6.0
Fair practice	411	82.2
Good practice	59	11.8
Total	500	100.0

Age was not statistically significant to the knowledge of modifiable risk factors for cardiovascular diseases among the respondents (p=0.237) (Table 8). Likewise, there no significant relationship between the gender of the respondents and their level of knowledge of modifiable risk factors for cardiovascular diseases (p=0.135, Table 9). A significant relationship was found between respondents' sex and knowledge of prevention of cardiovascular diseases (p=0.027, Table 10).

Table 8. Relationship between respondents' age and knowledge of modifiable risk factors for cardiovascular diseases

Variable	Knowledge about modifiable risk factor for cardiovascular diseases				Chi-square
Age (in years)	Poor knowledge (n=42)	Fair knowledge (n=176)	Good knowledge (n=282)	Total (N=500)	
<20	2 (3.2)	18 (29.0)	42 (67.7)	62 (12.4)	f = 5.188
20-29	39 (9.2)	154 (36.4)	230 (54.4)	423 (84.6)	p = 0.237
>29	1 (6.7)	4 (26.7)	10 (66.7)	15 (3.0)	

f – Fisher's exact test

Table 9. Relationship between respondents' sex and knowledge of modifiable risk factors for cardiovascular diseases

Variable	Knowledge of modifiable risk factor for cardiovascular diseases				Chi-square
Gender	Poor knowledge (n=42)	Fair knowledge (n=176)	Good knowledge (n=282)	Total (N=500)	
Male	23 (9.5)	94 (38.7)	126 (51.9)	243 (48.6)	$\chi^2 = 4.002$
Female	19 (7.4)	82 (31.9)	156 (60.7)	257 (51.4)	df = 2
Total	42 (8.4)	176 (35.2)	282 (56.4)	500 (100.0)	p = 0.135

Tab. 10. Relationship between respondents' sex and knowledge of cardiovascular diseases prevention

Variable	Knowledge of cardiovascular diseases prevention				Chi-square
Gender	Poor knowledge (n=42)	Fair knowledge (n=176)	Good knowledge (n=282)	Total (N=500)	
Male	29 (11.9)	95 (39.1)	119 (49.0)	243 (48.6)	$\chi^2 = 7.225$
Female	29 (11.3)	73 (28.4)	155 (60.3)	257 (51.4)	df = 2
Total	58 (11.6)	168 (33.6)	274 (54.8)	500 (100.0)	p = 0.027*

* Significant at p<0.05

Findings also showed that there was no significant relationship between knowledge of modifiable risk factors for cardiovascular diseases and lifestyle practices (p=0.275, Table 11). There was no significant relationship between knowledge of cardiovascular diseases preventive behaviours and lifestyle practices (p=0.308, Table 12).

Discussion

The majority of respondents were young adults and they were ideal targets for prevention interventions against CVDs because they are in the process of establishing lifestyle habits, which track forward into adulthood.[12] According to Zachariah and Alex, physical inactivity is a modifiable risk factor for cardiovascular diseases, and respondents in the study appear to be active and engage in some measure of walking.[13] This finding was similar to that of Oyerinde et al., Mustapha and Sanusi.[14,15] A majority also reported that their parents and family members had no history of hypertension. This finding was in contrast to that of George and Andhuvan where they found that majority of the respondents were not aware of the association between age and family history with cardiovascular disease (like hypertension) when in fact these risk factors are early predictors for the same.[16]

Table 11. Relationship between respondents' lifestyle practices and knowledge of modifiable risk factors for cardiovascular diseases

Variable	Lifestyle practice				
Knowledge of modifiable risk factors for cardiovascular diseases (CVD)	Poor practice (n=30)	Fair practice (n=411)	Good practice (n=59)	Total (N=500)	Chi-square
Poor knowledge	3(14.3)	16(76.2)	2(9.5)	21(4.2)	f = 4.839
Fair knowledge	10(4.2)	195(82.6)	31(13.1)	236(47.2)	p = 0.275
Good knowledge	17(7.0)	200(82.3)	26(10.7)	243(48.6)	

f – Fisher's exact test

Table 12. Relationship between respondents' knowledge of cardiovascular diseases preventive behaviours and lifestyle practice

Variable	Lifestyle practice				
Knowledge of preventive behaviours for cardiovascular disease	Poor practice (n=30)	Fair practice (n=411)	Good practice (n=59)	Total (N=500)	Chi-square
Poor knowledge	5(8.6)	47(81.0)	6(10.3)	58(11.6)	$\chi^2 = 4.803$
Fair knowledge	7(4.2)	135(80.4)	26(15.5)	168(33.6)	Df = 4
Good knowledge	18(6.6)	229(83.6)	27(9.9)	274(54.8)	p = 0.308

Knowledge of modifiable risk factors for cardiovascular disease

The majority of the respondents was able to define heart disease from a general knowledge point of view and could even mention some examples of cardiovascular diseases. This finding corroborated that of George and Andhuvan.[16] Some of the participants who were studying non-directly health-related courses showed a reduced level of knowledge of cardiovascular diseases. This finding was similar to that of Ammouri et al. and Bucholz et al., where coronary heart disease-related knowledge was found to be particularly low among the study population.[17,18]

Smoking, excessive alcohol consumption, stress, fatty food intake, hereditary, lack of exercise, obesity, age, gender, race and diabetes were among risk factors that predispose people to heart diseases as mentioned by the respondents. This finding corroborated the previous studies where risk factors for CVDs included alcohol dependency, which has greater potential to compound comorbid heart disease.[19] In a Nigerian study; habitual alcohol consumption had been documented among 9.0% of patients with cardio-vascular diseases.[20]

Eating an unhealthy diet, overweight and sedentary lifestyle, smoking, ineffective management of stress, uncontrolled blood pressure or high blood cholesterol levels, physically inactive are common among Nigerians and unfortunately, many do not know the signs of CVDs.[6] A WHO report revealed that approximately 3.2 million people die each year due to insufficient physical activity and people who do not take enough exercise have a 20 to 30 per cent increased risk of dying prematurely.[20,21] However, some other studies indicated that between 30.3% and 74.6% of Nigerian children and youth aged 5-25 years, respectively engaged in some form of physical activity daily.[14,22]

The current study identified smoking as a modifiable risk factor for cardiovascular diseases. It, therefore, corroborated a previous study that showed that about 80% of university students started smoking before the age of 18 years.[23] Smokers' chances of developing coronary heart disease are 2-4 times higher than that of non-smokers and people who smoke a pack of cigarettes a day have more than twice the risk of heart attack than people who have never smoked.[24]

Knowledge of cardiovascular disease preventive behaviours

Qualitative findings show that avoiding foods that contain high fat and cholesterol could reduce the chances of developing any form of heart disease. This finding was similar to previous studies, which found that knowledge of making healthy food choices can reduce the risk of getting CVD. According to the WHO, foods people eat directly have an impact on other controllable risk factors like cholesterol, high blood pressure, diabetes, and being overweight. Low fruits and vegetable intake is estimated to cause 31% of coronary heart disease and 11% of stroke worldwide Arts and colleagues reported that dietary lifestyle formed early in life will develop into adulthood and are strongly associated with risk of cardiovascular diseas-

es.[12,25] The change from adolescence to young adulthood is usually seen as a high-risk period because of low intake of quality diets and gain in body weight.[26] According to Arts and colleagues, this period of transition is crucial when students are entering higher institutions; living away from home for the first time with increased freedom or independence and responsibility for food choices. If adolescents or young people go through this transition period with unhealthy diets or poor quality diets, the chances of making positive changes in their diets without any intervention are slim.[12]

The majority of the respondents indicated that regular exercise is a preventive behaviour against cardiovascular diseases. This was not fully in line with another study where it was reported that only 15% of the subjects recognised lack of exercise as a modifiable factor against heart disease.[18] The majority also mentioned hypertension as the most common known risk factor for stroke. The finding was similar to the study conducted by Oladapo et al., where they found that hypertension was mentioned as one of the most common known risk factors for stroke.[18] The findings also established that being overweight or obese increases a person's risk of developing heart disease. This corroborated other findings that show that obesity has been confirmed as one of the risk factors causing heart disease.[27] Obesity has been shown to increase morbidity and mortality and therefore, reducing life expectancy.[28] A majority of heart diseases could be prevented through diet and lifestyle modification.[12] Individuals can eat healthier food, rich in vegetables, fruits, and lean meats, along with a steady exercise routine.[29] Most respondents indicated that regular medical screening of one's blood pressure could reduce the risk of heart disease. This finding was in line with the statement from the Centers for Disease Control and Prevention, which stressed the importance of getting one's blood pressure checked regularly.[31] According to this report; the cost of "high blood pressure and its adverse health outcomes constitute economic burden to many nations".[31]

Lifestyle practices associated with modifiable risk factors for cardiovascular disease

Findings from both qualitative and quantitative data were consistencies in terms of lifestyle of the study population. Qualitative data show that participants admitted eating fatty foods or empty calorie foods. Results from the quantitative data also showed that most respondents ate fast foods, though occasionally. These buttressed the findings of Arts and colleagues, where young adults reported consumption of solid fats, added sugars and sodium; in addition to inadequate intakes of fruits and vegetables.[12,31,32]

Since the respondents are young population, they are in a high-risk phase of their future life development and unhealthy habits, especially unhealthy dietary pattern and lifestyles that are formed during this period of life may be difficult to change when they enter adulthood stage.

Thus, young adults must change their behaviour to reverse the possible trend of increasing risk factor levels susceptible to cardiovascular diseases. Knowledge is a necessary condition for behaviour change because without knowledge, there is no motivation to change. Knowledge of the modifiable risk factors against cardiovascular diseases is a pre-requisite to achieving successful prevention and treatment goals. The findings from this study provide an insight into the fact that as much as knowledge is very essential in health promotion interventions programmes, it may not on its own bring the expected change. Effective intervention needs to consider behavioural change communication strategies and provision of the enabling environment that will encourage university undergraduates have a change of reasoning and adopt behaviour change that will foster healthy practices. These will include no smoking, healthy eating pattern and physical exercise. Environmental stimulus towards positive behaviour change may include using the students' meeting points and social media platforms of the university as points of engaging them within their institutional setting. These may include the use of recreation rooms/students' lounge and the university web-page to create more awareness on dangers associated with practices that may predispose to cardiovascular diseases. Peer group can be created to provide counselling to the undergraduates and health talk from the health workers from the university health center can be organised for evidence-based information from health practitioners that will focus on modifiable factors for cardiovascular diseases. The university General Study Program curriculum should contain information on healthy living and the course can be made compulsory to all the undergraduates. The course should focus more on add-on teachings, where undergraduates will be exposed to practical lessons on physical exercise, healthy diets, determination to quit smoking and consumption of alcohol among others, which will promote practice in addition to the basic knowledge on prevention of cardiovascular diseases.

Conclusion

The result of this study revealed that there was good knowledge of modifiable risk factors against cardiovascular diseases and knowledge of preventive behaviours among the undergraduates. However, some of these undergraduates still engaged in unhealthy dietary practices and lifestyles. Therefore, the findings from this study have supported the evidence that gaps exist among the respondents regarding translating knowledge to practice. This was revealed through poor dietary practices, smoking and consumption of alcohol and intake of fatty

foods, which negate healthy lifestyle practices; despite having the requisite knowledge.

Control measures against non-communicable diseases are possible with proper prevention and treatment strategies focusing on the modifiable environmental causes, and personal habits. This information can be applied to individuals and groups to improve health and to stall the anticipated epidemic of non-communicable diseases among the study population. Health promotion and education interventions, which target the modifiable risk factors for cardiovascular diseases, especially dietary intake and lifestyle modifications will go a long way in reducing the incidence and prevalence of cardiovascular diseases among this population.

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ORIGINAL PAPER

Paulina Hejda [1(ABCF)], Agnieszka Hubert-Lutecka [1(DEG)], Zdzisława Chmiel [1(ABH)], Adam Sidor [2(GEH)], Grażyna Iwanowicz-Palus [3(BEF)], Marcin Żal [4(CFD)], Agnieszka Koryl [5(DFG)], Monika Binkowska-Bury [1(BDG)]

Behaviors, attitudes and opinions of medical students in the field of smoking and anti-smoking counseling in two countries of Central and Eastern Europe

[1] Institute of Health Sciences, Medical College of Rzeszow University, Rzeszow, Poland
[2] Voivodship Sanitary and Epidemiological Station in Rzeszow, Rzeszow, Poland
[3] Medical University of Lublin, Lublin, Poland
[4] Provincial Military Staff in Krakow, Krakow, Poland
[5] Faculty of Sociology and History, University of Rzeszow, Rzeszow, Poland

ABSTRACT

Introduction. Europe is the region with the greatest proportion of deaths (16%) attributable to tobacco smoking worldwide. Medical students and physicians should set an example of tobacco-smoking abstinence for their patients.

Aim. The aim of the study was to compare opinions on behaviors and attitudes of Czech and Polish medical students about tobacco smoking and the position of a physician in anti-smoking counseling.

Material and methods. The Global Health Professions Student Survey (GHPSS) was conducted among 707 medical students in Czech Republic in 2011 and among 1164 medical students in Poland.

Results. Twety percent of polish and 25,7% of Czech medical students declared current tobacco smoking. Eighty-one percent in Poland and 60% in Czech Republic felt that physicians should be trained in smoking cessation techniques but only 27% of the medical students in Poland and 2,8% in Czech Republic , declared that such a course had been realized during the course of their education.

Conclusion. Over a fifth of Polish students and a quarter of Czech students declared themselves as active smokers. It is worrying that about half of Polish students were exposed to environmental tobacco smoke, while only one-fifth of Czech students declared such exposure. Polish and Czech students agreed that the doctor will play an important role in the patient's smoking cessation process and that physicians should give advice on quitting smoking.

Keywords. anti-smoking education, cessation training, ciggarete smoking, medical students, tobbaco smoking

Corresponding author: Paulina Hejda, e-mail: paulina.hejda@wp.pl

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Introduction

Smoking is a very important and current social and health problem throughout Europe and the main risk factor for most of the leading causes of death.[1] Tobacco smoking is a financial burden on economies and European healthcare systems.[2] Around eighty percent of the 1.1 billion smokers worldwide live in low and middle-income countries where the burden of tobacco-related illness and death is heaviest.[3] Every year more than 1.6 million Europeans die from smoking ciggaretes and it making Europe the region with the greatest proportion of deaths (16%) attributable to tobacco smoking worldwide.[4] In developed countries, smoking has been associated with a loss of at least a decade of life. Cessation before the age of 40 years, can dramatically reduce the risk of death and significantly improve quality of life.[5] Smoking has historically been and continues to be one of the key factors shaping the health of adult european people.[6] The term "smoking" is valid for people who have smoked more than 100 cigarettes over their lifetime and is one of the main and most common risk factors for many diseases.[7] Most European countries established laws against smoking in public places to protect from tobacco epidemic.[8] Early initiation of tobacco smoking is associated with increased risk of smoking-related mortality and morbidity.[9,10]

Smoking is one of the most important modifiable risk factors for cardiovascular disease and the leading cause of death in the European population. Even a small amount of tobacco smoke (eg several cigarettes a day, occasional smoking or passive smoking) increase the incidence of cardiovascular events. Smokers are burdened with a significantly higher risk of abdominal aortic aneurysm, coronary heart disease, sudden cardiac death and peripheral atherosclerosis. Smoking is one of the main modifiable causes of stroke, it is also an important factor in the development of dementia and Alzheimer's disease. The prevalence of tobacco smoking is still declining in Europe, which is mainly related to more restrictive national regulations that have been introduced over time.[11-13] Second-hand smoke is the smoke that fills restaurants, offices or other enclosed spaces when people burn tobacco products such as cigarettes, bidis and water-pipes. There are more than four thousents chemicals in tobacco smoke of which at least 250 are known to be harmful and more than 50 are known to cause cancer.[3,14] Second-hand smoking also known as environmental tobacco smoking, is the inhalation of smoke by a nonsmoker, released from the burning tobacco or exhaled by the smoker.[15,16] Passive smoking is the third after drinking alcohol and active smoking the cause of avoidable deaths. The main place of exposure to passive inhalation of tobacco smoke is the home environment. It is estimated that the number of deaths caused by exposure to tobacco smoke in homes is about ten times higher compared to exposure to environmental tobacco smoking only in the workplace. Non-smoking man, staying an hour in smoky room, absorbs such a quantity nitrosamines, which is found in the main stream of filter cigarettes, and benzopyrene, as much as he would have consumed by burning four cigarettes. A person exposed to daily smoke inhalation tobacco, has a 15% higher risk of death compared to a person without such exposure.[17-19] There is no risk-free level of secondhand smoke exposure.[20,21] Despite the transfer of socjety knowledge about the negative health consequences of tobacco use, a high percentage of adults continue to be addicted to this habit. Therefore, it seems justifiable to recognize risky behaviours in the area of the use of tobacco products among university students.[22] Particularly rich knowledge on topic of the negative impact of tobacco use on the state health should be demonstrated by medical students. Knowledge and related to the behavior of future physicians are particularly important for two reasons: first, this group should be a pattern of behavior for socjety pro-health, secondly in the future professional work will be obliged to provide comprehensive treatment (pharmacological and non-pharmacological: counseling and psychological support) of tobacco addiction.[23] Physicians as should set an example of tobacco-smoking abstinence for their patients. Tobbaco smoking among medical students, as well as physicians, has been a research subject for many years.[24] Treatment of tobacco addiction should be part of health care in which the role of a health care professional should be crucial in tobacco control advice - should range from short intervention at every contact with a smoking patient, to intensive and long-term treatment including both psychosocial and behavioral support as well as appropriate pharmacotherapies. According to the WHO recommendations, this formula should apply to all professions in clinical medicine - mainly to physician, nurses, pharmacists and dentists, and the costs of the activities carried out should be covered within healthcare systems. From an economic point of view, this would be one of the most cost-effective interventions in medicine.[25,26]

In the Czech Republic, approximately 22,000 people die annually as a result of diseases directly related to smoking, and most of them die prematurely before the age of 69. This means that smoking each year contributes to the premature death of 42% of men and 9% of women, which on average shortens the lives of smokers by about 15 years. The Czech Republic is in the group of 10 European countries where the incidence and mortality caused by malignant tumors is the highest. They are also in the lead of countries with the highest number of cigarettes smoked per one inhabitant. It is also disturbing that over 60% of Czech children are exposed to passive smoking in their family homes.[27-30] In Poland,

smoking is still a major health problem. Polish society occupies the third place in Europe in the consumption of tobacco per capita.[6,31]

Aim

The aim of the study was to compare opinions on behaviors and attitudes of Czech and Polish medical students about tobacco smoking and the position of a physician in anti-smoking counseling.

Material and methods

The basis of the analysis was a standardized international GHPSS study (Global Health Professions Student Survey) created by experts of the World Health Organization (WHO) and the United States Centers of Disease Control and Prevention (CDC). The Global Health Professions Student Survey (GHPSS) was developed in 2004 to collect data on tobacco use and cessation counseling among the medical students, it has a standardized methodology for selecting participating schools and classes. Methodology, questionnaires and scope of the study have been developed by experts from the Tobacco Free Initiative (TFI). The study population consisted of students of the third year of medical studies (medicine). These survey results have generated valuable information about attitudes, beliefs and behavior related to tobacco control among medical students, and provide a valuable source of information to develop tobacco control policies and intervention programs.[32] In Czech republic, GHPSS, which was carried out in 2011, covered 707 medical students from 11 medical universities. In Poland the survey was conducted in 2010 and covered 1219 medical students from 5 medical universities. In the study conducted in the Czech Republic, the response rate was 85.5% and in Poland 89,9% among medical students.

