

Estimation of Liver Enzymes and Ammonia in Methamphetamine Abusers in Khartoum State

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Abstract:

➤ *Background:*

Substance abuse poses significant health challenges, including hepatic and metabolic disruptions. "Ice Crystal" (Shabu), a methamphetamine-based drug, is widely abused and associated with severe physiological effects. Despite its prevalence, limited research exists on its impact on liver enzymes and ammonia levels in users.

➤ *Aim:*

This study aimed to evaluate the effects of Ice Crystal (Shabu) use on liver enzyme activity and ammonia levels and to examine correlations between substance usage patterns, demographics, and biochemical changes.

➤ *Methods:*

A cross-sectional study was conducted from March to April 2022, involving 50 Ice Crystal users (test group) and 50 non-users (control group). Blood samples were collected from all participants, and liver enzyme activity and ammonia levels were assessed using an automated chemistry analyzer. Statistical analyses were performed to compare biochemical markers between the groups and identify associations with variables such as age, gender, usage method, and quantity.

➤ *Results:*

The results revealed a significant elevation in liver enzyme activity and ammonia levels among the test group compared to the control group, with p-values of 0.005 and 0.001, respectively. Furthermore, positive correlations were observed between substance usage patterns (method and quantity), demographic factors (age and gender), and biochemical changes.

➤ *Conclusion:*

Ice Crystal (Shabu) use is significantly associated with elevated liver enzymes and ammonia levels, highlighting its potential to cause liver damage and metabolic disturbances. These findings emphasize the urgent need to raise awareness about the adverse health effects of methamphetamine abuse and advocate for preventive interventions to safeguard public health.

Keywords: Liver Enzymes, Ammonia, Methamphetamine Abusers, Khartoum State.

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I. INTRODUCTION

Methamphetamine is a strong synthetic stimulant known for its high addictive potential⁽¹⁾. While the U.S. Food and Drug Administration (FDA) permits its limited use in treating attention deficit hyperactivity disorder and managing short-term obesity. The majority of methamphetamine encountered worldwide is illicitly produced⁽²⁾. The substance is appearing as either a powder or crystalline form known as "ice". This drug can be consumed through multiple routes, including smoking, snorting, injection, or oral ingestion⁽³⁾. Short-term use typically enhances alertness, sociability, and euphoria, while suppressing appetite⁽⁴⁾. Chronic use, however, is linked to severe health complications, including accidental overdose⁽⁵⁾.

The liver, the largest internal organ in humans, performs numerous vital functions, such as metabolism, detoxification, digestion, and the elimination of harmful substances^(6,7). These synthetic, excretory, and metabolic activities are crucial for maintaining homeostasis⁽⁸⁾. One unique characteristic of the liver is its ability to regenerate after short-term injury. Nonetheless, persistent damage over time can result in irreversible alterations that compromise normal liver function^(9,10).

Ammonia is generated during the breakdown of amino acids in protein metabolism⁽¹¹⁾. Under physiological conditions, the liver converts ammonia into urea for safe excretion, and residual ammonia is eliminated by the kidneys, where it helps buffer urine^(12,13). Disruption of this process may have significant clinical consequences.

Evaluation of liver function commonly involves measuring enzyme activities in the blood. Alkaline phosphatase (ALP) is a cell-surface enzyme present in multiple tissues, including the liver, intestine, bone, spleen, placenta, and kidney⁽²⁾. Elevated ALP levels are particularly informative in assessing hepatobiliary and bone disorders. Aspartate aminotransferase (AST), a member of the transferase enzyme family, is found abundantly in liver, cardiac, and skeletal muscle tissues, with smaller amounts in kidney, pancreas, and red blood cells^(8,14). Clinically, AST is used primarily to assess hepatocellular and skeletal muscle disorders⁽¹⁵⁾. Alanine aminotransferase (ALT) shows enzymatic activity similar to AST and is highly concentrated in the liver, making it more liver-specific^(6,7). Gamma-glutamyl transferase (GGT) is an enzyme found in hepatocyte canaliculi and bile duct epithelial cells which participate in transferring glutamyl residues to amino acids and peptides, and is present mainly in liver, kidney, pancreas, brain, and prostate tissues. It was one of the most sensitive enzymatic markers of liver and bile duct pathology⁽¹⁶⁻¹⁸⁾.

Therefore, this study aimed to estimate liver enzymes (ALP, AST, ALT, and GGT) and ammonia levels among methamphetamine abusers in Khartoum State.

II. MATERIALS AND METHODS

➤ Study Design:

A cross-sectional case-control study was conducted in Khartoum State, Sudan, from March to April 2022.

➤ Study Population:

A total of 100 Sudanese adults were enrolled, comprising 50 methamphetamine ("Ice Crystal") users (case group) and 50 healthy non-users (control group). Individuals with pre-existing liver disease, alcoholism, or schistosomiasis were excluded.

