Wydawnictwo UR 2024
ISSN 2544-1361 (online)
doi: 10.15584/ejcem.2024.1.10

http://www.ejcem.ur.edu.pl
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2024; 22 (1): 68–72

ORIGINAL PAPER

Assessment of serum creatinine, urea, and aminotransferase levels among methamphetamine addicted individuals in Khartoum State

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ABSTRACT

Introduction and aim. Methamphetamine-use disorder is a pressing global public health issue. In Sudan, the escalating methamphetamine (METH) consumption has become a significant social and health problem. This study aims to evaluate liver and kidney biomarkers in methamphetamine addicts in Khartoum state

Material and methods. The study was an analytical prospective cross-sectional hospital-based study. One hundred participants were enrolled in this study, fifty were cases (methamphetamine addicts), and others were healthy non-METH users as a comparative group.

Results. METH users had a mean age of (27±7) years and had been using METH for an average of (14±9) months. Urea and creatinine levels were also significantly elevated in METH users compared to non-users, with $p<0.001$ and $p=0.044$, respectively. Their aspartate transaminase (AST) and alanine transaminase (ALT) levels were significantly higher compared to non-users, with $p<0.001$.

Conclusion. There was significant increases in creatinine, urea, and aminotransferases levels in the case group. ALT showed a moderate positive correlation with abuse duration, while AST showed no significant correlation. Urea and creatinine levels had strong and moderate positive correlations with abuse duration, respectively.

Keywords. aminotransferases, creatinine, methamphetamine, urea

Introduction

Methamphetamine (METH) nowadays is at the top of abused drugs worldwide. It is a widely-abused and addictive psychostimulant.[1] It has become a major social problem causing a substantial economic burden. METH is associated with many disorders and it is metabolized mainly in the liver and excreted by the kidneys.[2] Urea is the non-protein nitrogen compound found in the blood at the highest concentration. It serves as the primary excretory product of protein metabolism. The liver synthesizes urea through the enzymatic conversion of amino groups and free ammonia produced during protein breakdown, a process known as the urea cycle.[3]

Creatinine is synthesized from creatine and creatine phosphate within muscle tissue and is subsequently released into the bloodstream at a consistent rate

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Received: 6.09.2023 / Revised: 4.11.2023 / Accepted: 6.11.2023 / Published: 30.03.2024

Al-Tayeb A-NO, Abubakr MH, Elrheima HA, Habbani AK, Elrasul RYH. Assessment of serum creatinine, urea, and aminotransferase levels among methamphetamine addicted individuals in Khartoum State. *Eur J Clin Exp Med.* 2024;22(1):68–72. doi: 10.15584/ejcem.2024.1.10.

proportional to the individual's muscle mass. The concentration of creatinine in the plasma is inversely correlated with the glomerular filtration rate, which serves as an indicator of renal filtration function. Despite its limitations, plasma creatinine is frequently employed as a means to evaluate renal filtration function.[3]

Aspartate aminotransferase (AST) is ubiquitously present in various tissues such as the liver, brain, pancreas, heart, kidney, lung, and skeletal muscle. In the event of tissue damage in any of these organs, AST is released into the circulatory system.[4]

Alanine aminotransferase (ALT) is predominantly localized in the liver. Elevated levels of ALT are consistently regarded as a matter of concern; however, they do not necessarily imply a serious condition. An increased ALT level may suggest mild or severe liver impairment.[5]

Neurotoxic doses of METH can induce liver necrosis and increase blood levels of ammonia.[4] additionally, one of the kidney's primary functions is the filtration and discarding of waste products from the blood. The measurements of elevated blood urea and creatinine indicate decreased renal function, (reduced clearance).[2,6]

Aim

Therefore, this study was conducted to measure creatinine, urea, and aminotransferases in methamphetamine addicted individuals.

Material and methods

The study was a prospective analytical cross-sectional, hospital-based study conducted in Khartoum during the period from 1st June 2022 to 1st October 2022. Before the examination, participants were given a verbal explanation of the study's goals and procedures. They were then asked to sign a formal consent form. The study was approved by University of Medical Sciences and Technology (IRB UMST/EG/2022/18, approval date 11/01/2022), and all participants were provided with a verbal explanation of the study's objectives and procedures and they were verbally approved.

This study aimed to compare aminotransferase, urea, and creatinine levels among methamphetamine users (case group) and healthy non-users (as a control group).

A total of one hundred participants were recruited for this research investigation, with fifty individuals classified as cases (ICE addicts) undergoing a rehabilitation program for ICE addiction (the period of rehabilitation was not considered). The remaining fifty participants were selected as a control group, consisting of healthy individuals without any history of substance abuse.

Participants with autoimmune diseases, take oral contraceptives, cancer, renal failure, dehydration, liver disease, alcoholics, pregnant women, those with any disorder affect aminotransferase, urea, and creatinine levels, and those who are not willing to agree to participate in the study were excluded.