The questionnaire

The tool used in this study was validated anonymous and self-administered the The Global Health Professions Student Survey questionnaire. The tool used in this study was from the The Global Health Professions Student Survey questionnaire. The original version (English version) of the questionnaire was used in Czech Republic. The questionnaire for Polish students has been translated from English and tested by the WHO department in Poland. The WHO collaborators adapted, a questionnaire by adding questions about local forms of tobacco, native language questionnaires were back-translated to English - to check compatibility with the main questionnaire. Questionnaires were administered during regular class sessions in accordance with the protocol developed by WHO. The questionnaire was an anonymous, self-administrated, filled in by the students during regular classes. Questionnaire contained 42 questions covering six categories. The first one concerned the current cigarette smoking by the respondent, the second - exposure to environmental tobacco smoke, the third included questions regarding the attitudes of the respondent to the smoking ban and the role of health care workers in the field of antitobacco counseling, the fourth related to nicotine addiction and attempts to break with addiction, fifth - it included questions about the level of education of the subject in the field of anti-tobacco intervention obtained during studies, and the last category was created for obtaining socio-demographic data. As a current smoker, the respondent was defined who declared that he had smoked cigarettes at least once during the 30 days preceding the examination. The GHPSS questionnaire had questions about local forms of tobacco consumed in each country. The section called: "Current use of tobacco products other than cigarettes" was defined as using bidis, pipes, snuff, e- cigarettes, cigars and chewing tobacco on one or more days during the past 30 days. The students' attitudes towards the total ban on smoking in restaurants, nightclubs and music clubs and bars were analyzed, as well as the position regarding the ban on smoking in all public places. Special attention was paid to the attitudes of students regarding the position of the doctor in creating patients' attitudes with particular emphasis on his role in providing anti-smoking advice and help in giving up smoking - including the status of smoking by the doctor and the frequency of his advice encouraging patients to quit addiction. The next analyzed variables concerned the trainings in the field of techniques supporting the quitting of smoking and the respondents' expectations regarding the education and significance of using educational materials for patients in this field. Additional variables included in the analysis included socio-demographic characteristics: gender and age of students.

Statistical analysis

The main purpose of statistical analysis was to compare the opinions of medical students in Poland and the Czech Republic regarding smoking and the position of a physician in the process of quitting smoking. Opinions were also analyzed regarding the usefulness of the anti-nicotine counseling suggested by the physican, and his practical skills. Student attitudes regarding total smoking bans in public places were also assessed and compared. The chi square test of independence was used to calculate p values. Statistical analyzes were performed using STATISTICA 13. Given the lack of data on smoking status for 4 medical students in the Czech Republic and 55 in Poland, a total of 703 and 1164 students were included respectively.

Results

More than 95% of the medical students in Poland and nearly 93% medical students in Czech Republic were 20-24 years (Tab.1). Sixty five percent of the medical students in Czech Repulic and 64% of the medical students in Poland were women (p<0.05).

Table 1. Characteristics of the study sample, exposure to secon-hand smoke, prevalence and regulations of smoking at the universities, attitudes toward smoking in public places

Variable		Czech Medical Students N=707	Poland Medical Students N=1219	p
Age (years)	≤20	6	47	–
	20-24	655	1157	
	≥25	45	12	
Gender	male	247	433	0.754
	female	459	780	
Currently smoked cigarettes	Yes	137	313	–
	No	566	851	
Exposed to second-hand smoke at home within past week	Yes	190	597	–
	No	517	619	
Exposed to second-hand smoke in public places within past week	Yes	333	867	–
	No	374	350	
School had ban on smoking in school building	Yes	696	1120	–
	No	111	89	
Tobacco-free environment is enforced at University	Yes	660	704	–
	No	40	502	
Ever smoked cigarettes in school buildings during the past year	Never	185	419	–
	Yes	61	51	
	No	460	660	
Smoking should be banned in restaurant	Yes	640	1027	0.135
	No	61	125	
Smoking should be banned in discos/bars/pubs	Yes	469	781	0.750
	No	232	374	
Smoking should be banned in all enclosed public places	Yes	571	886	0.012
	No	131	274	

Tobbaco smoking was declared by 20% of medical students in the Czech Republic and 25.7% of medical students in Poland. Exposure to Environmental Tobacco Smoke (ETS) in the home during the last week preceding the survey was declared by 26.8% of medical students of Czech universities and as many as nearly half (49.1%) of medical students surveyed in Poland, while exposure to this factor in public places indicated 47% and 71.2%, respectively. The existence of a smoking ban in the university building was indicated by 98.4% of respondents in the Czech Republic and 91.9% of the medical students in Poland. About 94% of Czech students and only 57.7% of Polish students said that compliance with this prohibition is enforced by the university authorities, in addition, nearly 9% of Polish and 5% of Czech students declared smoking in the university building during the last year . Over 90% of Czech students declared support for a total ban on smoking in restaurants, 67% of medical students support smoking in bars, nightclubs and music, and nearly 80% of respondents are for a total ban on smoking in all public places. Substantial relations were noted in the case of smokers and non-smokers. In Poland, support for a total ban on smoking in restaurants was declared by 89% of the medical students. Fewer students (over 65%) expressed support for the ban on smoking in bars, pubs and nightclubs. Support for a total ban on smoking in all public places was declared by more than 76% of the students (p<0.05).

Table 2. Opinions of medical students from Poland and the Czech Republic regarding the role of a physician in the process of smoking cessation of their patients, practical skills in the anti-tobacco counseling obtained during the education

Variable		Czech Medical Students N=707	Poland Medical Students N=1219	p
The physician serve as role models for their patients	Yes	369	1006	-----
	No	333	140	---
The physician have a role in giving advice or information about smoking cessation to patients	Yes	574	981	0.016
	No	127	159	
The physician who smoke is less likely to advice patients to stop smoking	Yes	463	649	-----
	No	238	495	---
Patients have more chances to quit smoking if advised by physician	Yes	480	865	0.004
	No	222	295	
The physician should regularly advise smokers to quit	Yes	633	1074	0,063
	No	70	87	
The physician should get specific training in cessation techniques	Yes	423	928	-----
	No	280	219	---
Any formal training in smoking cessation approaches to use with patients in their medical school training	Yes	20	311	-----
	No	682	850	---
Training about importance to provide educational materials to support smoking cessation to patients who want to quit	Yes	258	409	0,851
	No	442	714	

Only slightly more than half of the medical students in the Czech Republic (53%) and nearly 88% of the polish students felt that a physician plays an important role in creating patients' attitudes (Tab. 2). However, 82% of czech students and 86 % polish medical students admitted that the physician plays an important role in advice on quitting tobacco and said that patients have a better chance of quitting if they get doctor's professional advice on anti-smoking therapy (68% of medical students in Czech Republic and 75% in Poland) (p<0.05). The majority, i.e. 68% of medical students in Czech Republic and 56,7% in Poland, claimed that, in the case when a physician smoked, he was less inclined to provide their patients with smoking cessation advice. A similar proportion of the respondents saw an import-

ant role in providing anti-tobacco advice to patients and nearly 90% polish students and 82% czech students believed that physicians should provide smoking cessation advice ($p<0.05$). In Poland 57% and 66% of the medical students (66% in Czech Republic) claimed that, in the case when a physician smoked, he was less inclined to provide their patients with smoking cessation advice. Majority of the respondents expressed the opinion that the patients' chances of quitting smoking increased if a heath professional advised them to quit (75% medical students in Poland and 68% in Czech Republic). Most of the surveyed students (81% of the medical students in Poland and 60% in Czech Republic) felt that physicians should be trained in smoking cessation techniques. Unfortunetly, much smaller percentage of the respondents declared that such a course had been realized during the course of their study (27% of the medical students in Poland and only 2,8% in Czech Republic). A low percentage of the students declared that during their studies they had learned that it is important to provide the patients who want to quit smoking with educational materials to support smoking cessation (36% of the polish students and 37% of the czech medical students).

Discussion

The study showed that 19.8% of medical students studying in the Czech Republic were smoking cigarettes and nearly 26% of students were exposed to secondhand smoke in the home environment. Among Polish medical students, the percentage of smokers is as high as 26%. For comparison, China is the world's largest producer and consumer of tobacco products but analyzes carried out by Yang et al., indicate that the smoking prevalence among third-year medical students was relatively low (7.0%). The smoking prevalence among the third-year medical students was lower than rates reported in most other countries (over 10%). However, researchers have shown that the smoking prevalence among physicians is much higher (23%) in China.[32] In 2015, the World Health Organization's report on tobacco smoking reported that the percentage of people currently smoking in the Czech Republic was close to 29 in the group of adults and 30.6% in the group of youth in the age group 13-15. The World Health Organization in a report from 2017 reported that 24% of the Czech population smoked cigarettes.[27] The positive is, that the percentage of students smoking cigarettes in the analyzed study was lower than in the general population of smokers in the Czech Republic. Similar to the results obtained in the population of Czech medical students, it was observed in a study conducted in Latvia (19.6%), Slovenia (18%), higher in Germany (28%), Slovakia (29%), Spain (29%), Lithuania (30%) and in Italy (31%), while the highest percentage of students smoking cigarettes among the European countries covered by the GHPSS survey was recorded in Moldova (65%), Macedonia (53%) and Bulgaria (52%).[33-35] The percentage of smoking polish medical students (26%) in the study was high and similar to the nationwide survey on smoking attitudes (in 2011, the percentage of smokers in our country was 31%, in 2017 - 24%), similar results were obtained in the GATS study for the 20-29 age group - 32% of people smoked cigarettes. The World Health Organization published similar results - in 2017 tobacco smokers constituted one fourth of the Polish population. Analyzes carried out by Warren et al. indicate that in the majority of European countries in which this study was conducted, students who smoke are more than a third of the respondents.[33,36] In the analyzes carried out by Warren et al. out of more than 40 countries in which the GHPSS survey was carried out, in 50% of these countries, the percentage of students declaring current smoking exceeded 20%. Similar results to those observed in the population of Polish and Czech students were recorded in a study conducted in Italy (29%), Lithuania (30%), Slovakia (29%) and lower in Germany (22%) and Spain (16%). A higher percentage of smoking students was observed in Bulgaria (52%), Greece (39%) and Russia (65%).[37-39] Differences in the distribution of smoking in various countries may result from cultural differences - in China, there is practically no smoking occurrence among women who study at medical universities because it is related to cultural tradition and sanctions against women who smoke, especially unmarried women. Factors such as social acceptance, the lack of provisions sanctioning smoking in public places, conditions for advertising of cigarettes, economic conditions (low prices of tobacco products, better accessibility) and the level of medical care and public education regarding the harmfulness of smoking also contribute to the differences between countries. Similar results to those observed in our analyzes (among Czech and Polish medical students), regarding passive exposure to environmental tobacco smoke at home and in public places were recorded for other countries where the study was conducted in accordance with the GHPSS methodology (for example over 50% of medical students declared exposure to the environmental tobacco smoke (in home) and more than 70% in public places (in 29 out of 48 countries). In our analyzes, similarly to those recorded in Lithuania, Slovenia and Slovakia, over 90% of students indicated that the area of the university is subject to regulations prohibiting smoking. The lower percentage of students indicating the occurrence of these regulations was noted in other European countries. In the Czech population, over 90% of future physicians supported the ban on smoking cigarettes in restaurants, slightly less, about 80% of those polled expressed support for the introduction of such a ban in all public places. A large majority of Polish students also supported the ban on smoking in public plac-

es. The results obtained in the group of medical students are higher than for the general Polish society obtained in the GATS study, where 58% declared support for the ban on smoking in restaurants, while in bars, nightclubs and music clubs – only 37% of respondents. Higher than in Poland, the percentage of students supported the ban on smoking in public places in Germany and in Italy, lower - in Spain.[40,37] A significantly higher percentage of respondents in both populations was exposed to environmental tobacco smoke in the home environment and public places. It should be mentioned that in the Czech Republic during the research the least restrictive law regarding smoking in public places was in force. Compared to most European countries, in the Czech Republic it was possible to smoke cigarettes in places where it is strictly forbidden in other European countries. Currently, the Czech government has introduced a law banning smoking in all restaurants, pubs and bars. The vast majority of both Polish and Czech students declared that the physician plays an important role in anti-tobacco counseling and about 90% of Czech students and 92% of Polish students decided that he should give advice on quitting tobacco addiction. Similarly to the results we analyzed, over 80% of students expressed the opinion that the physician plays an important role in giving advice on quitting smoking in 42 out of 46 countries in which the study covered medical students. A significant percentage of students in both Poland and the Czech Republic, as well as in other countries, claim that a doctor should be trained in anti-tobacco techniques and advice. In spite of this, only close to 3% of the surveyed students in the Czech Republic and less than 27% of medical students in Poland pointed to the training during the studies in the field of techniques supporting the quitting of cigarettes. Only in 2 out of 48 countries included in the GHPSS study, over 40% of medical students declared participation in such training.[34,37,38,41]

Conclusion

Smoking by medical students in Poland and the Czech Republic is not uncommon. Analyzes carried out in the Czech Republic and Poland, as well as in other countries covered by the GHPSS study, indicate the urgent need to include practical activities during medical studies in the field of anti-smoking counseling. Over a fifth of Polish students and a quarter of Czech students declared themselves as active smokers. It is worrying that about half of Polish students were exposed to environmental tobacco smoke, while only one-fifth of Czech students declared such exposure. The overwhelming majority of students from these two countries confirmed the existence of a smoking ban in the university building, but worrying her that only more than half of Polish students said that the ban was observed (compared to Czech future doctors, where compliance with this ban was indicated by more than 90 percentage of students). Students representing both surveyed nationalities mostly agreed in favor of a total ban on smoking in all public places. The vast majority of Polish students expressed the opinion that the physician plays an important role in shaping the attitudes of the health of patients among Czech citizens a little more than half of the students expressed this conviction. Polish and Czech students agreed that the doctor will play an important role in the patient's smoking cessation process and that physicians should give advice on quitting smoking. Over twenty percent more Polish students compared to students studying in the Czech Republic expressed the opinion about the need to train future doctors in the techniques of quitting smoking. A significant difference was visible in the case of students' declarations regarding such training during their studies. More than one-fifth of Polish students declared that they would undergo it, while Czech students declared that they did not undergo such training, however, they recognized that it could have a significant role in the process of quitting smoking by patients. Students are aware of the fact that future physicians have an important social role to play in disseminating knowledge in the field of public health and propagating preventive actions, including in the field of anti-tobacco counseling. Despite this, the classes carried out as part of medical studies do not include education in specific techniques, acquiring skills and knowledge necessary to help patients who want to quit smoking. The fight against tobacco addiction should be part of a broader strategy implemented by the all medical staff and aimed at reducing the overall risk of tobacco-related diseases, and consequently reduce mortality, morbidity and disability resulting from their occurrence.

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REVIEW PAPER

Kinga Szlachetka [1(ABDFG)], Paulina Kut [1(ABDFG)], Agnieszka Stępień [1,2,3(ABDFG)]

Cytotoxic and anticancer activity of *Moringa oleifera*

[1] Dietitians' Scientific Club section Food safety at Department of Dietetics, Institute of Health Sciences, College of Medical Sciences, University of Rzeszow, Rzeszów, Poland
[2] Centre for Innovative Research in Medical and Natural Sciences, Laboratory of Innovative Research in Dietetics, College of Medical Sciences, University of Rzeszow, Rzeszów, Poland
[3] Department of Dietetics, Institute of Health Sciences, College of Medical Sciences, University of Rzeszow, Rzeszów, Poland

ABSTRACT

Introduction. Given its very strong antioxidant properties, *Moringa oleifera* is particularly noteworthy among medicinal plants. The high contents antioxidants in the *M. oleifera* determining her antioxidant activities deciding for very important anticancer properties.

Aim. The aim of the paper is to provide an overview of the cytotoxic and anticancer activity of *Moringa oleifera*.

Material and methods. This review was performed based systematic analysis of literature.

Analysis of the literature. The results of scientific research conducted *in vitro* indicate that extracts from *Moringa oleifera* significantly affect the development of human cancer cells such as myeloma, leukemia, cervix, breast, colon, lung, liver, neuroblastoma, pancreas, colorectal, epidermoid, oral, ovarian, muscular, prostate, skin.

Conclusion. This indicates *Moringa oleifera* as that they may be used as a therapeutic agent to support oncological therapies.

Keywords. anticancer activity, cytotoxic activity, Moringa oleifera

Introduction

Owing to their highly-valued curative properties, herbaceous plants have been used in folk medicine. Medicinal effect of herbs depends on their contents of bioactive compounds with antioxidant properties.

Antioxidants, substances known for their health promoting properties, neutralise excess free radicals, this way preventing oxidative stress in the organism. Long-lasting oxidative stress increases a risk of inflammation which causes numerous diseases, e.g. cancer, heart failure, circulatory system disorders, and many more, that is why antioxidants are so important in preventing these conditions. Medicinal plants are a natural source of antioxidants, such as polyphenols, flavonoids, terpenes, saponins and azulenes.[1]

Given its very strong antioxidant properties, *Moringa oleifera* is particularly noteworthy among medicinal plants.

Corresponding author: Agnieszka Stępień, e-mail: astepienurz@gmail.com

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Moringa oleifera (synonyms: Guilandina moringa L., *Moringa moringa* (L.) small, *Moringa pterygosperma* Gaertn., MO, *Moringa oleifera Lam*), also referred to as horseradish tree or miracle tree, drumstick tree, ben oil tree, benzolive tree, moringa is the most commonly cultivated tree representing the monogenetic family *Moringaceae;* it reaches approximately 10 metres in height and is grown in Africa, Asia and Latin America (fig.1.). All parts of the tree are edible and they have high contents of amino acids, vitamins, and minerals, such as calcium, potassium, zinc, magnesium, iron, and copper.[2-5] Particularly notable, however, are the bioactive compounds contained including vitamins A, C and E, which are strong antioxidants, as well as polyphenolic compounds – quercetin and kaempferol, terpenoids, glycosides, tannins and saponins.[6-14] The high contents this antioxidants in the *M. oleifera* determining her antioxidant activities deciding for antiplatelet, hypotensive, antimicrobial, antiulcerous, anti-inflammatory, hypocholesterolemic, and hypoglycemic properties, and very important anticancer properties.[15-23]

Fig. 1. Dried herb leaves *Moringa oleifera* (photograph by Kinga Szlachetka)

Numerous scientific studies have shown that *M. oleifera* contains many bioactive compounds, among others alkaloids, flavonoids, and phenolic compounds determining the antioxidant and anti-cancer. These bioactive ingredients cause changes in the cycle of cancer cells. By inducing in the cell the mechanism whose main element is the pathway covering the process of apoptosis, i.e. programmed cell death causing cell contraction, DNA fragmentation, cell membrane changes, chromatin, consequently leading to death of the apopoptotic cell. Antioxidants also have an effect on inhibiting the proliferation of cancer cells. Molecular change observed in cancer cells is a decrease of the proliferation (cytostatic effect) and the like and decrease in cell survival rate due to the induction of apoptosis (cytotoxic effect) significantly affecting the properties of anti-cancer and cytotoxic *M. oleifera*.[18,24,25]

Aim

In this paper, we present the results of an analysis of the scientific literature of *in vitro* studies confirming the cytotoxic and anti-tumor properties of *Moringi oleifera* resulting from the ability to inhibit proliferation, induce apoptosis and cell cycle arrest.

Analysis of the literature

Parvathy and Umamaheshwari investigated the effects of extract from *Moringa oleifera* leaves in human multiple myeloma cell lines (U266 B1 human B-lymphocyte plasmacytoma). The cells were incubated with MO leaf extract dissolved in methanol, ethanol, ethyl acetate and chloroform, and cytotoxicity testing was performed using neutral red dye uptake assay. The findings showed that methanol extract was characterised by the highest cytotoxic activity related to these cells. It was observed that even its small quantity significantly inhibited proliferation of these cells, which suggests its high anti-cancer activity.[26]

Another study also reports anticancer effect of *Moringa oleifera* leaf extract observed in primary cell lines of acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL), collected from patients, as well as a line of hepatocarcinoma cells (HepG2). Khalafalla et al. in their study identified anticancer effects of hot water, cold water and 80% ethanol extracts of moringa leaves in the primary cells of the two types of leukaemia and liver cancer. The findings related to cytotoxicity of these extracts, determined using MTT (the tetrazolium dye, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, showed the highest activity of the ethanolic extract with respect to both AML and ALL cells, while the hot water extract was more active than the cold water extract. In the case of HepG2 cells, hot water extract showed the strongest anticancer activity. [27]

A study by Varalakshmi and Nair examined anticancer properties of aqueous, methanol and hexane extracts of *Moringi oleifera* leaves with respect to cervix cancer cell line (HeLa) and normal human lymphocytes. Following incubation with *M.oleifera* extract, antiproliferative effects were assessed using MTT assays and trypan blue dye. Based on DNA fragmentation analysis performed using acridine orange–ethidium bromide (AO/EB), they identified apoptotic effect of these extracts. The findings showed good cytotoxicity of aqueous extract, depending on its concentration, with respect to cancer cells, compared to methanol and hexane extracts. However, aqueous extract produced the lowest cytotoxic effects in lymphocytes.[28]

Sreelatha et al. also evaluated the effects of an aqueous extract from *M. oleifera* (MO) leaves on a human tumor (KB) cell line derived from glandular cancer of cervix. After incubation of the KB cell culture with MO extract (0-200 ug/ml), based on the cell viability assess-

ment (MTT test) they showed its inhibitory effect on the cell proliferation increasing with concentration. The anti-proliferative effect of this extract resulted from the induction of apoptosis and morphological changes of cells determined by DAPI and propidium iodide staining. The authors point to the strong antiproliferative effect of *M. oleifera* leaf extract on cells of this type of cancer.[29]

In another study described the effects of *Moringa oleifera* seed methanolic extract on human cancer cell lines such as lung (A-549), liver (Hep-2), colon (502713 and HT-29) and neuroblastim (IMR-32). The cytotoxicity of this extract (100 μg/ml) was determined by these sulforhodamine B (SRB) dye test on this tumor cell lines. Growth inhibition was observed in the lung, colon HT-29 cell line and neuroblastima 80%, 95% and 93% respectively. In contrast, the results showed no cytotoxicity to the Hep-2 line, and the maximum for the colon cell line 502713.[30]

Likewise, a study by Tiloke et al. provided supporting evidence showing anticancer effects of aqueous extract of *Moringa oleifera leaves* in human cell line of lung cancer (A549). Following 24 h incubation of human cancer cell lines with MO extract the researchers assessed the level of oxidative stress (TBARS method) and the level of glutathione. Proapoptotic effect of aqueous extract of MO, on the other hand, was reflected by significantly increased expression of p53 protein and mRNA p53.[31]

In addition, subsequent studies determined the antitumor properties of the *Moringa oleifera* aqueous leaf extract against two human pancreatic cancer cell lines (Panc-1 and COLO-357). It was determined by means of colorimetric analysis and flow cytometry that MO extract inhibited the growth of pancreatic cancer cells of both tested lines. Test results showed that the highest inhibition of Panc-1 and COLO-357 cell growth was observed at a concentration of ≥0.75 mg/ml extract.[32]

Charoensin et al. investigated anticancer properties of *M. oleifera* leaves in relation to human cell lines of hepatocarcinoma (HepG2), colorectal adenocarcinoma (Caco-2) and breast adenocarcinoma (MCF-7). Cytotoxicity of methanol and dichloromethane extract with respect to cancer cell lines was assessed using MTT assay, and chemoprevention was examined using quinone reductase induction testing. The findings showed greater anticancer effect of dichloromethane extract in the cells of Hep G2 and MCF-2 as well as greater chemopreventive effect.[33]

In subsequent studies, Jung et al. have shown anti-tumor activity of *Moringi oleifera* leaf extract against human cancer line lung (A549). They observed that an aqueous extract (300 mg/ml) of MO strongly induced apoptosis, inhibited the growth of cancer cells and lowered the level of internal reactive oxygen species (ROS) in human lung cancer cells.[34]

Activity of *Moringa oleifera* leaves and bark in relation to human cancer cell lines of breast (MDA-MB-231) and colorectal (HCT-8) was investigated by Al-Asmari et al. They determined that the extracts, by inducing apoptosis and inhibiting cell cycles, produced phenotype changes in the cells of both cancers and cell death.[35]

Similarly, a study carried out by Jung presented evidence for antiproliferation effect of extract from *Moringa oleifera* leaves. Following incubation of human cell line of hepatocellular carcinoma (HepG2) with aqueous extract of *Moringa* leaves, flow cytometry was applied to assess effects in DNA content and cell cycle stages. It was found that the extract induced apoptosis of cancer cells.[36]

Other studies have determined the antitumor effect of extracts (n-hexane, chloroform, ethyl acetate, 50% methanol) from *M. oleifera* leaves and 15 fractions of ethyl acetate extract (F1 to F15) against human epidermoid cancer cell line (Hep2). After incubation, cell viability was assessed by sulforodamine B staining. Among all tested MO extracts and fractions, the isolated F1 fraction showed the highest cytotoxic activity against tumor cells. It was found through the use of *High-Performance Thin-Layer Chromatography* (HPTLC) technique that F1 contains a large amount of antioxidants – phenolic compounds that affect these properties.[37]

Kaur et al. analyzed the chemical composition of the obtained methanolic extract from *M.oleifera* leaves. They isolated and identified on the basis of melting point, Nuclear Magnetic Resonance (13C-NMR, 1H-NMR), Infrared Spectroscopy (IR), Fast Atom Bombardment Mass Spectrometry (FAB-MS) chemical compound β-D-glucopyranosidetetradecanoate belonging to the group of antioxidant flananoids. They then evaluated its cytotoxic activity against human cancer cell line colon (Colo-320DM), oral (KB-403), ovary (PA-1), breast (MCF-7). After incubation, the cytotoxicity of this compound was assessed by the MTT test on the tested tumor lines. Inhibition of cell growth of the Colo-320 DM line was observed already at a concentration of 2.52 μg/ml of this flanovide, while for KB-403 at 3.62 μg/ml, for Pa-1 at 6.46 μg/ml and MCF-7 at 10.00 μg/ml. The results indicate that this compound has the highest cytotoxicity against colon cancer compared to the other 3 lines.[38]

Milungo et al. examined the antiproliferative activity of extracts (50% methanol in dichloromethane) from *Moringa oleifera* leaves against human liver (Hep-G2) and muscular (RD). After incubation with the MO leaf extract, tumor cell viability (crystal violet staining and Optical Density measurement) was assessed. Significant inhibition of cell growth of both tumor lines was observed already at 0.017 mg/ml extract concentration for the RD line and at 0.50 mg/ml higher concentration for Hep-G2.[39]

In subsequent studies, researchers analyzed the effect of *M.oleifera* leaf extract on human cancer cell lines ovarian (A2780CP20) and prostate (PC3). By using colorimetric analysis with the AlamarBlue dye after exposure of both tumor cell lines with extract, their viability was assessed. It was observed that the concentration of the extract inhibiting the growth of A2780CP20 cells was 0.27 mg/ml and for prostate cancer cells 0.17 mg/ml.[40]

Madi et al. presented the results of research on the antitumor activity of *Moringi oleifera* leaf extract against human cancer cell line lung (A549), liver (Hep-G2), colon (CaCo2), leukemia-associated T cells (Jurkat). All tumor cell lines were incubated with an aqueous extract (dried leaf powder soaked in hot water) of varying concentration (0.05-2.5%). Subsequently, after incubation, cell viability was determined by MTT test and the anti-proliferative effect of MO extract on them was assessed. It was observed that the MO extract caused a decrease in the viability of all tested cell line types depending on the concentration of the extract. However, the most cytotoxic effect was already determined at 0.05% of the extract used versus A549 compared to Jurkat, Caco2, Hep2 at 0.1-0.4%.[41]

Guon and Chung conducted scientific studies to evaluate the effect of *Moringa oleifera* fruit extract on human melanoma cells (A2058). It was observed thanks to the MTT test that the Moringa oleifera fruit extract significantly inhibited the viability of A2058 cells and propagated their apoptosis depending on the concentration (0-200 μg / ml). It was determined that at concentrations of 150 and 200 μg/ml MO extract there was a significant reduction in the proliferation of these cells, to 11.3 and 10.1%, respectively. Thanks to the double staining test for Annexin V-PI to distinguish the stages of apoptosis, it was found that *Moringa oleifera* fruit extract effectively induces mitochondrial apoptosis of A2058 cells.[42]

Subsequent results of the conducted tests showed the cytotoxic properties of *Moringa oleifera Lam* leaves against the colon cancer cell line (HCT116). The obtained methanolic MO leaf extract was fractionated by column fraction chromatography (MOL1-MOL4). It was determined by MTT and Western blotting that the fractions showed high antiproliferative activity against HCT116 cells especially MOL2, MOL3 and MOL4.[43]

Adebayo et al. analyzed the cytotoxic activity of *Moringa oleifera* seeds on a breast cancer cell line (MCF7). The obtained aqueous and ethanol extracts from MO seeds were divided into 4 fractions (hexane solvent, dichloromethane, chloroform and n-butanol). It was determined by MTT that all fractions showed high antiproliferative activity on MCF7 cells. The MO seed extracts analyzed inhibited the multiplication of MCF7 cells, aqueous at 280 μg/ml, respectively, and the hexane fractions 130 μg / ml and dichloromethane, respectively 26 μg/ml.[44]

Jinghua et al. investigated antioxidative potential of extract from MO leaves and they described molecular mechanisms associated with its anticancer activity. Following incubation of human cell line of colon cancer with hexane extract from MO leaves, the researchers assessed toxicity using MTT assay, and examined apoptotic effects by measuring caspase activity. The findings showed cytotoxic effects of extract from MO leaves in these cancer cell lines. The study demonstrated that extract from leaves of *Moringa* significantly inhibits proliferation of colon cancer cells and induces cell death via mitochondrial pathway of apoptosis. The research shows the potential for using extracts from MO leaves in prevention and treatment of this type of cancer.[45]

In their research, Ndungu et al. evaluated the cytotoxic activity of *Moringa oleifera* leaf extracts against human breast cancer cell lines (HCC 1395), prostate (DU145) and cervix (Hela) and the non-cancer cell line (Vero). The presence of alkaloids, terpenoids, tannins, flavonoids, glycosides, phenols and saponins was determined in MO extracts. The effect of MO on the inhibition of tumor cell growth was assessed by MTT. It was observed that the methanol-dichloromethane extract of *M. oleifera* was characterized by higher activity than aqueous. All MO extracts showed antiproliferative activity against all cancer cell lines tested, and for the DU145 line already at 66.290 μg / ml. In contrast, *M. oleifera* extracts were not cytotoxic to Vero cells.[46]

However, Ali and et al. in their study they evaluated the cytotoxic activity against the human cancer cell line breast (MCF-7) extract from *Moringi oleifera* leaves. The study reported exposure of MCF-7 cell lines with seven types of extracts obtained. MO leaf extracts were obtained using two methods: extraction (ethanol, 2-propanol, acetone, petroleum ether, water-solvent) and soaking (ethanol, boiling water-solvent). Only the obtained extract (water as solvent extraction techniques) 81.77 ± 6.05 μg/ml showed cytotoxic activity against MCF-7 among all extracts used.[47]

In their research, Vipul and Vishal analyzed the antitumor effect of the extract (water: methanol, 30:70 v / v) of *Moringa oleifera* leaves on human cancer cell lines, prostate (DU-145), breast (MCF-7), hepatoma (HEP- 3B), myelogenous leukemia (K-562) and colorectal (HCT-15). It was determined by MTT that MO leaf extract induced dose-dependent inhibition of K-562 (32.43 μg/ml), DU-145 (42.74 μg/ml), and HCT-15 (5.21 μg/ml) cell proliferation), MCF-7 (24.76 μg / ml), HEP-3B (29.37 μg / ml). It was also determined that at these concentrations a significant fragmentation of DNA fragmentation for K-562, DU-145 and HCT-15 cell lines.[48]

Whereas Ju at el. focused their research on assessing the properties of the extract (water: ethanol, 20:80 v/v) of Moringa oleifera flowers against human prostate cancer (PC-3) cell lines. Observed thanks to the MTT test

and assessment of cell cycle progress using flow cytometry that this MO extract had significant activity on PC 3 cells at a dose of 6.25 μg / ml (48 h). It induced G1 phase cycle arrest and apoptosis as confirmed by Annexin V staining, and detected markers of immunoblot apoptosis lead to increased protein expression in caspase-3 activity, indicates induction of apoptosis. Researchers based on the obtained research results that extracts of *Moringa oleifera* flowers lead to phosphorylation / activation of AKT, which affects the upregulation of the BCL-2 and BCL-XL prosurvival genes; which binds and inhibits caspase 3/7/9 required for induction of apoptosis in prostate cancer.[49]

Research team Podesta et al. evaluated the effects of *M. oleifera* aqueous leaf and seed extract on human cell line lymphoid (Jurkat E6-1), monocytic leukemia patient (THP-1) and peripheral blood mononuclear cells (PBMC) from healthy donors. The results of this study showed antiproliferative assessment by the trypan blue and proapoptotic effect of aqueous extracts obtained from *M. oleifera* leaves and seeds on tumor lines but not against peripheral blood mononuclear cells (PBMCs). The proapoptotic effect of the MO seed extract (MOE-S) was associated with decreased expression of B-lymphoma protein (BCL2) and sirtuin-1 (SIRT1), which are involved in apoptosis.[50]

In other studies, the cytotoxic activity of the obtained ethanol extract from *M. oleifera* leaves and then fractionated with n-hexane against human breast cancer cell line (T47D) was determined. Hexane fraction MO extract (hMO) was shown at 235.58 μg/ml cytotoxic effect and inhibition of T47D cell proliferation. It was observed that the apoptosis of these cells determined by flow cytometry induced their slow death and cell cycle arrest at the G0-G1 and G2-M phases. However, thanks to immunocytochemical tests, hMO has been shown to reduce the expression of anti-apoptosis protein, Bcl-2 and cell cycle regulating protein, cyclin D1, in a concentration-dependent manner.[51]

Further researchers Tiloke et al. focused on assessing the apoptosis-inducing effect of an aqueous MO leaf extract on human liver hepatocellular carcinoma (HepG2) cells. Exposure of HepG2 cells to an aqueous MO extract resulted in a decrease in viability at 4.48 mg/ml (MTT test). It was also observed that it significantly increased lipid peroxidation (TBARS test), DNA damage (comet test). It was determined that in their cell cycle a significant decrease in G1, S and G2-M phases due to flow cytometry. Increased caspase-9, -3/7 activity was determined by luminometry, with a significant decrease in ATP levels indicative of apoptosis. And thanks to western blot analysis, a significant reduction in c-myc, p-Bcl2 and Hsp70 protein expression and a significant increase in Bax, Smac/DIABLO and PARP-1 cleavage also confirmed the pathway of apoptosis. Numerous results of the above studies indicate that MO water extract has the ability to induce cell cycle arrest and apoptosis in HepG2 cells.[52]

Do et al. evaluated the effect of the aqueous extract of *Moringa oleifera Lam* leaves. human malignant melanoma cells (A375), human metastatic melanoma cell (A2058) focusing on the assessment of molecular mechanisms (preventing proliferation, induction of apoptosis). It was determined by the WST-1 test that MO extract inhibited the growth of A375 cells more than A2058 cells in a dose-dependent manner (0 to 200 μg/ml). This cytotoxicity of the MO extract towards the A375 line decided that the researchers conducted further analyzes only for it. It was confirmed by Annexin V FITC test that MO extract induces apoptosis of A375 cells. The study results also showed that the MO extract increased the Bax / Bcl-2 ratio, decreased the mitochondrial membrane potential, and activated caspase 3/7, caspase 9, PARP and AIF translocation which led to apoptotic cell death.[53]

Conclusion

The results of scientific research presented in this review suggest the *Moringa oleifera* may be highly valued in medicine for its her the properties anticancer and cytotoxic. This suggests that M.oleifera could be used in the prevention and treatment of various types of cancer. However, it is necessary to conduct additional clinical tests involving human subjects, in order to confirm the positive contribution of *M. oleifera* in treatment of cancer, and it is equally important to assess its interactions with medication administered to patients with these conditions.

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REVIEW PAPER

Piotr Czarnecki [1(ABFGH)], Justyna Podgórska-Bednarz [1(ABFGH)], Lidia Perenc [1(ABFGH)]

Forms of physical activity of the elderly

Institute of Health Sciences, Medical College of Rzeszów University, Rzeszów, Poland

ABSTRACT

Introduction. Physical activity is known to be an important factor influencing health throughout human life. This issue has become crucial for public health due to the aging of the population in both developed and developing countries.

Aim. is to present a literature review on the forms of physical activity undertaken by the elderly, as well as on issues related to physical activity and the population aging.

Material and methods. The study was prepared on the basis of a review of Polish and foreign literature. The following databases and data sources were used: EBSCO, ScienceDirect and Google Scholar. An additional source of data were the websites of the Central Statistical Office. Strictly defined key phrases were used during the collection of literature. The work has been divided into thematic subsections on the aging of the society, the impact of physical activity on health and the main topic, i.e. forms of physical activity selected by the elderly.

Analysis of the literature. The number of elderly people in Polish society has increased by almost 3.7 million over three decades. Therefore, an important topic is prophylaxis aimed at increasing the number of days in good health, largely covering the broadly understood activation of the elderly. The available data indicate that only 12% of elderly people undertake physical activity once a week. The most common form of spending free time actively is walking (as many as 73% of people in this population declare this form of physical activity in one of the presented studies).

Conclusion. Organized forms of physical activity are undertaken much less frequently by the analyzed age group mainly due to financial limitations and limited availability of sports infrastructure.