Data for this study were obtained using a structured questionnaire administered to the participants. Additionally, the history of any previous drug abuse was extracted from the patients' medical records. Then about three mL of venous blood samples were collected in a plain container from all participants using disposable syringes after clearing the skin with 70% alcohol. Then samples were separated by centrifugation at 3000 RMP for three minutes, and serum was obtained.

Aminotransferases were quantified utilizing the kinetic method as per the SPINREACT (Barcelona, Spain) protocols, employing a spectrophotometer BTS 305. Urea levels were determined using the enzymatic urease method following the BioScien (Egypt) procedures with a spectrophotometer BTS 305. On the other hand, creatinine concentrations were assessed using the kinetic Jaffe reaction in accordance with the spectrum procedures using a spectrophotometer BTS 305. The precision and accuracy of all methods used in this study were checked by commercially prepared control (normal and pathological control sera).

Statistical analysis

The data was entered and organized in a Microsoft Office Excel 2010 spreadsheet. The Statistical Package for the Social Sciences software (version 22.0; IBM SPSS Inc.) was used for analysis. The information collected from the questionnaire was coded as variables. The normality of the data was tested using the Kolmogorov-Smirnov test. Descriptive and inferential statistics, including analysis of independent variables, were then conducted.

Results

This was prospective analytical cross sectional study to estimate serum urea, creatinine, AST and ALT levels in METH users. The study enrolled 50 METH users (case group) and 50 non-users (compare group). The mean age of the case group was (27±7) years, while the mean age of the control group was (29±9) years (Table 1). The mean duration of METH abuse was (26±5) months, with a minimum of 3 months and a maximum of 48 months.

Table 1. Distribution of the study group according to age and duration

		Number	Minimum	Maximum	Mean	SD
METH users	Age	50	18	47	27	7
	Duration (months)	50	3	48	26	5
Non users	Age	50	23	43	29	9

The mean creatinine level was significantly higher in case group (1±0.1 mg/dL) when compared to control group (0.8±0.02 mg/dL, p=0.04), whereas the mean urea

level was significantly higher in METH user (42±4 mg/dL) compared to non-users (20±0.5 mg/dL, p<0.001) (Table 2).

The mean ALT level was significantly higher in METH users (37.8±10.6 U/L) compared to the non-users (24.7±2.4 U/L, p<0.001), also AST level was significantly higher in METH users (41.7±9.1 U/L) compared to the non-users (28.7±4.2 U/L, p<0.001).

Table 2. Mean difference of creatinine, urea, ALT and AST levels between users and non-users*

	Creatinine (mg/dl)		Urea (mg/dl)		ALT (U/L)		AST (U/L)	
	M±SD	p	M±SD	p	M±SD	p	M±SD	p
METH users n=50	1.0±0.1	0.04	42±4	<0.001	37.8±10.5	<0.001	41.7± 9.0	<0.001
Non users n=50	0.8±0.02		20±0.5		24.7±2.4		28.7±4.17	

* Data are expressed as mean±SD

There was no significant mean difference of creatinine among tetrahydrocannabinol (THC) and Tramadol (TML) positive and negative group p=0.08 and p=0.79 respectively, whereas mean urea level is higher in THC positive group when compared to THC negative group p=0.04, but no significant difference in the mean of urea among TML positive and negative group (p=0.63) (Table 3 and Table 4).

Table 3. Mean difference of creatinine, urea, ALT and AST levels between THC positive and negative*

	Creatinine (mg/dl)		Urea (mg/dl)		ALT (U/L)		AST (U/L)	
	M±SD	p	M±SD	p	M±SD	p	M±SD	p
THC positive n=15	0.8±0.06	0.08	30 ±12	0.02	36.4±3.18	0.399	40.3 ±8.0	0.447
THC negative n=35	0.8±0.02		46 ±35		38.4±12.4		42.3±9.5	

* Data are expressed as mean±SD

Table 4. Mean difference of creatinine, urea, ALT and AST levels between TML positive and negative

	Creatinine (mg/dl)		Urea (mg/dl)		ALT(U/L)		AST(U/L)	
	M±SD	P	M±SD	P	M±SD	p	M±SD	p
TML Positive n= 2	1.1±0.15	0.79	34 ±18	0.63	41±2.82	0.292	36.5±0.7	0.414
TML Negative n = 48	1.0±0.12		42 ±31		37.7±10.7		41.9±9.2	

There was no significant mean difference of ALT among THC and TML positive and negative group p=0.399 and p=0.292, respectively.

Additionally, there was no significant mean difference of AST among THC and TML positive and negative, p=0.447 and p=0.414, respectively.

There was a moderate positive correlation between creatinine and duration of addiction (r=0.496, p<0.001), and a strong positive correlation between urea level and duration of abuse (r=0.877, p<0.001) (Table 5).