Keywords. aging, epidemiology, physical activity

Introduction

Aging is a biological and natural process, however, means of extending the number of days older people maintain in good health are still being sought. Numerous studies show unequivocally that the process of structural and functional changes can be slowed down by selecting appropriate preventive methods resulting in the long-term maintenance of independence.[1,2] Adequate physical activity and its frequency positively affect the health of the elderly, the quality of their life and its duration which is in line with the goals of gerontological prevention.[3-5] Professional literature highlights that maintaining the health of the elderly at the highest possible level is crucial issue of the "successful aging". It has

Corresponding author: Piotr Czarnecki, e-mail: pier_czarneccki@interia.pl

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long been known that health, quality of life and physical activity are closely related to each other. In the case of an organism aging, various types of pathophysiological changes occur, which have a negative impact on functional abilities. This stage of life is inextricably linked with a gradual decline in physical fitness, an increase in the frequency of limitations resulting in disability and chronic diseases. It should also be remembered that in the world literature numerous reports indicate not only the essence of physical exercise as a factor of primary prevention, but also of secondary prevention in the case of many non-communicable diseases. In turn, the lack of physical activity is the so-called population-attributable risk (PAR).[4] However, it should be borne in mind that there is no amount of physical activity that can completely stop the natural aging process of the organism. There is also extensive evidence of the beneficial effects of physical activity not only on the physical sphere in the elderly, but also on the psychological and cognitive ones.[5] Moreover, long-term cohort studies conducted by Wen. et al. clearly confirmed the positive effect of physical activity on the decrease in mortality regardless of the cause. It also seems important that even a smaller amount of time than the recommended 150 minutes a week can also bring positive health effects. 15 minutes of daily physical activity (or 90 minutes on a weekly basis) of moderate intensity can be beneficial for those at risk of cardiovascular disease.[6] Thus, increasing the level of physical activity in older people is an important factor in supporting public health institutions and relieving the healthcare and social system.[7-8]

Aim

The aim of the present literature review is to show the forms of physical activity in the elderly. Additionally, the study covers issues related to physical activity and aging of the society.

Material and methods

The study was prepared on the basis of a review of Polish and foreign literature. For this purpose, the following databases and data sources were used: Medline, ScienceDirect and Google Scholar. An additional source of data were the websites of the Central Statistical Office.

Key phrases were used in the course of literature search. They included the following phrases: forms of physical activity of the elderly, the role of physical activity in maintaining health in the elderly, aging of the population or guidelines for physical activity of the elderly. They were created on the basis of the main keywords: physical activity, epidemiology, the elderly, aging, health. The following keywords were precisely used: a) demographic data: demography, elderly people, Poland, European Union; b) forms of physical activity of the elderly: physical activity, forms of activity, the elderly, health. Next, out of all papers found, the research team selected those that were relevant to the aim of the paper. The study presents data from various types of reports: research papers, reviews, analyzes of demographic data, and recommendations for physical activity in the elderly. A detailed description of the studies cited in the paper is presented in Table 1. Demographic data and some information on the physical activity of older people come from the databases of the Central Statistical Office, EUROSTAT, Public Opinion Research Center, World Health Organization and the Info Senior Report - Bank Association Polish.

The study was divided into thematic subsections on the aging of the society, the impact of physical activity and the main issue, i.e. forms of physical activity selected by the elderly. The presented literature includes items from the last 20 years in order to fully achieve the aim of the study.

Aging of the population

The aging of the population is a serious problem that Poland and other the European Union member states face. In Europe, as well as in highly developed non-European countries, the statistical life expectancy has increased by approx. 30 years compared to the beginning of the 20th century. These changes result from the technological progress and improved medical and hygienic conditions as well as access to food. Additionally, a low birth rate is observed in Poland, which becomes economic as well as social challenge for the state governments.[9-10] The life expectancy of Poles has been systematically extending, this tendency was particularly visible after 1991. Over the last 10 years, it has increased for men by over 4 years, and for women by over 3 years. In 1950, there were over 2 million people over 60, which constituted 8.3% of the total population of Poland, while in 2001, almost 6 million, i.e. 16% of the population. This group amounted to slightly over 9 million in 2017, which is 24% of the total population. Over the course of 3 decades, the number of elderly people in the society has increased by almost 3.7 million. The number of people in very old age, i.e. over 80 years of age, is also growing faster and faster.[9]

The share of the 65+ population is growing successively in each EU Member State (European Union), EFTA (European Free Trade Association) countries and candidate countries. Over the last decade (the period of 2007-2017), the share of the above-mentioned age group in the general population has increased by 2.4 percentage points across the EU. Eurostat (EUROPOP2015) forecast showing the aging of the population indicates that the EU population will be around 528.6 million in 2050, in 2080 there will be a significant decline to 518.8.[11] There is also a significant shift in the increase in the percentage of people aged 80 and 80+ in

Table 1. Comparison of papers cited in the study

Study type	Numer of patients/ participants/ cases	Randomi-zation	Control	Demographics of importance (age, sex)	Main outcome	Measures
Barbosa de Lira CA, Viana Taveira H, Rufo-Tavares E et al. Engagement in a Community Physical Activity Program and Its Effects Upon the Health-Related Quality of Life of Elderly People: A Cross-Sectional Study. Value Health Reg Issues – cross-sectional study	100 (active group) 100 (sedentary group)	-	yes	physical activity [PA] group: n = 50 woman, 30 men; sedentary [S] group; n = 50 woman, 30 men;	Mortality due to all-causes declined by 4% (95% CI 2·5-7·0) and all-cancer mortality by 1% (0·3-4·5) with every additional 15 min of exercise over the minimum amount of 15 min a daily training	36-Item Short-Form Health Survey (SF-36)
Wen CP, Wai JP, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. Lancet – prospektywne cohort study	416 175	-	-	199 265 men, 216 910 women	The risk of mortality was increased in inactive individuals - 17% (HR 1·17, 95% CI 1·10-1·24) compared with low intensity PA group	self-administered questionnaire
Wyszyńska J, Dereń K, Hausner I, Mazur A. Selected factors influencing the level of physical activity in the elderly. Eur J Clin Exp Med - survey research	100	-	-	85 women 15 men	Lack of correlation was found between the level of total physical activity and sex, place of residence and BMI of participants	IPAQ, questionnaire developed by the authors
Gosik B. Rekreacja i aktywność ruchowa starszych osób. Przykład mieszkańców województwa łódzkiego. Space - Society – Economy – survey research [Recreation and physical activity of elderly people. example of the inhabitants of the Lodzkie Voivodship] (in Polish)	400	-	-	252 women 148 men	Only 28.6% of seniors express the willingness to undertake physical activity, while 45.2% only to some extent, and 26.2% do not feel such a need at all.	questionnaire developed by the authors
Baj-Korpak J, Różański P, Soroka A, Wysokińska E. Motywy i bariery uczestnictwa osób starszych w rekreacji ruchowej. Rozprawy Społeczne – badanie ankietowe (diagnostic survey) [Motives and barriers of older people's participation in physical recreation.] (in Polish)	110	-	-	110 women	94% of the respondents declared taking up active forms of recreation. Cycling (50%), Nordic walking (22%) and swimming (20%) were the most frequently undertook.	questionnaire developed by the authors
Łysak A, Walentukiewicz A, Drabik J, Dąbrowski A, Rowiński R, Aktywność fizyczna i niektóre jej uwarunkowania w populacji seniorów województwa pomorskiego. Hygeia Public Health – survey research[Physical activity and some of its determinants in the population of seniors in the Pomeranian Province] (in Polish)	249	-	-	120 women 129 men	The most popular activity were short walks around the home. 66.8% of the respondents declared taking up such an activity a few times or more per week. Poor health conmdition or lack of need to be physically active were main obstacles.	questionnaire developed by PolSenior
Marchewka A, Junkiewicz M. Aktywność fizyczna w młodości a jakość życia w starszym wieku. Gerontologia Polska. – survey research[Physical activity in youth and the quality of life in old age.] (in Polish)	59	-	-	39 women 20 men	The level of physical activity declared >the age of 35 years has great statistical influence for the quality of life at the old age.	questionnaire developed by the authors
Hu L, Smith L, Imm K.R, Jackson S.E, Yang L. Physical activity modifies the association between depression and cognitive function in older adults. Journal of Affective Disorders – survey research	2604	-	-	1327 women 1277 men	Moderate-to-vigorous physical activity modifies the depression-cognition relationship and helps to preserve cognition function.	National Health and Nutrition Examination Survey
Wiech M, Prusik K, Kortas J, et al. Changes in the ranges of motion in the joints of the upper and lower extremities in elderly people under the influence of the Nordic walking training. Zmiany zakresów ruchów w stawach kończyn górnych i dolnych u osób starszych pod wpływem treningu Nordic. Journal Of Health Sciences – intervention study	56	-	-	46 women 10 men	3-month training program turned out to bring the expected results by increasing the range of motion in the joints	measurements of range of motion in selected joints with SFTR method using a goniometer
Stankiewicz B, Majchrowski A, Zukow W. Nordic Walking as an alternative form of physical recreation = Nordic Walking jako alternatywna forma rekreacji ruchowej. Journal of Health Sciences - survey research	40	-	-	36 women 4 men	Nordic Walking as a form of physical activity is suitable for a wide range of individuals, diverse in terms of age and efficiency.	questionnaire developed by the authors
Duana Y, Wagnerb P, Zhanga R, Wulffb H, Brehmc W. Physical activity areas in urban parks and their use by the elderly from two cities in China and Germany. Landscape and Urban Planning – observational study	Hong Kong n=317, Leipzig n=311	-	-	Hong Kong 148 women, 169 men Leipzig 182 women, 129 men	Males demonstrated more intensive and frequent physical activity than women in both cities. The preferred physical activity of the elderly in the parks was walking or cycling.	questionnaire developed by the authors

the EU population. Estimates indicate that in the period 2017-2050 this percentage will double and will amount to 12.7% (for comparison: 5.5% - the initial, actual value for 2017).[12]

Physical activity of the elderly

The level of activity of people aged 65+ in Poland is much lower than in other EU countries. The analyzes carried out by Eurostat show that only 16% of this group undertakes physical activity within the time range from 1 to 149 minutes a day (detailed data are presented in Table 2). The reasons for such low activity of seniors may be health factors such as: injuries, general poor health, disability, communication, movement and economic barriers. The data from 2017 state that the average amount of retirement pension paid under the Social Insurance Institution benefits was PLN 2,133 (calculations for March 2017). Its average value in the group of men was PLN 2,700, and for women PLN 1,615 (the average difference for the group of men and women was slightly over PLN 1,000). Statistical data for Poland indicate that the average monthly household budget surplus is PLN 328.[13] Therefore, the economic factor should not constitute the main barrier to the elderly people taking up physical activity, especially due to the fact that many forms of activity do not require additional financial outlays apart from costs of sport outfit and footwear.

Table 2. Time spent on health-promoting aerobic (non-work-related) physical activity by degree of urbanization after the age 65 - 2014 data[14]

	0 min.	1-149 min.	150-299 min.	150-300 min.	300 min. and more
Average (for city/suburbs/rural areas)	76.9	15.8	3.4	7.3	3.9
City	81.9	10.7	3.3	7.4	4.1
City and suburbs	75.1	17	3.4	7.9	4.5
Rural areas	73	20.2	3.4	6.8	3.5

A correlation was found between the place of residence and the level of activity of the elderly.

Gosik et al. focused on physical activity of seniors in the area of the former Łódź Province. One of the aspects of the study were the reasons why elderly people take up physical activity. The most frequently mentioned reasons were the improvement of well-being and fitness, which was declared by 25.9% of the respondents. Sequentially, the elderly indicated: medical recommendations (18.8%), improved sleep quality (16.8%), body weight normalization (8.1%) and better appearance (4.5%). Moreover, the researchers also asked about the reasons why elderly people do not take up physical activity. The percentage breakdown of responses for this aspect was as follows: 32.7% of seniors stated that they could not define them (no causes), 23.8% declared that it was due to poor health, only 2.1% stated that it was the lack of access to equipment/facilities. The respondents also mentioned other less frequent limitations, such as: lack of financial resources, preferring passive forms of rest, lack of company and laziness, with a similar low number of indications.[15]

Forms of activity of the elderly

According to Małgorzata Halecka and Jerzy Halecki study, active forms of spending free time by the elderly can be divided into 5 groups:

1. recreation and hobby including outdoor activities such as walking or gardening, and sports activities. This group also includes activities undertaken as a part of taking up passions and interests. A number of sedentary activities such as – going to the cinema, theatre, doing crafts, etc. are also covered here.

2.receptive - i.e. activities undertaken at home, such as: watching TV, listening to the radio, reading, etc.

3.public oriented - including public, political, social or parish activities,

4.integration - consisting in active support for the work of local societies or participation in scientific and training activities as a part of e.g. seniors' clubs or the University of the Third Age,

5. other types of activity - other individual forms not mentioned above.

These authors also identified the most common leisure time activities of the elderly and so successively: slightly over 84% of seniors watch TV, 64% listen to the radio, 54% read the press, 51% go for a walk, 35% visit friends and 39% relax in the garden.[16] These data were also confirmed by the study of the Public Opinion Research Center (CBOS), where 98% of seniors watch TV, 87% meet friends (at home), 81% go to church, 81% listen to music, 80% read, 77% visit relatives (outside home), 76% meet friends (outside home), 73% go for a walk and hike, 55% do gardening, 44% take care of grandchildren or great-grandchildren, 34% help with household chores, 29% support the family's economic activity, 22% look after ill or disabled relatives.[17]

Baj-Korpak et al. proved that the elderly more and more often choose active recreational activities of higher intensity, such as: cycling (50% of the respondents), Nordic Walking (22%), swimming (20%), jogging, dancing or fitness classes were chosen less frequently.[18] On the other hand, the analysis of the results of the study by Łysak et al. aimed at determining the most frequent forms of physical activity undertaken by the elderly showed that 66.8% walk, 32.3% do gardening and 22.2% go hiking.[19]

Analyzing the above results, it can be concluded that the elderly do not meet the recommendations of the World Health Organization (WHO) for this age group regarding physical activity. The forms of physical activ-

ity they choose are mainly sedentary and low-intensity physical effort. Note that many of the forms of physical activity mentioned in the study will depend on factors such as the season and weather conditions. In the literature on the subject, education, the level of social status or the type of previously performed work are mentioned as factors conditioning undertaking physical activity.[20]

An important aspect of participation in organized forms aimed at social activation and increasing the physical activity of this group of people is the positive impact on the quality of life. The study by Orzechowski indicated that participation in the classes of the University of the Third Age (UTA) can be a factor in preventing depression. Czopko et al. also pointed to the improvement of the quality of life of those participating in UTA classes.[21-22]

The aging process is an unavoidable biological process in which physical activity is an important preventive factor. According to Drabik, the optimal dose of physical activity in connection with the health assessment are important for prophylactic purposes [21,23], due to the previously mentioned fact of the increase in the population of people aged 65+. The purpose of using physical exercise in people aged 65 and over has not changed significantly. According to The American College of Sports Medicine and the American Heart Association, recommendations for physical activity remain the same for the general population, but the WHO proposes to supplement the guidelines with additional exercises to prevent falls (at a frequency of twice a week) (Table 3).

Table 3. Recommendations for the time of physical activity (PA) [24-26]

	WHO	ACSM/AHA	Tudor-Locke
Medium Intensity PA	at least 150 minutes a week	30 minutes at least 5 times a week	
High Intensity PA	at least 75 minutes a week	20 minutes at least 3 times a week	6,000 – 8,500 steps a day for healthy people
Mixed PA	possibility to split the duration into at least 10 minutes or longer PA throughout the day		3,500 – 5,500 steps a day for people with chronic diseases and the disabled
Strength training	8–10 strength exercises of large muscle groups, 8 to 12 repetitions performed 2–3 times a week		
Flexibility and balance training	At least twice a week		Minimum 200–300 kcal/training Over 1000 kcal/week Optimally above 2000 kcal/week
Resistance training		at least 2 x a week, 8-10 sets of exercises, 10-12 repetitions	

Abbreviations used in the tables: PA - physical activity, WHO – World Health Organization, ACSM - American College of Sports Medicine, AHA - American Heart Association

Physical activity plays a very important role in human life - exercise improves the biological state of the body, which translates into improvement in the mental, intellectual and social spheres.[27] It has also been proven that moderate and high intensity physical activity modifies the relationship between the incidence of depression and affects the level of cognitive functions. The studies indicate that as little as 150 minutes of moderate or high-intensity physical activity per week can prevent cognitive decline in people with symptoms of depression in an older age.[28]

Among seniors, various forms of exercise are promoted, they are intended to slow down the biological aging process of the body, prevent diseases typical of this period of life, counteract physical limitations, perform a recreational form or return to fitness from before the disease / injury.[29] It is recommended that the elderly performed exercises that primarily affected such aspects as endurance, balance, strength and flexibility. The literature on the subject mentions many forms of physical activity, the most frequently chosen ones are: walking, jogging, gymnastics, swimming, cycling, hiking, skiing, walking, yoga and ballroom dancing.[30]

At this point, it is appropriate to quote the results of the study by Fries, started in 1984, the main purpose of which was to determine the impact of regular running on the aging body. On the basis of monitoring the health of 500 regularly running elderly people for a period of 20 years, compared to the non-running controls, it was noted that: in the study group the number of deaths caused by cancer is lower, infections, cardiovascular diseases, nervous system diseases and other entities are less frequent . It has also been reported that running has a positive effect on life expectancy and maintaining overall physical fitness (thus delaying the time of dependency on other people's help).[31]

Recently, Nordic Walking has been very popular in this age group, hence Stankiewicz et al. conducted research on the impact of this form of exercise on the health of seniors.[32-34] Based on the analysis of the study results, they found a positive effect of Nordic Walking on body posture, weight loss and reduction of pain in the locomotor system. This activity also increases the circulatory and respiratory capacity of seniors. An important feature of its impact is the reduction of muscle tension and pain in the neck area and shoulder girdle. Nordic Walking involves almost 90% of all muscles, reduces the load on the joints of the lower extremities, and increases the mobility of the spine. March with poles also improves agility, balance and coordination.[34]

Another form of activity for the elderly considered to be one of the safest with holistic impact on the body is exercise in the water. Its natural properties are used while

exercising in an aquatic environment, such as: displacement (non-weight bearing activity), resistance and density (strengthening of muscle groups). This form of activity has a very beneficial effect on seniors. An additional advantage of exercising in an aquatic environment is the ability to perform movements that would be much more difficult or impossible to perform in other conditions.[35]

The literature on the subject also draws attention to the fact that the infrastructure is used to support various forms of physical activity. An interesting analysis in this regard was carried out by Duana et al., who studied the use of city parks as important places related to PA of seniors. The researchers took into account 6 city parks located in two cities of Hong Kong (China) and Leipzig (Germany). It has been shown that the most exploited part of the parks are the paths where the people observed most often walked (in the case of both cities) and cycled (only in the case of Leipzig). Sports fields and playgrounds were used more often by people surveyed in Hong Kong. In general, in both cities, older people undertook low-intensity PA, and statistically more often they were men. The authors of the work emphasized in their conclusions that such data should be taken into account when designing urban recreational areas.[36]

Haskell in his works emphasizes that the selection of an appropriate activity may depend on many physiological, demographic and environmental factors. He emphasizes the regularity that too small a "dose" will not have a positive effect on the functioning of the body, and too high will have a negative effect on its functioning. Many publications refer to health training involving large muscle groups, which is continuous (uninterrupted for several to several minutes) - aerobic training. This type of activity includes: marching, walking, cycling, cross-country skiing, swimming, rowing and running. Systematic aerobic training improves the efficiency of the system. In addition to this type of exercise, resistance exercises (strength) and stretching exercises should be included. The first part of the exercises should be a 7-10 minute warm-up, the final part should be low-intensity breathing and calming exercises that last 7 to 10 minutes.[37]

Conclusion

The aging of the society is a phenomenon important from the socio-political perspective. The governments should be guided by the very current motto of Juwenalis "Mens sana in corpore sano" - "In a healthy body, healthy mind" and through integrated social efforts aimed at the physical activation of the elderly aimed at improving their health and functional state should fulfil the constitutional duty of the state which is to provide health care to specific groups such as children, pregnant women, disabled people and the elderly [art. 68 of the Constitution of the Republic of Poland].

The data available in the literature show that 1% of elderly people regularly practice sports, and 30% regularly walks. Overall, only 12% of people at the age of 60+ undertakes physical activity at least once a week.[38] The choice of PA itself is often determined by the existence of financial, social and health limitations, especially the relatively high costs of activities offered by the fitness club in relation to monthly unused funds remaining in households. However, it should be borne in mind that thanks to various pro-health programs and support from governmental and non-governmental organizations, the availability of various infrastructure facilities, e.g. outdoor gyms, which are a part of land development, both in cities and in rural areas, or health paths enabling cost-free undertaking of physical activity.

Certainly, it would be not without significance to promote physical activity as a preventive and health-enhancing measure in this social subpopulation.[39-42] These efforts should be undertaken by people who are authorities in the field of health, such as primary care physicians. Going further, the availability of various organized forms of physical activity strictly dedicated to the elderly should be improved.[43-47] Also in rural areas, thanks to systemic support solutions.[48] All these activities will result in a modification of the current style of spending free time by seniors, and this in turn should translate into a delay in the negative effects of the aging process in the coming years, as well as a reduction in state budget funds allocated to convalescence and care among people over 65 years of age. Programs dedicated to the elderly should take into account individual interests and needs.[49]

The well-known fact that PA is a relatively accessible, cheap and simple form of maintaining the body in good health is increasingly used in various prevention programs and programs aimed at activating the elderly, but there is still a need for many changes, which can be summarized as follows [25, 50- 51]:

1. Social awareness of the importance of regular physical activity for health, fitness and mental condition should be increased,
2. It is necessary to implement popularizing and preventive programs activating the elderly,
3. It is important to encourage older people to participate in such programs by showing them tangible benefits,
4. It seems crucial to involve doctors in the cooperation, promoting movement among their patients as one of the methods of counteracting the negative effects of aging,
5. An important aspect is to increase the variety of classes in fitness clubs, while encouraging older people to take advantage of the rich offer,
6. Consideration should also be given to improving the accessibility to activities organized in the autumn and winter period,

7. The share of financing costs related to physical activity of the elderly by local governments should be increased.

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CASUISTIC PAPER

Fatma Hüsniye Dilek [1(ABDF)], Furkan Tosun [2(CG)], Arif Atay [2(DG)], Osman Nuri Dilek [2(AFG)]

Pancreatic tumor metastasis to the navel in a case with three primary tumors – case report and review of the literature

[1] Department of Pathology, School of Medicine, İzmir Katip Celebi University, İzmir, Turkey
[2] Department of Surgery, School of Medicine, İzmir Katip Celebi University, İzmir, Turkey

ABSTRACT

Introduction. Sister Mary Joseph nodule (SMJN) is a metastasis that can occur in the umbilical region due to many tumors in the abdomen. Most of the cases are of gastrointestinal system origin and are often an indicator of poor prognosis. It can be seen in 1-3% of intraabdominal and pelvic malignancies. In the literature, around 300 studies are presented, mostly in the form of case reports. Very few (7-9%) of the cases with SMJN are from pancreatic origin. In our literature review, we found that in the majority (>90%) of SMJN cases due to pancreatic tumors, the lesions originated from the pancreatic tail and/or body, and tumor marker Ca-19.9 was very high in most cases (>90%).

Aim. Here, the case of SMJN seen in a patient with three different primary tumors was discussed in the light of the literature data.

Description of the case. Here, our case, whose third primary malignancy was detected in the pancreas in the PET/CT examination performed to investigate the origin of SMJN in a 68-year-old female patient who had undergone surgery due to breast in 2011 and endometrium cancers in 2018 and came with umbilical metastasis, is presented in the light of the literature data.

Conclusion. As a result, in our case, which was followed up due to two primary tumors, it became important to know the origin of the SMJN that occurred due to the third primary tumor detected during the CT and PET/CT examination due to the newly emerging SMJN. It is important to know the origin and histopathological features of the SMJN in order to determine the treatment to the patient.

Keywords. breast, endometrium, multiple primary tumor, pancreas, Sister Mary Joseph's nodule, umbilical mass

Introduction

Sister Mary Joseph nodule (SMJN) is a metastasis that can occur in the umbilical region due to many tumors in the abdomen. The tumor is thought to metastasize to the umbilical region through lymphatic ducts, blood vessels, neighborhood and embryonic residues (1). The majority of cases (75-90%) are adenocarcinoma. It constitutes 30-60% of malignant tumors located in the umbilical region. It can be seen in 1-3% of intraabdominal and pelvic malignancies. Although most of the cases originated from the gastrointestinal tract, cases of biliary tract, endometrium, ovary, lung, bladder and appendix have also been reported.[1-5] Although the average survival time of patients with SMJN is 11 months, this

Corresponding author: Osman Nuri Dilek, e-mail: osmannuridilek@gmail.com

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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period may exceed 2 years in patients who have the chance of chemotherapy and surgical treatment (<15%). In the literature, around 300 studies (about 450 cases) are presented, mostly in the form of case reports.[1,2]

Aim

Here, the case of SMJN seen in a patient with three different primary tumors was discussed in the light of the literature data.

Description of the case

A 68-year-old female patient underwent modified radical mastectomy in 2011 due to invasive ductal carcinoma. Hysterectomy was applied in 2018 due to endometrioid type endometrium cancer. During her periodic follow-up, the patient applied to her physician a month ago with complaints of swelling and discharge in the navel (Figure 1).

Fig. 1. Sister Mary Joseph nodule in the navel

As a result of abdominal CT performed to the patient referred to our clinic, a malignant mass in the pancreatic tail and a lesion showing involvement in the navel were identified (Figure 2).

No genetic predisposition was detected in his family's questioning. The presence of hypermetabolic involvement in both lesions was demonstrated by PET/CT (Figure 3).

Radiological findings related to local recurrence of breast and endometrium tumors were not found. Serum Ca 19.9 value of our patient was found to be very high (65.951 U/mL). As a result of histopathological examination of the incisional biopsy specimen made from the mass in the navel; Malignant tumoral tissue forming glandular structures was seen under the skin. Tumor cells had hyperchromatic nuclei, large eosinophilic cytoplasms, some with secretions. It was thought to be compatible with a pancreatobiliary type adenocarcinoma morphologically. As a result of the immunohistochemical study; Diffuse positive staining was detected with cytokeratin 7, cytokeratin 19 and GATA3, while negative staining was detected with cytokeratin 20, estrogen receptor, progesterone receptor, mammoglobulin, GFCD, WT1 and CDX2 (Figure 4).

Contrary to expectations, the lesion was not due to breast or endometrium, but to pancreatic origin. The patient has been receiving chemotherapy protocols for 3 months. As a routine procedure, Written-signed informed consent form was obtained from the patient for treatment modalities and publication.

Discussion

Sister Mary Joseph's nodule is a phenomenon accepted by surgeons as an indicator of poor prognosis.[1] The diagnosis of SMJN can usually be made easily by physi-

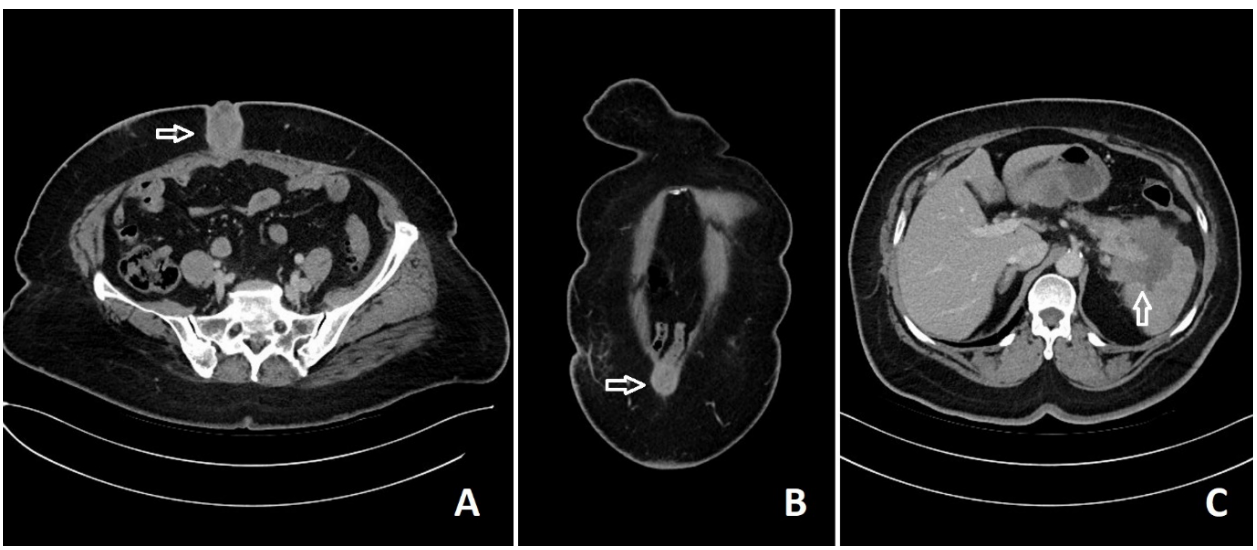

Fig. 2. The abdominal CT axial (A) and coronal (B) sections show the appearance of SMJN, and the axial section (C) shows the tumoral lesion (Arrows) in the tail of the pancreas

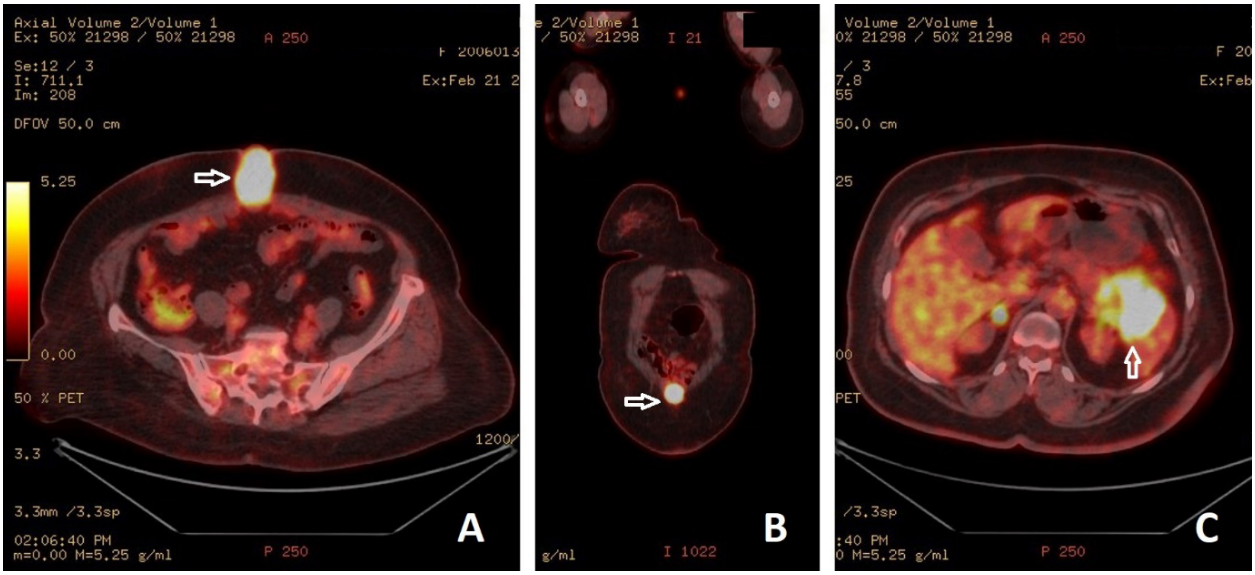

Fig. 3. PET/CT axial (A) and coronal (B) sections show the appearance of SMJN, and the axial section (C) shows the tumoral lesion (Arrows) in the tail of the pancreas

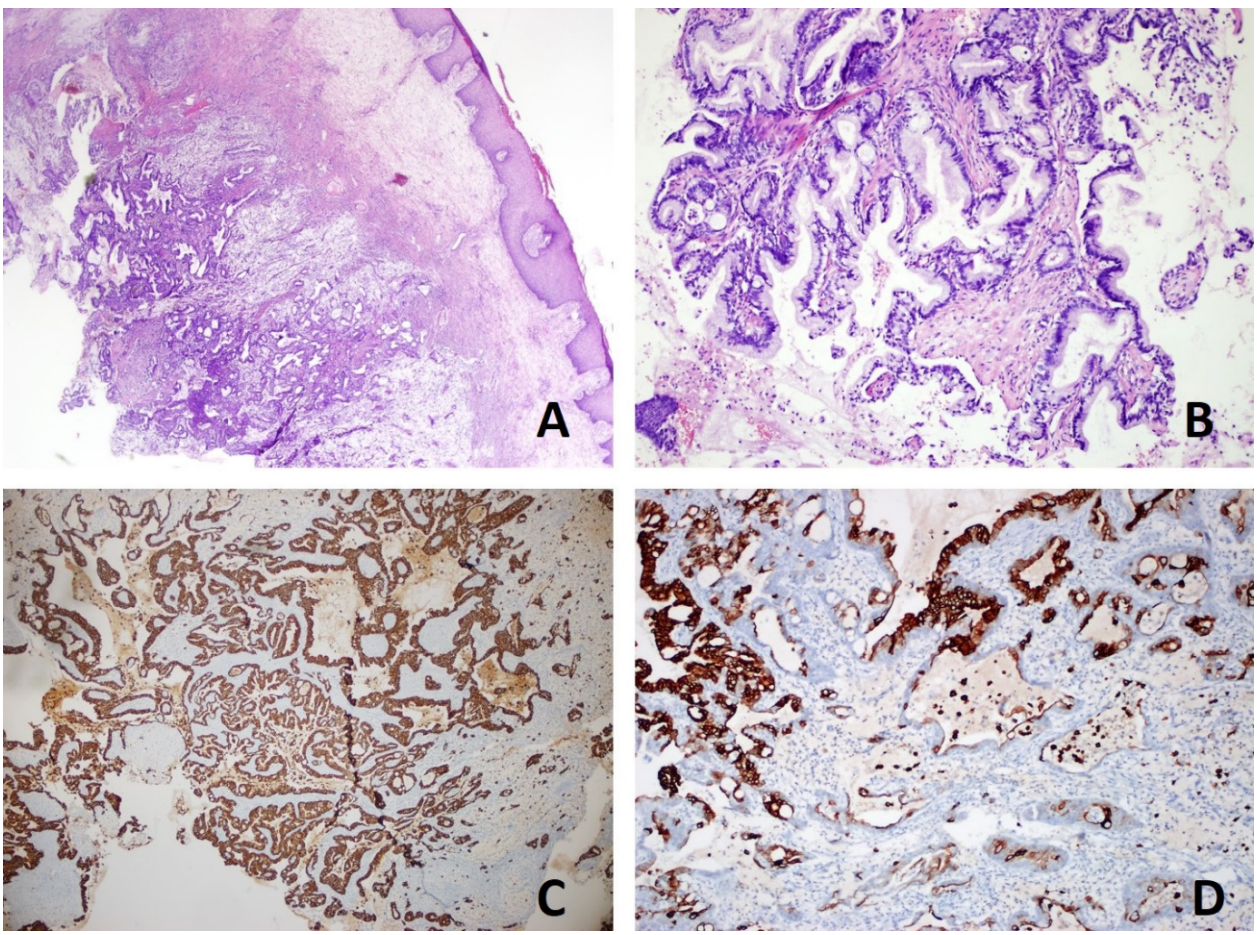

Fig. 4. These pictures show the presence of adenocarcinoma (A) under the skin tissue (HE x 20). Some of the irregular adenoid structures (B) contain mucin-making cells (100x) (H&E stain). Adenocarcinoma shows diffuse cytokeratin 19 (C) positivity (CK-19 x 40), and patch-style cytokeratin (D) positivity (100x) (CK-20)

cal examination. Mass-forming lesions can be revealed by radiological examinations.[6] The diagnosis of SMJN can usually be made easily by physical examination. Mass-forming lesions can be revealed by radiological examinations. While more than half of the cases with SMJN (52-55%) originate from digestiv system organs

and 28-30% from reproductive system organs, primary focus may not be found in 15-20% of the cases.[2,7] 7-9% of SMJN cases reported in the literature are of pancreatic origin.[1,2,4] We did not encounter three primary tumor cases and SMJN cases with pancreatic tumor.[8,9] We think that our case is the first case in the literature with these features.[3,4] Microscopic examination of our case showed that tumor had simple, large glands are lined by a single layer of cells with round nuclei. Some glands have abundant mucinous cytoplasm and are remarkably well formed. This pattern resembles carcinomas of the pancreas and bile ducts not endometrial or breast carcinoma. Commonly used breast markers such as mammaglobin, gross cystic disease fluid protein, ER,PR were negative. There is a high rate of expression in breast carcinoma of GATA3, and ER, PR in endometrial cancers. Our case was not showed expression for ER,PR. Also, CK7 and CK19 expressed relatively diffusely and strongly in the vast majority of pancreatobiliary-type ampullary adenocarcinoma, and diagnosis was diagnosis was determined in compatible with pancreatobiliary type adenocarcinoma metastasis.

In our literature review, we found that the majority (>90%) of lesions defined as pancreatic SMJN were lesions originating from the tail of the pancreas and less than the body of the pancreas (2,3,5). In 4 cases of pancreatic tumors and SMJN series of Ozaki et al., All of the cases were defined as pancreatic body and tail origin.[3] It was noteworthy that most of the patients (>90%) with pancreatic tumors with SMJN whose blood tumor markers were examined had a high level of Ca 19-9.[1-3,9,10] It was also found to be very high in our patient. Most of the patients with SMJN (>90%) diagnosed in the literature also had liver metastases. Our patient also had metastases in the liver.

Conclusion

As a result, in our case, which was followed up due to two primary tumors, it became important to know the origin of the SMJN that occurred due to the third primary tumor detected during the CT and PET/CT examination due to the newly emerging SMJN. It is important to know the origin and histopathological features of the SMJN in order to determine the treatment to the patient.