There was a week positive correlation between AST levels of the METH users and duration of use, r=0.196, the correlation was statistically insignificant, p value 0.174. Moreover, there was a moderate positive correlation between ALT levels of the METH users and duration of use, r=0.300, the correlation was statistically significant, p=0.034.

Table 5. Correlation between urea, creatinine, ALT and AST with duration of use among the case group, n=50

	Variables	Urea (mg/dl)	Creatinine (mg/dl)	ALT (U/L)	AST (U/L)
Duration of use (months)	Correlation coefficient	0.877	0.496	0.300	0.196
	Sig. (2-tailed)	<0.001	<0.001	0.034	0.174
	Number	50	50	50	50
	Strength	Strong	Moderate	Weak	Weak
	Direction	Positive	Positive	Positive	Positive

Discussion

The misuse of METH places a significant financial strain on families, resulting in a range of societal issues. Moreover, it gives rise to various detrimental health effects such as heart problems, liver and kidney failure, as well as neurodegenerative disorders.[7] Hepatocellular enzyme serum concentrations and creatinine, urea levels can be utilized as selective biomarkers for hepatic tissue damage and kidney damage respectively.[8]

This study aimed to measure creatinine, urea, AST and ALT serum levels among METH addicted individuals in Khartoum state.

In the present study, there were significant increase in urea and creatinine levels among METH users when compared to control group. Similar observation has been recorded by Basile et al., and Baradhi et al.[9,10] They suggested multiple factors that contribute to the development of acute kidney injury in cases of methamphetamine intoxication. These include vasoconstriction, instability in hemodynamics, depletion of fluid volume, hyperthermia, and the development of pigment nephropathy due to rhabdomyolysis.[11,12]

Nephrotoxicity can occur with both prescribed medications and illicit substances. Methamphetamine is an example of a drug that can cause nephrotoxicity, potentially resulting in kidney failure. This failure can manifest as either chronic over a prolonged period or acute suddenly. Drug-induced nephrotoxicity, including methamphetamine use, is a frequently observed cause of sudden kidney failure.[10]

Furthermore, the study revealed significant increase in hepatocellular enzymes (AST and ALT) in METH addicted case group when compared to the non-users control group. These findings were in accordance with

results of Halpin et al. and Chian et al. their studies included individuals who exhibited a diverse array of clinical manifestations, including both acute and chronic hepatitis, as a consequence of methamphetamine addiction.[13,14] Also the findings were in match with a study performed by Shannon et al., who concluded that liver injury can be an effect of methamphetamine abuse.[13]

Possible mechanism of liver injury in methamphetamine includes; lipid peroxidation and toxic effects on liver cells.[15]

However, the present findings were inconsistent with Nazari et al. and Zhao et al., who stated that, there were no differences in ALT between the two groups.[16,17]

This may be attributed to variations in the research design (differences in sample size, and participant demographics) and contextual factors (geographical location and time period of the study) which may influence the outcomes. Moreover, the study showed that there was a strong positive correlation between urea levels and duration of the METH abuse and a moderate positive correlation between creatinine levels and duration of METH abuse

Additionally, there was a moderate positive correlation between ALT levels and duration of use. METH-induced hepatocellular damage maybe the consequence of the direct effects of the drug on the liver and the relatively prolonged duration of abuse.

The study encountered several limitations. Firstly, the stigma surrounding the study population presented challenges in data collection. Additionally, the timing of sample collection proved to be a significant obstacle. Furthermore, the study faced limitations due to the limited availability of admitted addicts for inclusion. Moreover, the lack of complete patient history and data accessibility further constrained the study.

Further investigation is strongly recommended, encompassing a comprehensive assessment of renal and hepatic functionalities. To accurately gauge the extent of renal impairment, it is advised to employ more specific renal markers such as cystatin C, estimated glomerular filtration rate, neutrophil gelatinase–associated lipocalin, and kidney injury molecule-1. Additionally, measuring ammonia levels is recommended to evaluate the severity of liver damage. Also, it is highly recommended to enhance public awareness regarding the use of METH, the contributing factors to its abuse, and the associated health complications.

Conclusion

There was significant increase in creatinine, urea, ALT and AST levels among METH addicts, strong positive correlation between duration and urea levels, and moderate positive correlation between the duration and creatinine and ALT level. However, AST levels showed no significant correlation with the duration of abuse.

Declaration

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors. This study was funded by the authors; no special funds were received.

Author contributions

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

Conflicts of interest

The authors have no conflicts of interest to declare.

Data availability

All datasets are available upon request from the corresponding author.

Ethics approval

The study was approved by the ethical committees of the University of Medical Sciences and Technology (IRB UMST/EG/2022/18, approval date 11/01/2022). Verbal consents were obtained from all participants, and approval was granted by the hospital administration through the office of the medical director.

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