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CASUISTIC PAPER

Natalia Leksa [1(ABDFG)], Adam Uryniak [2(ABDFG)], David Aebisher [3(BDFG)], David Leksa [2(ABDFG)], Dorota Bartusik-Aebisher [4(ABDFG)]

Vascular surgery and an occurrence of stroke

[1] Department of Anatomy, Medical College of Rzeszów University, Rzeszów, Poland
[2] Rzeszów Center for Vascular and Endovascular Surgery, Rzeszow, Poland
[3] Department of Photomedicine and Physical Chemistry, Medical College of Rzeszów University, Rzeszów, Poland
[4] Department of Biochemistry and General Chemistry Medical College of Rzeszów University, Rzeszów, Poland

ABSTRACT

Introduction. The brain responds to metabolic disorders with a limited array of symptoms and signs. The brain has enormous needs in terms of substrate and blood flow.

Aim. This paper presents a case report reporting episode of stroke.

Description of the case. The incidence of cerebral vascular episodes in the form of strokes, transient episodes of cerebral ischemia is reported.

Conclusion. The chemical constituency of the brain are generally quite different from those of other tissues. Stroke is a clinical syndrome characterized by sudden focal or generalized brain dysfunction.

Keywords. cerebral arteries, diagnosis, stroke

Introduction

There are many systematic medical illnesses that can affect the central nervous system. These include such common affiliation as diabetes, heart failure, cirrhosis of the liver, and chronic obstructive pulmonary disease. There is however a subgroup of medical illness that has major and important systematic manifestation in the central nervous system. These disorders can and most certainly do affect other bodily systems but the central nervous system manifestation are such that serious that serious injury, disability or even death can result. Stroke is the third most common cause of rubbish after heart disease and cancer today. The incidence of stroke is an infarct of a portion of the brain, most often secondary to occlusion of a major or minor blood vessel. The sequelae of a particular stroke depend to a large extent on the location of the blood vessel the extent of tissue damage and the collateral circulation. As a sequele of stroke there is tissue death of a portion of the brain. Within the initial few hours after a stroke and for a period perhaps 1 to 3 days there will be variable but progressive tissue edema and death in the area around the zone of infraction that is partially fed by the occluded vessel. Stroke is one of the main causes of mobility impairment and the second most common cause of dementia.[1-3] Discomfort persists over 24

Corresponding author: Natalia Leksa, e-mail: leksanatalia@gmail.com

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hours or leads to death with no cause other than cerebral. However, if the ailments persist for less than 24 hours and disappear spontaneously, we are talking about TIA (transient ischemic attack) - a transient episode of cerebral ischemia.[4-6] Diagnostics primarily includes assessing cardiovascular fitness by measuring blood pressure, ruling out cardiac arrhythmias (Holter RR, Holter ECG, echocardiography), atherosclerosis of the cerebral arteries (duplex carotid ultrasound and transcranial ultrasound) and laboratory tests (glycemia, parameters renal, lipids profile assessment and others).[7- 10] In patients, an abrupt fall in blood pressure may induce cerebral ischemia, sometimes resulting in stroke.[11] The fundamental therapy for the treatment of ischemic -hypoxic injury is to correct the cause. May other therapies have been advocated for brain injury of hypoxic ischemic region. None has been found to restore function without neurologic deficit. It has been thought that osmotic diuretics might be successful in case of brain swelling after hypoxic injury.[12 -16] It is recognized that at the time of ischemic hypoxic injury there is often an associated loss of autoregulation of cerebral circulation such that further injury may be indicated. Many patients are initially misdiagnosed and are felt to have primary cerebral pathology, such as subdural hematoma. In the hyponatremic patients the diagnosis must be made on clinical grounds but appears to be the most likely cause of the relapsing encephalopathy, with either death or a persistent vegetative state as the usual outcome.[17] In the last years there have been a large number of studies of patients with hyponatremia who have developed cerebral demyelinating lesions. Some of these investigators have suggested an association between hyponatremia or its therapy and central pontine myelinolysis. Cerebral demyelination occurring in hyponatremic subjects is usually secondary to a combination of anoxia-hypoxia band increased intracranial pressure. The clinical manifestation is sometimes delayed until after treatment has been completed giving a false appearance of some relationship between cerebral demyelination and the therapy of hyponatremia. Calcium channel blockers has been proposed as a treatment for hypoxic ischemic brain injury based on the hypothesis discussed above that calcium loading of cells leads to necrosis.[18-25] The brain depends on a stable internal environment for optimal function. To some extent the other systems in the body serve the brain. They provide nutrients to the brain, remove products of metabolism from the brain and protect the brain from external perturbations.[17-20]

Aim

The goal of this study was to presents diagnosis and treatment of the stroke.

Description of the case

A 68-year-old patient was admitted to the Department of Neurology because of severe dizziness with nausea, feeling of numbness and weakening of the muscular strength of the right upper limb, which has persisted since morning hours. In the history of nicotinism, otherwise not treated chronically.

The admission neurological examination revealed: conscious, verbal contact, full orientation, meningeal and root symptoms, nystagmus, isochoric, in the cranial nerve area: no abnormalities, in the limb area: discrete global paresis of the right upper limb, otherwise without irregularities, deep correct symmetrical reflexes, bilateral correct reflexes. Imaging (CT of the head and MR of the head) imaged fresh ischemic lesions of the left hemisphere of the brain. For the diagnosis of cerebral vascular episodes, an ultrasound examination of the brain vessels was performed, in which 80% of the left internal carotid artery stenosis was described. Diagnosis was extended to an CT scan of the intracerebral arteries, which confirmed the above stenosis (Figure 1).

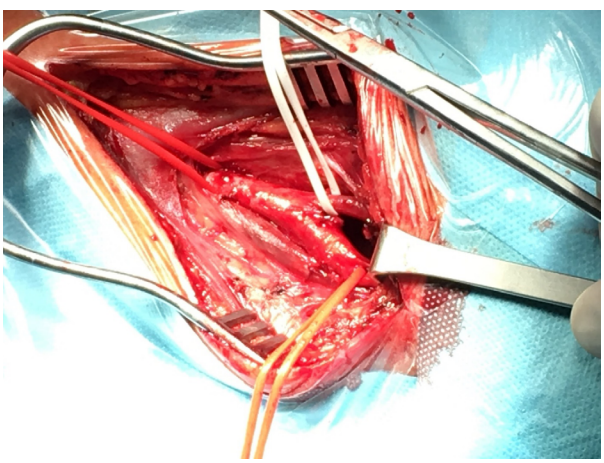

Fig. 1. The vascular surgey by the classical method – endarterectomy

The patient was transferred for further treatment to the Department of Vascular Surgery, where he was operated by the classical method - endarterectomy.

Discussion

Due to the fact that one of the main causes of stroke is the narrowing of the intracerebral arteries caused most often by atherosclerotic plaques, each patient after an episode of stroke or after an episode of transient cerebral ischemia should have an ultrasound examination of the intracerebral arteries and a transcranial ultrasound. If any of these methods is not possible, then computed tomography angiography or magnetic resonance angiography are routinely performed.[1] These methods allow the assessment of flow velocity, the ratio of velocity at the stenosis site to the velocity outside the stenosis

and assessment of the plaque morphology (echogenicity, surface, ulceration).[5] The degree of narrowing can be assessed in a variety of ways, but the NASCET (North American Symptomatic Carotid Endarterectomy Trial) method is most commonly used. About 10-15% of strokes are caused by carotid stenosis, but they are not always symptomatic. Symptomatic stenosis is one where symptoms occur up to 6 months after falling ill, while asymptomatic for more than 6 months. The analyzed patient developed symptomatic stenosis. Due to the location of the atherosclerotic plaque restricting blood flow through the vessel, the method of classical surgery, i.e. endarterectomy (CEA), was decided - Figure 2.

Fig. 2. An MRI picture imaged fresh ischemic lesions of the left hemisphere of the brain

According to current guidelines, this method is preferred in patients with minor neurological symptoms, male, with cortical and hemispheric symptoms, and with concurrent internal load and age over 70 years. The above patient met most of these criteria. The second possible method of intracerebral artery surgery is CAS (carotid stenting), which involves the implantation of a stent within a diseased vessel with access usually through the femoral artery. CAS has an advantage over CEA in the following cases: previous radiotherapy of the area, recurrent stenoses, recurrent laryngeal nerve palsy, difficult surgical access (stenoses located very high within the internal carotid artery). In the study Carotid Revascularization Versus Stenting Trial (CREST), Endarterectomy Versus Angioplsty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S), Stent Protected Angioplasty Versus Carotid Endarterectomy (SPACE) and International Carotid Stenting Study (ICSS) associated with 30-day risk stroke in connection with surgery using the CEA or CAS method, it was proved that a significantly lower risk was associated with the surgery using the classical endarterectomy method.[6] It should also be noted that in patients operated on by the CEA method - it is recommended to use acetylsalicylic acid chronically after surgery or in the case of resistance to clopidogrel. However, in the case of CAS-acetylsalicylic acid surgery together with 1. however, clopidogrel therapy should not be longer than 3 months. stroke is a complex clinical picture caused by extreme elevation of body temperature.[20-25]

Conclusion

Due to the high incidence of cerebral vascular episodes in the form of strokes, transient episodes of cerebral ischemia, detailed diagnosis of the causes of the disease in each of the above cases is necessary. For symptomatic carotid stenosis, the only effective method is the surgical method. The choice of surgical method due to the location of the atherosclerotic plaque, concomitant diseases and general condition of the patient always belongs to the vascular surgeon.

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CASUISTIC PAPER

Dominik Godlewski [1(ABCDEF)], Patryk Pszczółkowski [1(ABCD)], Tadeusz Fedus [1(ABCD)], David Aebisher [2(EF)]

Bladder leiomyoma: diagnostics, laparoscopy, and treatment

[1] Clinical Department of Urology and Oncological Urology Clinical Provincial Hospital No.1, Rzeszów, Poland
[2] Department of Photomedicine and Physical Chemistry, Medical College of Rzeszów University, Rzeszów, Poland

ABSTRACT

Introduction. Leiomyosarcoma is the most common benign tumor of the bladder. However, it is only a small percentage of all proliferative changes of this organ.

Aim. Presentation based on two clinical cases of diagnostics and surgical treatment from laparoscopic access of bladder leiomyoma.

Description of the cases.

Case 1. The work contains a diagnosis based on transvaginal ultrasound (TVUS), cystoscopy and computed tomography (CT), as well as partial laparoscopic bladder re section of leiomyoma in young women.

Case 2. The case of young women with the histopathological result confirmed bladder leiomyoma.

Conclusions. Leiomyoma is a rare bladder cancer. Laparoscopic bladder resection is a safe method that leads to healing.

Keywords. bladder leiomyoma, endometriosis, laparoscopic surgery

Introduction

Leiomyoma is a benign tumor of mesenchymal origin. Although the bladder is the most common localization of leiomyosarcoma in the urinary system and is the most common benign lesion of this organ (35%), leyomioma is only 0.5% of all bladder tumors.[1-4] The disease occurs three times more common in women than men[2] with a peak incidence between the third and eighth decade of life. The average age of diagnosis is 45 years.[5-9] Symptoms of leiomyosarcoma are non-specific and depend on the size and location of the tumor. The most common are: impaired urination (49%), dysuria (38%), lumbar pain (13%) and hematuria (11%). In 19%, the change can be completely asymptomatic and constitutes an accidental diagnosis. In 57% of women, these tumors are palpable in a two-handed study.[3,7,8,10]

Diagnosis is based on physical examination, imaging techniques and cystoscopy. Helpful in the diagnosis of imaging include transabdominal or transvaginal ultrasound, which is usually the first diagnostic step, as well as computed tomography and magnetic resonance imaging.

In the differential diagnosis, the presence of leiomyosarcoma or other bladder tumors and urinary endometriosis should be taken into account.

Corresponding author: Dominik Godlewski, E-mail: dogod@o2.pl

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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Aim

Presentation based on two clinical cases of diagnostics and surgical treatment from laparoscopic access of bladder leiomyoma.

Description of the cases

Case 1.

In a 30-year-old woman preparing for pregnancy, during a follow-up visit to the gynecologist, an asymptomatic tumor of the anterior bladder wall was found on ultrasound. In an interview, delivery by caesarean section 2 years ago. The patient did not report dysuria or cyclic hematuria, however, the change in the bladder described in ultrasound could suggest endometriosis due to the patient's gynecological history.

The patient is in good general condition, without any complaints or perceptible pathologies in the physical examination. Blood and urine tests without deviation from the norm. Computed tomography (CT) scan with contrast of the abdominal cavity and pelvis was performed as part of diagnostic imaging. It showed the presence in the anterior wall of the bladder of a tumor with smooth outlines and dimensions of 14 x 28 x 27 mm, undergoing slight contrast enhancement (up to 22 JH), having densities similar to the uterine endometrium, which would suggest a focus of endometriosis (Figure 1).

Fig. 1. Leiomyoma of the anterior wall of the bladder

Peritoneal implants were not disclosed, and no pathological features were found in the other abdominal, retroperitoneal and pelvic organs. Lymph nodes of the retroperitoneal space and the pelvis minor enlarged.

On the basis of the above tests, it was decided to schedule the patient's admission to the Urology Clinic of the Provincial Specialist Hospital in Rzeszów for cystoscopy and possible qualification for surgical treatment. In endoscopic examination under general anesthesia, prior to the planned surgery, only the anterior wall impression was suggested suggesting its external modeling or the existence of an intramural lesion, which was confirmed by the CT image. There are no lesions that could be subjected to transurethral resection. Both sides were equipped with DJ catheters for easier intraoperative identification of ureters and decided to laparoscopic tumor resection. A Foley 16Fr catheter was left in the bladder. Patient lying in Trendelenburg position, deflected to 15°, after peritoneal optical trocar (10mm) was introduced by minilaparotomy in the navel, peritoneal pneumothorax was created. Two more working trocars (10 mm and 5 mm) were placed on both sides in the projection of the lateral edges of the straight abdominal muscles, two fingers below the navel. Adhesions were found in the lower part of the peritoneal cavity after caesarean section, which were released revealing the anterior wall of the bladder. After filling it with physiological saline, the tumor was identified. The lesion was excised with a healthy tissue margin (Figure 2).

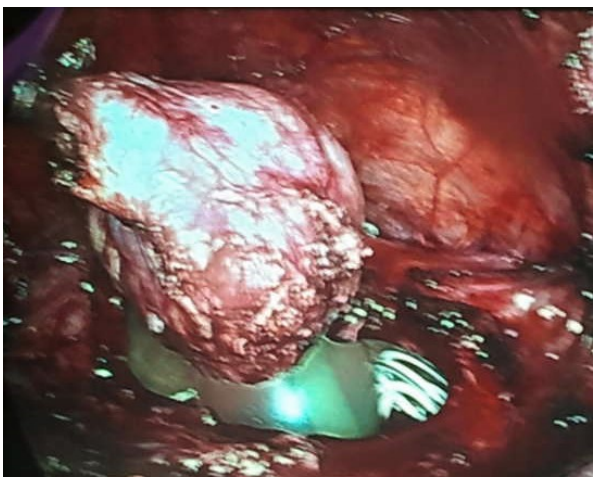

Fig. 2. Leiomyoma of the anterior wall of the bladder

The anterior wall of the bladder was sutured with a laparoscopic 2-layer continuous 3-0 suture.

Bladder tightness was checked, Redon drain was left. Intraoperative blood loss was trace, not significant. Postoperative course without complications. The drain was removed on the second day after surgery. The patient was discharged from the clinic on the fourth postoperative day with the Foley catheter and DJ stents left behind.

As a result of histopathological examination, a 1.5x0.5x2.5cm leiomyoma-type bladder lesion was described - a tumor excised with a healthy tissue margin. Immunohistochemical tests: DES (+), SMA (+), S100 (+/-), CD-34 (-), CD-117 (-), VIM (-). The patient was admitted again after two weeks. Cystography was performed giving 170 ml of contrast. Smooth-walled bladder, no contracting defects, no leakage of contrast.

The Foley catheter and ureteral catheters were removed. No bladder retention after voiding.

The patient quickly returned to full activity, and two months after the surgery resumed sports training.

Case 2.
Another patient, aged 30, was referred by a urologist because of computed tomography of a 31x31x28 mm bladder tumor adjacent to the vaginal wall and located near the left ureteral outlet, (Figure 3).

Fig. 3. Leiomyoma of the left bladder wall - CT II-phase image- 31x31x28 mm bladder tumor

The initial diagnosis was based on an ultrasound examination made for recurrent haematuria. The patient did not report any other ailments. The renal calf-pelvic system without stasis in imaging (USG, computed tomography).

During hospitalization, the patient was consulted gynecologically - a tumor palpable was found through the left vaginal vault, and TVUS revealed the above-mentioned change in the bladder wall. In cystoscopic examination, visible mass penetrating into the lumen of the bladder covered with unchanged mucosa over the left ureteral opening (Figure 4).

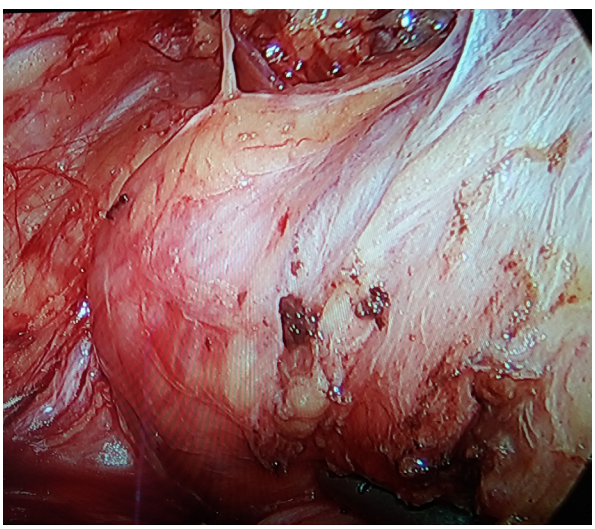

Fig. 4. Leiomyoma of the left bladder wall - laparoscopic image. 31x31x28 mm bladder tumor

It was decided to have surgery - partial laparoscopic resection of the bladder. The left ureter was stent under anesthesia to facilitate its intraoperative identification. Then four trocars were introduced. The tumor was reached laterally from the lateral umbilical fold. Using the Thunderbeat® device, a lesion was removed with an unchanged tissue margin (Figure 5).

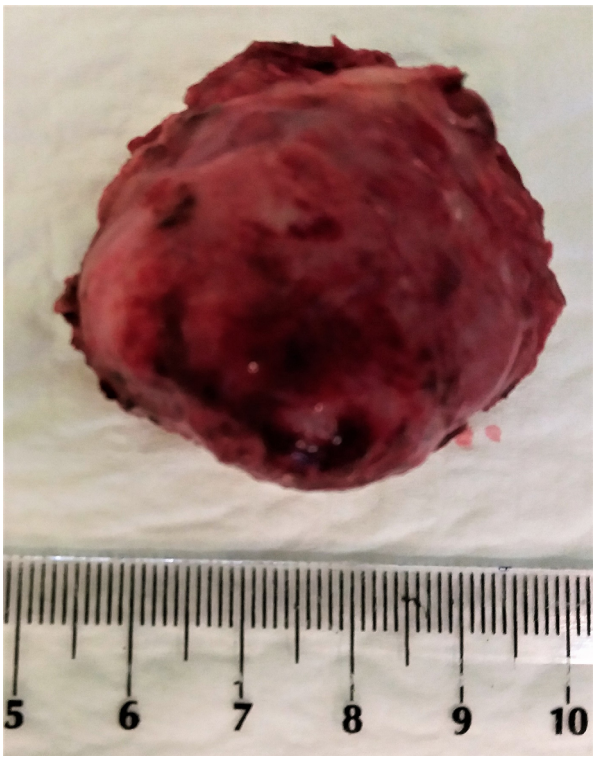

Fig. 5. Leiomyoma of the left bladder wall - condition after removal of the tumor

The bladder was sutured with a continuous suture, its tightness was checked. Postoperative course without complications, drainage removed on the third day after surgery. Foley's catheter was left and removed along with the DJ catheter 10 days after surgery. No adverse effects were found.

The histopathological result confirmed bladder leiomyoma. The picture corresponded to a poor cell, spindle cell tumor in the muscularis of the bladder wall. Mitosis and necrosis were not found. In immunohistochemistry, strongly actin and SMA positive cells, few estrogen positive cells, CD 117 and S 100, negative for CK Pan, Ki67 about 1%. Urothelial epithelium without dysplasia. A tumor cut out entirely with a margin.

Discussion

63% of the bladder leiomyosarcoma occurs submucosa, and the mucosa covering it is unchanged in the cystoscopic image. 11-30% of lesions are located in the subserum and 7-17% are intramural.[7,10,11] The etiology of the disease remains unclear. The accepted hypotheses are

a chromosomal defect, hormonal disorders (which may explain the more frequent occurrence in women), recurrent detrusor infections, vasculitis, or dysontogenesis.[12,13] Available data are quite scarce. In the available English literature since 1953, only about 250 cases of the described disease were reported.[14] Submucosal tumors have the appearance of peduncular polyps, whereas intramural masses have the character of a capped lesion surrounded by a bladder wall.[14]

In diagnostics, per vaginam and per rectum tests are used, as well as various imaging tests - transabdominal or transvaginal ultrasound, computed tomography or magnetic resonance imaging, and cystoscopy.[1,3,8,11,14,17-22] Ultrasound examination reveals homogeneous echogenicity of the tumor with scanty vascularization in Doppler examination. CT allows differentiation between the solid and cystic nature of the lesions and accurately assesses the attitude towards surrounding tissues, showing weak amplification to 25 - 50 Hounsfield units, which confirms poor vascularization of the lesions.[11,14] MRI has greater specificity for mesenchymal components, allows to assess the relation to neighboring structures. This image shows homogeneously strengthening tumors, others with cystic degeneration with a hyperintensive signal in T2-dependent images. It is worth emphasizing that none of the imaging tests exclude the malignant nature of the lesion, so it should be obligatory to obtain material for histopathological examination, whether by biopsy during cystoscopy or by complete removal of the tumor. Percutaneous, suprapubic biopsy in a pregnant patient has also been described.[14,22] In the histopathological picture, degenerative changes, hyalinization, necrosis, fat metaplasia and mucilage can be observed.[5] In the differential diagnosis, first of all, the leiomyosarcoma change should be taken into account, since in the form of high-grade mortality accounts for up to 50% with an observation period of 22-47 months.[5,6] In addition, differentiation applies to other bladder tumors, its diverticula and cysts, and endometriosis. The method of treatment is determined by the location of the tumor. In submucosal localization, transurethral resection (TURBT) is possible, while in intramural and subserum position resection by open surgery, laparoscopic, or be robotic. [3,5-8,10,11,14-19] In the case of complete leiomyoma excision, no tumor recurrence or malignancy are observed.[2,3,5,6,8] Barayan and Nassir report the need for re-TURBT in 18% of patients due to incomplete transurethral resection and the lack of such necessity after open surgery.[3] Considering the excellent imaging that allows close and enlarged assessment of resection borders, as well as easy access to lesions located both on the anterior wall, the top of the bladder and on its back wall, reduction of postoperative pain and quick recovery of laparoscopic operations constitute an effective and minimally invasive method of treating this type of tumor. The risk of complications in the form of damage to surrounding structures, including abdominal organs (transperitoneal access) is largely dependent on the skill and experience of the operator.

Conclusions

Surgical treatment of bladder leiomyoma is the method of choice because it allows complete removal of the lesion, providing material for histopathological examination, which is important due to the differentiation of pathological mass with leiomyosarcoma and other bladder tumors or endometriosis. Excellent treatment effectiveness is observed, i.e. a very low recurrence rate, resolution of symptoms, as well as very good long-term prognosis.

Laparoscopic surgery for intramural and sub-serous lesions is a minimally invasive, precise method of treatment (excellent insight into the surgical field), allowing the patient to quickly return to daily functioning - as in the described case, also to actively play sports. In centers with experience in laparoscopic techniques, previous pelvic surgery, as in the case of the Caesarean section, is not a contraindication to choosing this method of treatment.

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CASUISTIC PAPER

Natalia Leksa [1,2(ABDFG)], Dawid Leksa [3(FG)], Łukasz Gałuszka [3(FG)], Adam Uryniak [3(FG)], David Aebisher [4(DFG)], Sabina Galiniak [5(FG)], Dorota Bartusik-Aebisher [5(DFG)]

An iliac artery aneurysm

[1] Department of Neurology, MSWiA Hospital, Rzeszów, Poland
[2] Department of Anatomy, Medical College of Rzeszów University, Rzeszów, Poland
[3] Rzeszów Center for Vascular and Endovascular Surgery, Rzeszów, Poland
[4] Department of Photomedicine and Physical Chemistry, Medical College of Rzeszów University, Rzeszów, Poland
[5] Department of Biochemistry and General Chemistry Medical College of Rzeszów University, Rzeszów, Poland

ABSTRACT

Introduction. Isolated common iliac artery aneurysms (CIAs) are rare. The rarer are rupture of the common iliac artery. We can treat them surgically: classic or endovascular. Open surgery has a main role in the management of aneurysms not suitable for repair by endovascular techniques.

Aim. The aim of the study is to present the possibility of occurrence of such a disease at a young age, to indicate non-characteristic symptoms that may predict the above-mentioned disease entity at the level of a primary care physician or SOR. Review of medical publications from 2000-2019 regarding guidelines or methods of conduct in that cases.

Description of the case. A patient 39 years old, admitted to the Department of Vascular Surgery, in an interview: about 15 years ago severely beaten, as a result of injuries total loss of hearing, memory and basic skills such as: speech, writing, reading, hospitalized over 6 months.

Conclusion. Good rehabilitation and patient persistence restored cognitive skills. Advances in surgical has lowered the mortality and morbidity rates even in patients.

Keywords. arteriography, iliac artery aneurysms, intravascular therapy, Stent-Graft

Introduction

A number of complications are directly related to the endovascular treatment method for common iliac artery aneurysms.[1-3] In some cases, due to the extent of the aneurysm, we take into account that it may be necessary to extend the covered stent or leg of the Stent-Graft to the external iliac artery (EIA), in order to avoid type I leakage, it is necessary to close the internal iliac artery (IIA) by means of interventional covering her ostium or intra-operative embolization.[4] IIA obstruction is often associated with gluteal claudication and erectile dysfunction - up to 55% and 46% of patients, respectively.[5-8] In rare cases, it may lead to gluteal necrosis, spinal cord ischemia or colon ischemia. Intra-operative iodine contrast may lead to post-contrast nephropathy. The frequency of this complication is estimated at 1.2-1.6% of patients who received

Corresponding author: Natalia Leksa, e-mail: leksanatalia@gmail.com

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intravenous or intra-arterial contrast agent. The tortuous course of the iliac arteries can hinder or even prevent the correct positioning of the vascular prosthesis, and as a result of unfavorable anatomical conditions it may be enough to perforate or detach the vessel.[9-11] Not without significance is the fact that endovascular procedures require highly specialized medical equipment and qualified medical staff, which may limit access to such procedures. In some cases, the anatomical structure of the iliac arteries does not allow the use of intravascular therapy or significantly increases the risk of complications.[12-17] Due to the exclusion of IIA, the patient's quality of life often worsens. However, it is a method that in the experienced center gives a great chance to survive the patient during rupture of such an aneurysm from a small incision or even puncture of the artery below the inguinal ligament. In some cases, the anatomical structure of the iliac arteries does not allow the use of intravascular therapy or significantly increases the risk of complications.[18] Due to the exclusion of IIA, the patient's quality of life often worsens. However, it is a method that in the experienced center gives a great chance to survive the patient during rupture of such an aneurysm from a small incision or even puncture of the artery below the inguinal ligament. Classical treatment is not free of any complications. The most important factors are anatomical conditions, type of access, extent of the procedure, collision with large venous vessels, which in a significant percentage with very changed anatomy caused by hematoma in a tight area (pelvis) can be damaged, which causes a significant slowdown of the procedure, urinary system, sex structures.[19-23]

Aim

The goal of this research was to present the most important factors of iliac artery aneurysms.

Description of the case

The patient was admitted to the Department of Vascular Surgery in the emergency room mode to the Emergency Room with edema of the left lower limb, where iliac vein thrombosis was diagnosed and femoral in doppler ultrasound. Anticoagulation and compression therapy were included. After identifying the potential cause of the patient's local condition, he was discharged home. The treatment started did not bring a good effect, the pain gradually increased in the left lower abdomen, there was a fever and increased levels of leukocytes in the blood. Due to severe pain, the limb was forced involuntarily in the left hip joint. The patient was once again admitted to the Admissions Room, where laboratory tests and abdominal angio-CT examination were performed. An imaging study described an inflammation of the left common iliac artery. The patient was then referred to the Vascular Surgery Department. An in-depth analysis of the Angio-CT image of the abdominal cavity allowed for a change in diagnosis - fractured left iliac artery aneurysm. The decision was made to treat the rupture with a stent graft (coated stent) from access by exposing the femoral artery. Such a method requires preliminary diagnostics on the operating table - arteriography, which can also provide additional information about the location and the extent of arterial wall injury, thus it does not take away the possibility of transition to classical treatment if necessary, it also gives the chance to temporarily close blood flow outside the vascular bed. Accordingly, arteriography was performed on the basis of which the size of the damaged vessel was dimensioned and the patient was qualified for intravascular treatment. The Stent-Graft was implanted into the left common iliac artery and the coils implanted to turn off the left internal iliac artery, leaving it would cause Type I leakage. In the postoperative period, the patient's general condition remained good, while elevated inflammatory parameters (leukocytosis and CRP) and elevated body temperature were observed. Empirical antibiotic therapy was included. Blood cultures were obtained that were sterile. Contracture and forced flexion of the lower left limb in the hip joint resolved after three days. The patient was discharged home in good condition. Due to persistent fever of unclear etiology in the early period after discharge from the vascular ward, he was referred by the primary care physician to the Department of Infectious Diseases, where full diagnostics was carried out without obtaining a response regarding the etiology of fever. Currently, the patient remains in outpatient control in good general condition, without fever. The control angio-CT scan showed normal flow through the Stent-Graft hip vessels, the pressure symptoms completely disappeared.

Discussion

In the above description of the young man's case, it is noteworthy that the ailments with which he reported to the Admissions Room were non-characteristic. Beginning with the forced bending of the left lower limb caused by hematoma exerting pressure on the ilio-lumbar muscle, then iliac vein thrombosis caused by pressure on the venous vessels. Leukocytosis and elevated body temperature were most likely associated with pressure on the ureter, which resulted in a disorder of the urinary outflow from the left kidney or an inflammatory (bacterial or fungal) factor that could have caused an artery wall rupture in 39-year-olds. Also a potential cause of selective rupture of the iliac artery in the absence of pathology in other vessels is mechanical trauma, which could probably have occurred 15 years earlier during beating.

Conclusion

Review of the literature did not show numerous similar cases and lack of information about long-term effects

of endovascular or classical treatment in young people. This case contributes to a better underestanding and characterization of a rare pathology. This case is demonstrating that both surgical and endovascular treatment can be performed with efficient and good result.

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CASUISTIC PAPER

Beata Chmielewska [1(AB)], Natalia Leksa [1,2(ABF)], David Aebisher [3(BDFG)], Sabina Galiniak [4(FG)], Dawid Leksa [5(FG)], Seweryn Bartosz [1(F)], Dorota Bartusik-Aebisher [4(BDFG)]

Stroke masks – a case report

[1] Department of Neurology, MSWiA Hospital, Rzeszów, Poland
[2] Department of Anatomy, Medical College of Rzeszów University, Rzeszów, Poland
[3] Department of Photomedicine and Physical Chemistry, Medical College of Rzeszów University, Rzeszów, Poland
[4] Department of Biochemistry and General Chemistry Medical College of Rzeszów University, Rzeszów, Poland
[5] Rzeszów Center for Vascular and Endovascular Surgery, Rzeszów, Poland

ABSTRACT

Introduction. Stroke is a common vascular disease encountered in the work of a practitioner. Despite this, his differentiation is difficult. This is due to a variety of diseases that can be a "mask" for stroke. These are neurological diseases other than vascular (brain tumors, epilepsy), head injuries and a number of metabolic disorders (fluctuations in glucose, electrolytes).

Aim. This work aims to approximate the differentiation of this common disease entity. Case reports show both clinical view and diagnostic difficulties.

Description of the cases.

Case 1. The patient 59 years old treated for bipolar disorder, hypertension and alcohol abuse.

Case 2. The patient 68 years old treated for type 2 diabetes, hypertension, ischemic heart disease, cholecystolithiasis – cholecystectomy.

Conclusion. Stroke is a significant clinical and social problem both in Poland and in the world. Despite this, its diagnostics and especially differentiation is difficult. When analyzing the case of each patient with suspected sudden CNS vascular disease, all of them should be remembered. It should also be borne in mind that differential diagnosis cannot delay specific treatment for stroke.

Keywords. brain metabolic disorders, MRI, stroke

Introduction

Stroke is a significant clinical and social problem because it remains the first of the main causes of morbidity and long-term disability, and the second most frequent cause of death.[1] In the world, about 17 million people suffer from stroke every year, in Poland the figure is 90,000.[2] In order to reduce the risk of stroke, it is necessary to eliminate risk factors for vascular diseases in the population of healthy people and to identify and effectively treat diseases that increase this risk.[3] Fast implementation of effective treatment in the early stages of the disease such as thrombolytic and endovascular treatment (mechanical throm-

Corresponding author: Natalia Leksa, e-mail: leksanatalia@gmail.com

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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bectomy) is of key importance for reducing the degree of disability and mortality after stroke.[1] Many non-vascular and metabolic neurological diseases can be associated with suddenly appearing focal neurological symptoms. These are, among others tumors, brain abscesses, seizures, migraine, glucose fluctuations, renal impairment, electrolyte imbalance, alcohol and drug effects, and injuries.[4] Their differentiation is of key importance because the above-mentioned thrombolytic and endovascular treatment, apart from its effectiveness, carries a risk of complications. Intravenous thrombolytic therapy is associated with a 5- to 7-fold increase in the risk of secondary haemorrhage of a heart attack.[1] Medical history plays an important role in the diagnosis of people with sudden focal neurological symptoms. Provides information on the circumstances of illness (loss of consciousness, injury, contact with a person with an infectious disease), existing diseases (diabetes, kidney disease, epilepsy), lifestyle (alcohol, drugs). The next element should be the assessment of the patient's basic life functions: arterial pressure, pulse, saturation, body temperature, blood glucose level (test strip made of capillary blood), ECG.[1-7] Then, laboratory tests should be performed with venous blood (morphology, coagulogram, glycemia, electrolytes, creatinine, C-reactive protein, transaminases) and imaging (CT or possibly MR of the head).[1] In patients qualified for intravascular treatment, angio-CT or angio-MR examination of the intracerebral arteries is performed.[8] Specialized procedures are also performed in differential diagnostics lumbar puncture and EEG test. It should be remembered that all the above-mentioned tests should be carried out in the shortest possible time. The therapeutic window for the implementation of thrombolytic therapy from the onset of stroke symptoms is 4.5 hours. However, the results of the meta-analyzes clearly show that the shorter this time, the better the clinical effect.[1] Therefore, differential diagnosis of stroke should not delay specific treatment.

Aim

This work aims to approximate the differentiation of this common disease entity. Case reports show both clinical view and diagnostic difficulties.

Description of the cases

Case 1.

The patient 59 years old, brought by ZRM due to babbling speech after night, imbalance with a tendency to fall to the right, general weakness, confluent sweat. Until now, he was treated for bipolar disorder, hypertension, alcohol abuse. Takes: Trazodone 50 mg, Betahistine 16 mg, Hygroton 50 mg, Daneb 5 mg. In the neurological examination: conscious, sleepy, in logical contact, blurred speech, tongue deviates to the right, narrower eyelid gap of the right eye, paresis of a low degree of LKG, without pathological symptoms. Qualification for thrombolytic treatment was performed: in CT scan of the head grooves of the brain bends atrophic wider, without focal and ischemic changes. Due to the unknown time of onset, single heads, small nonspecific foci, subcortical vascular origin were performed in both hemispheres of the brain. In laboratory tests, significant hyponatraemia of 102 mmol/L (norm 136-145 mmol/L), and intra-intramuscular 2.5 mmol/L (3.5-5.1 mmol/L). Due to electrolyte disturbances and the lack of fresh ischemic lesions in the MR examination, thrombolytic treatment was initiated, the patient was referred to O. Internal Medicine. The treatment used concentrated salt solution, supplemented potassium deficiency, modified treatment of hypertension (thiazide diuretic discontinued). During hospitalization, the patient admitted that he had had balance disorders, headaches, dizziness, nausea and vomiting for a week. After electrolyte imbalance due to intentional tremor, he was consulted neurologically again. In the neurological examination: conscious, logical contact, correct speech, narrower eyelid gap in the right eye, in the area of remaining cranial nn without abnormalities, in the limbs without paresis, intentional tremor of the upper limbs of pronounced severity. Based on the whole clinical picture, it was suspected that the above-mentioned tremor is the result of damage to the cerebellum, caused by a toxic background. Alcohol abstinence and control at the Neurological Outpatient Clinic were recommended.

Case 2.

Patient 68 years old, brought because of babble speech, which appeared after a 1.5 hour nap (the patient was last seen healthy about 3 hours before arrival in the emergency room). Until now, he was treated for type 2 diabetes, hypertension, ischemic heart disease, cholecystolithiasis - cholecystectomy. Consumers: Amaryl 4 mg 1x1 tabl, Siofor 850 mg 3x1 tabl, Beto 25 ZK 1x1 tabl, Tritace 10 mg 1x1 tabl, Amlozek 5 mg 1x1 tabl. In the neurological examination: conscious, medium-grade mixed aphasia, selectively fulfills the instructions, isokoria, meningeal symptoms, in terms of remaining cranial nn with no abnormalities, in limbs without paresis, pathological symptoms, nb. Qualification for thrombolytic treatment was carried out: in measurements with SOR: RR 157/92 mmHg, temperature 36.7 degrees C, glucose 38 mg% (test strip made of capillary blood). In CT of the head in both hemispheres of the brain subcortical and periventricular small foci of chronic vascular lesions. Due to hypoglycemia, thrombolytic treatment was abandoned, the patient was referred to O. Internal Medicine. In laboratory tests obtained from venous blood, glucose 32 mg%. Concentrated glucose solutions were used in the treatment, treatment of type 2 diabetes was modified. After glycemic control, neurological re-evaluation was performed: conscious, in verbal con-

tact, normal speech, isokoria, meningeal symptoms, in the scope of remaining cranial without abnormalities, in limbs without paresis, pathological symptoms.

Discussion

Stroke is a common clinical problem, but its diagnosis is still there providing many problems. When starting the diagnosis of sudden hemiparesis, we count with stroke most.[4] Tumor and brain abscess symptoms usually develop over days or weeks, but the onset may also be acute. The neurological symptoms in this case result from the presence of the abnormal "mass". They are the result of increased intracranial pressure, which is a consequence of limited possibilities of abnormal tissue growth within the brain, they also form a set of symptoms resulting directly from damage to certain structures.[5] In the CT of the head, hypodense, "finger" swelling may be visible – so-called ischemic stroke cancer mask. After administration of the shading agent, the tumor mass is enhanced by contrast, and the hypodense zone of edema around the tumor does not change.[6] The advantages of MR in relation to CT are the ability to obtain images of brain structures with high spatial and contrast resolution.[7] The non-invasive and repeatability of the MR examination allows it to be used both in the diagnosis of CNS tumors during the initial assessment of the nature of the tumor (lesions typically benign or suspicious of malignancy), biopsy planning, qualification for neurosurgical surgery, as well as monitoring after treatment – both surgical and after radiation therapy.[8] Contemporary neuroimaging due to the use of functional MRI sequences – diffusion-weighted imaging (DWI), nerve fiber (DTI, diffusion tensor imaging, tractography), perfusion (PWI, perfusion weighted MRI), spectroscopy (MRS, magnetic) resonance spetroscopy) and functional MR (fMRI), allows for multifaceted assessment of the tumor – its structure, both macroscopic and coexisting features within retrograde changes, biochemical features, microcirculation and changes at the cellular and molecular level.[7] In the cases described above, imaging studies showed small nonspecific, vascular origin; no suspected focal length shift. Seizures are rare signs of acute stroke.[8, 9] The neurological deficit that appears immediately after the seizure disappears mimics that caused by vascular disease. Interview regarding illness, disturbed consciousness, retrograde amnesia, and tongue biting symptoms are helpful in diagnosis.[4] The EEG test is of great importance, as it may be normal in the inter-seizure period. You can then perform provocative tests (photostimulation, hyperventilation or sleep deprivation). Sometimes it is useful to conduct a so-called Holter EEG, i.e. several hours or even several days of continuous recording of brain bioelectrical activity.[10] In the described clinical cases, the collected history did not indicate loss of consciousness. Migraine, in particular migraine with aura is one of the postulated risk factors for ischemic stroke in the population of young people.[10] Risk factors have been identified that increase the likelihood of stroke in people with migraine with aura. The most frequent in this case is the high frequency of bouts of headache, smoking and the use of hormonal contraceptives. Despite this, ischemic stroke is rare in this disease (it accounts for 0.5–1.5% of all strokes).[11] Migraine usually causes visual symptoms that run through the field of view within 5-20 min. Sometimes the migraine aura takes the form of sensory disorders also moving within 10-20 min along the limb. The rate of spread of the discomfort in some cases usually makes it possible to distinguish between aura and stroke, in which the spread of the discomfort is minimal or very fast.[12] The biggest problem in differential diagnosis is the differentiation of migraine stroke with a seizure of hemiplegic (hemiplegic; FHM) migraine, especially its sporadic form and/or the first episodes of this disease in life. In some cases, FHM equivocal imaging studies differentiate the above disease entity from stroke. MR FLAIR and T2-dependent images may (although not always) show signs of edema in the opposite hemisphere to symptoms. The DWI study did not always show changes, whereas the study using ADC maps usually did not show deviations from the norm.[13] In one of the described clinical cases, the patient reported headaches. But they occurred for a week before the appearance of the focal symptoms neurological. In addition, speech disorders and paresis of the limb did not appear simultaneously, they were not of a sequential nature.[4] The biggest problem in differential diagnosis is the differentiation of migraine stroke with the attack of hemiplegic (hemiplegic; FHM) migraine, especially its sporadic form and/or the first episodes of this disease in life. In some cases of FHM, imaging studies ambiguously differentiate the above disease entity with stroke. MR FLAIR and T2-dependent images may (although not always) show signs of edema in the opposite hemisphere to symptoms. The DWI study did not always show changes, whereas the study using ADC maps usually did not show deviations from the norm.[13] In one of the described clinical cases, the patient reported headaches. However, they occurred for a week before the appearance of the focal symptoms neurological. In addition, speech disorders and paresis of the limb did not appear simultaneously, they were not of a sequential nature. Migraine was therefore excluded. In the event of coma, glucose fluctuations associated with metabolic disorders, renal impairment, electrolyte levels, infection, alcohol and drug effects should be considered. In some patients with diabetes, in the clinical picture of its complications which is the hyperglycemic-hypermolal state, focal neurological symptoms (hemiparesis, hemiparesis, speech disorder) and seizures predominate. Other characteristic clinical symptoms include: strong thirst, anorexia, orientation disorder, drowsiness, stupor, hypotension, tachycardia, tremor, fever.[14] In treatment, it is im-

portant to correct fluid and electrolyte deficiency as well as insulin therapy.[15] Hypoglycemia is diagnosed when blood glucose levels fall below 55 mg/dL (3.0 mmol/L).[16] Clinical signs that make the diagnosis include: neuroglycopenia (insufficient glucose supply for the proper functioning of the central nervous system) leading to confusion with the features of impaired thinking ability, dizziness, drowsiness, weakness, aggression, anxiety, speech disorders, orientation disorder, stupor, loss of consciousness and coma; and also increased activity of the sympathetic nervous system (tachycardia, increase in blood pressure, confluent sweat, wide pupils, hyperkinesia, tremors and increase in muscle tone, convulsions) and decreased activity of the parasympathetic system (nausea, severe hunger).[15] The treatment uses 20% glucose solution and glucagon administered i.m. or s.c.[15] The most common neurological symptoms in uremic encephalopathy are: disturbance of consciousness, multifocal myoclonus, dysarthria, ataxia, intentional tremor and epileptic seizures. The fluctuating nature of the symptoms is typical.[17] There is also a positive relationship between the rate of increase of failure and the severity of neurological deficits. Hyponatraemia (plasma sodium below 135 mmol/L) is the most common electrolyte disorder that primarily causes CNS symptoms, especially when it develops rapidly. This is due to brain edema that occurs as a result of this disorder.[18] Hyponatraemia can be divided into: mild, usually asymptomatic; moderate when the sodium level drops to 120-130 mmol/l. Then there may be nonspecific symptoms in the form of dizziness and headache, nausea, general tiredness and weakness, muscle cramps. Severe hyponatraemia we recognize when the sodium concentration falls below 120 mmol/l. Such a low concentration causes headache, orientation disorder, epileptic seizures reduction of muscle tone, up to the disappearance of tendon reflexes, Babiński's reflex and even coma.[18,19] Hypernatremia is a condition in which the plasma sodium concentration is > 145 mmol/l. Symptoms include increased thirst, nausea, muscle weakness, fatigue, irritability, drowsiness, convulsions, and coma.[18] Hypokalemia is a condition of low potassium plasma levels below 3.5 mmol/L. Symptoms on the part of the nervous system result from impaired function, associated with changes in the membrane potentials of nerve cells caused by potassium deficiency.[18] We can observe hyperactivity, paresthesia, apathy, impaired concentration and drowsiness, as well as cold intolerance and thirst.[20] Symptoms of hyperkalaemia (blood potassium levels above 5.5 mmol/l) are most common in cases of significant potassium deficiency. We observe muscle disorders in the form of irritability, spasms and even muscle paralysis. Occasional numbness and symptoms of sensory damage may occur.[18-20] In the presented patients' metabolic disorders were the cause of neurological symptoms. The patient described in the first case experienced hyponatraemia resulting from probably prolonged alcohol abuse. Sodium levels were extremely low. The fact that the patient felt worse for several days prior to hospitalization and the worsening of symptoms indicate that hyponatraemia developed in a chronic manner. In the second patient, hypoglycaemia was the cause of neurological disorders. Glucose levels were also extremely low. The severity of the speech disorder suggested that the patient was partially adapted to hypoglycemia. Chronic alcohol abuse is thought to cause two types of change in central nervous system. In the case of direct changes that result from its neurotoxic effects, personality, mood and behavioral changes appear the earliest. Then there are cognitive disorders in the form of abstract thinking disorders, working memory disorders, time and space orientation disorders.[21,22] In the long-term effects of alcohol on the nervous system, vitamin B deficiency (mainly B1) and caloric deficiency are important. In these cases, in addition to neurological and psychiatric symptoms, there are symptoms of damage to the parenchymal organs, mainly the liver, as well as heart and symptoms of damage to the peripheral nervous system. The most common syndrome is Wernicke and Korsakow.[21,22] In the cases described above, the first patient was chronically abusing alcohol. However, the determined level of ethanol in venous blood was negative in both cases.

Conclusion

Stroke is a significant clinical and social problem both in Poland and in the world. Despite this, its diagnostics and especially differentiation is difficult. This is associated with a variety of diseases that can be a "mask" of stroke - from non-vascular neurological diseases (brain tumors, epilepsy) through injuries to very common metabolic disorders (hypoglycemia, hyponatraemia). When analyzing the case of each patient with suspected sudden CNS vascular disease, all of them should be remembered. It should also be borne in mind that differential diagnosis cannot delay specific treatment for stroke.

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LETTER TO THE EDITOR

Basavraj Nagoba (ABDFG), Ajay Gavkare (ABDFG), Nawab Jamadar (ADF)

Plasma Therapy: Why not for post – exposure prophylaxis in Health Care Professionals?

Maharashtra Institute of Medical Sciences & Research, Latur, India

Dear Editor,

The COVID-19 pandemic caused by SARS CoV-2, originated in China in December 2019, is creating havoc in almost all countries and has now become a major concern all over the world. In a battle against COVID-19 disease, health care professionals carry a higher risk of exposure. Health care workers represent one of the most vulnerable populations in terms of contracting the highly virulent disease. It has been observed that during the course of management of COVID-19 cases, many health care professionals have suffered from this dreadful virus. The report shows that many health care professionals from almost all countries with COVID-19 pandemic and in particular from China, United States of America, Germany, Italy, Spain, etc. have lost their lives because of COVID-19 disease. As per the report from WHO 22,073 healthcare workers across 52 countries were infected by COVID-19 as of April 12, 2020.[1] The percentage of infected health workers has almost doubled the number registered in China throughout the epidemic and as many as 100 doctors have succumbed to death in Italy after contracting the novel coronavirus while treating the patients of COVID-19 disease.[2,3] Almost 600 US Healthcare workers have died From COVID-19 as of June 9, 2020.[4] To protect the health of health care professionals must be the top most priority, especially in a current pandemic of COVID-19. Although hydroxychloroquine has been recommended for prophylaxis, there is no supportive evidence that it is an effective prophylactic option to offer protection against SARS CoV-2.[5] Artificially acquired passive immunity is used for treatment as well as for prophylaxis and is particularly useful in clinical emergencies where immediate and temporary protection is needed. The principle of passive immunization is mainly used for prophylaxis in suspected exposed cases and also for treating infected cases. Previously, the use of convalescent plasma has been reported to be successful in postexposure prophylaxis and/or treatment of various infectious diseases, including other coronavirus infections such as SARS-1, Middle East respiratory syndrome (MERS), etc.[6] In view of non-availability of a suitable vaccine and non-availability of defined/established treatment modality against SARS CoV-2, in a current outbreak convalescent plasma (CP) collected from recently recovered individuals from COVID-19 disease is coming up as one of the treatment options. The CP therapy has been proved to be effective in the management of COVID-19 cases with clinical benefits including radiological resolution of pulmonary pathology, reduction in viral loads and improved survival.[6-9] In view of non – availability of effective prophylactic option for health care pro-

Corresponding author: Basavraj Nagoba, e-mail: bsnagoba@gmail.com, dr_bsnagoba@yahoo.com

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fessionals for COVID-19 in a current situation, plasma therapy could be an effective option for post – exposure prophylaxis of health care professionals exposed to infection while treating these cases, as it has been found to be more effective and better in prevention as compared to the treatment/management of infected cases, and thus, has been more promising treatment option for COVID-19 cases with early symptoms and to prevent disease in those who are exposed to infection.[10-11] It has been observed that administration of convalescent plasma would be expected to be more effective before the patient develops its own antibodies to SARS-CoV-2; hence, it would be more effective option for post-exposure prophylaxis rather than treating the infected cases in which already antibodies are formed in response to infection.[12] In a review by Rojas et al., it has been suggested that the benefits of Convalescent Plasma therapy in neutralization of the virus, control of an overactive immune response and immunomodulation of a hypercoagulable state are expected to be better achieved in non-critically hospitalized patients.[13]

We hope that the use of convalescent plasma for post-exposure prophylaxis in health care professionals would be helpful to reduce the mental stress in them and give courage to work non-apprehensively to discharge better services in the present dreadful situation of COVID-19.

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LETTER TO THE EDITOR

Ali Banagozar Mohammadi [1(ACDEF)], Maryam Vahabzadeh [2(ABCDEFG)]

A concurrent outbreak of COVID-19 and methanol poisoning in Iran: Is this the time to make amendments to alcohol drinking laws?

[1] Sina Educational, Research and Treatment Center, Department of Internal Medicine, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[2] Medical Toxicology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Dear Editor,

In late 2019, cases of a highly contagious viral disease, namely coronavirus disease (COVID-19), were reported from China and shortly spread throughout the world population resulting in an unforeseeable pandemic. On February 19, 2020, Iran first reported two confirmed cases of COVID-19, both of which died. Along with other affected countries, partial lockdown and preventive measures were started to take action to help break the spreading chain of the deadly virus. Together with several hygienic recommendations published by health authorities, there was misleading information in social media regarding the disinfecting effect of alcohol ingestion on viruses entering the GI tract. Before long, numerous cases of poisoning with toxic alcohols were referred to Iranian clinical toxicology centers with a range of complications from GI symptoms like nausea and vomiting to more deadly effects such as end-organ failure, blindness, and even death.[1,2]

The World Health Organization (WHO) recommended "70% ethyl alcohol to disinfect reusable dedicated equipment and also sodium hypochlorite at 0.5% (equivalent 5000ppm) for disinfection of frequently touched surfaces in homes or healthcare facilities" along with several other countermeasures such as social distancing and wearing masks against virus transmission.[2] For this reason, the Iranian population rushed to use alcohols to disinfect hands and surfaces that lead to a shortage of alcohols in pharmacies. Based on false information from social media, many individuals began drinking alcohol in the hope of disinfecting the virus within their bodies. In Iran, however, any production, consumption or distribution of alcoholic beverages is prohibited by law since 1979, and alcohol utilization is limited to medical and industrial use. For this reason, alcoholic beverages are obtained through unlawful means such as personal home production and illegal imports from some neighboring countries.[3,4]

Such legislation not only makes it impossible for Iranian Food and Drug Administration authorities to control the quality of alcoholic beverages, but also creates a vicious cycle of supply and demand, providing sub-standard alcohols as a toxic mixture of methanol and ethanol to illegal consumers. Due to such a challenge, methanol poisoning is quite common in Iran. Because of the lack of a comprehensive toxicology registry system in Iran, there is no accurate number for methanol poisonings throughout the COVID-19 pandemic, and the precise mortality

Corresponding author: Maryam Vahabzadeh, e-mail: vahabzadehm@mums.ac.ir

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rates due to methanol poisoning might be under-estimated.[3] However, the Iranian Legal Medicine Organization (LMO) announced referral of 728 deaths between February 19 and April 19, 2020, due to alcohol poisoning, the majority of which involved methanol. Among these, 471 deaths were because of methanol poisoning comprising 422 men, and 49 women.[5] This was considered the greatest methanol mass poisoning nationally and internationally in such a short timeframe.[1] Outbreaks of methanol poisoning and COVID-19 have similarities regarding their high prevalence and there is a direct relationship between the degree of side effects and availability of treatment facilities for patients. In contrast, they have significant differences; for instance, the majority of COVID patients are elderly or those with comorbidities (e.g. hypertension, diabetes, coronary heart disease), while morbidity and mortality in methanol poisoning are most prevalent amongst young and healthy people.[6-12]

Therefore, until appropriate scientific policies for the prevention of alcohol poisoning have not been adopted, and appropriate diagnostic and treatment facilities have not been provided for the poisoned patients, particularly patients with methanol poisoning in Iran, this poisoning will continue. On the other hand, if proper arrangement and policies for alcohol consumption and trade be made and appropriate information provided for citizens, the rate of poisoning from toxic alcohols in Iran can be decreased. Although methanol poisoning is preventable, situations like COVID-related lockdown and stress can increase the risk of toxic alcohol poisoning in Iran.[13]

Considering new legislative measures for alcohol consumption and poisoning with toxic alcohols can prevent further irreparable consequences on public health.[3] Therefore, we recommend that: 1- The Ministry of Health of Iran pay special attention to providing essential facilities for timely diagnosis and treatment of poisonings along with proper training of poisoning course in medical education. International institutes such as WHO may help in this regard; 2- Legislators in Iran make amendments to the law for production, sale, and consumption of alcohols in order to improve the society health and prevent the production of toxic alcohols as beverages; 3- The Food and Drug Administration of Iran strengthen its supervision over pharmaceutical companies for production of alcohol-containing products.

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- The degree of respiratory muscles fatigue depends on the applied exercise protocol and the research group's fitness level. [1, 2] The greatest load with which a patient continues breathing for at least one minute is a measure of inspiratory muscles strength.[3]
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A citation should contain a maximum of 6 authors. Wnen an article has more than six authors, only the first three names should be given by adding 'et al.'. If the source

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Article from a journal, number of authors more than 6	Gonzalez ME, Martin EE, Anwar T, et al. Mesenchymal stem cell-induced DDR2 mediates stromal-breast cancer interactions and metastasis growth. Cell Rep. 2017;18:1215-28. 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;34:1678-88.
Article from an online journal	Coppinger T, Jeanes YM, Hardwick J, Reeves S. Body mass, frequency of eating and breakfast consumption in 9-13-year-olds. J Hum Nutr Diet. 2012;25:43-9. doi: 10.1111/j.1365-277X.2011.01184.x. Cogulu O, Schoumans J, Toruner G, Demkow U, Karaca E, Durmaz AA. Laboratory Genetic Testing in Clinical Practice 2016. Biomed Res Int. 2017;2017:5798714. doi: 10.1155/2017/5798714.
Websites	Cholera in Haiti. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/haiti-cholera/. 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	Naish J, Syndercombe Court D. Medical Sciences. 2nd ed. London, Elsevier;2015. Modlin J, Jenkins P. Decision Analysis in Planning for a Polio Outbreak in the United States. San Francisco, CA:Pediatric Academic Societies;2004.
Chapter in a book	Pignone M, Salazar R. Disease Prevention & Health Promotion. In: Papadakis MA, McPhee S, ed. Current Medical Diagnosis & Treatment. 54th ed. New York, NY: McGraw-Hill Education; 2015:1-19. Solensky R. Drugallergy: desensitization and Treatment of reactions to antibiotics and aspirin. In: Lockey P, ed. Allergens and Allergen Immunotherapy. 3rd ed. New York, NY: Marcel Dekker; 2004:585-606.

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