➤ Sample Collection:

Venous blood samples (2.5 mL) were collected from each participant. Serum was separated by centrifugation at 3600 rpm for 10 minutes and stored at 2-8°C until analysis. For ammonia measurement, plasma was obtained from EDTA-anticoagulated blood, immediately placed on ice, and centrifuged at 10,000 rpm for 2 minutes.

➤ Biochemical Analysis:

All parameters were measured using a Bio base automated chemistry analyzer according to the manufacturer's protocols.

- ALT and AST: Measured using standard kinetic methods based on the rate of NADH oxidation, monitored at 340 nm. Activity is proportional to the decrease in absorbance.
- ALP: Measured kinetically at 405 nm based on the formation of 4-nitrophenol from 4-nitrophenylphosphate.
- GGT: Measured at 412 nm based on the release of 3-carboxy-4-nitroaniline from a synthetic substrate.
- Ammonia: Measured enzymatically using glutamate dehydrogenase; the decrease in absorbance at 340 nm (NADPH consumption) is proportional to ammonia concentration.

➤ Statistical Analysis:

Data were analyzed using SPSS version 25. An independent t-test was used to compare means between groups, and Pearson's correlation was used to assess relationships between variables. A p-value ≤ 0.05 was considered significant.

➤ Ethical Considerations:

Ethical approval was obtained from Alzaiem Alazhari University. All participants provided written informed consent.

III. RESULTS

A total of 100 specimens were analyzed, consisting of 50 cases (amphetamine users) and 50 controls (non-users). Among the participants, 7 were females, and the remaining were males (Table-1).

The mean Alkaline Phosphatase (ALP) level in the case group was 140.9, compared to 65.5 in the control group. The difference was statistically significant ($p < 0.0001$; Table-2).

The mean Ammonia (NH₃) level in the case group was 45.7, compared to 25.4 in the control group. The difference was statistically significant ($p < 0.0001$; Table-2).

The mean Alanine Aminotransferase (ALT) level in the case group was 68.6, compared to 35.6 in the control group. The difference was statistically significant ($p < 0.0001$; Table-2).

The mean Aspartate Aminotransferase (AST) level in the case group was 77.5, compared to 32.9 in the control group. The difference was statistically significant ($p < 0.0001$; Table-2).

The mean Gamma-Glutamyl Transferase (GGT) level in the case group was 29.7, compared to 24.8 in the control group. The difference was statistically significant ($p = 0.047$; Table-2).

IV. CORRELATION ANALYSIS

Pearson’s correlation was used to analyze the relationship between age and biochemical parameters among amphetamine users:

- **ALP:** A correlation coefficient of 0.090 was observed, with a p-value of 0.5, indicating no statistical significance (Table-3).
- **NH₃:** A correlation coefficient of 0.071 was observed, with a p-value of 0.6, indicating no statistical significance (Table-3).
- **ALT:** A correlation coefficient of 0.142 was observed, with a p-value of 0.3, indicating no statistical significance (Table-3).
- **AST:** A correlation coefficient of 0.289 was observed, with a p-value of 0.04, indicating statistical significance (Table-3).
- **GGT:** A correlation coefficient of 0.231 was observed, with a p-value of 0.1, indicating no statistical significance (Table-3).

Comparison of enzymes levels means between categories of usage frequency among ice crystal abusers (Table-4).

The study demonstrates significant elevations in liver enzymes (ALP, ALT, AST, and GGT) and ammonia levels in amphetamine users compared to the control group. Correlation analysis revealed limited significant associations between age and biochemical parameters, except for AST, which showed a statistically significant relationship.

Table-1: Frequency of Gender Among the Study Groups

The study groups		Frequency	Percent
Amphetamine non users	female	7	14.0
	male	43	86.0
	Total	50	100.0
Amphetamine abusers	female	7	14.0
	male	43	86.0
	Total	50	100.0

Table-2: Comparison of ALP,ALT,AST,GGT,NH₃ Means Between Amphetamine Abusers and Non Users

Tests	Case Group Mean SD	Control Group Mean SD	P. Value
ALP IU\L	140.9 ± 30.7	35.5 ± 13.4	0.0001
NH ₃ IU\L	45.7 ± 6.5	25.4 ± 7.4	0.0001
ALT IU\L	68.8 ± 29.9	35.6 ± 9.1	0.0001
AST IU\L	77.5 ± 17.1	32.9 ± 7.2	0.0001
GGT IU\L	29.7 ± 14.5	24.8 ± 8.6	0.047

Table-3: Correlation of Age to Liver Enzymes and NH₃ Among Amphetamine Abusers

	Person correlation	P value
ALP IU\L	-0.090	0.5
NH ₃	-0.071	0.6
ALT IU\L	-0.142	0.3
AST IU\L	-0.289*	0.04
GGT IU\L	0.231	0.1

Table-4: Comparison of Enzymes Levels Means Between Categories of Duration Abuse Among Ice Crystal Abusers

	Duration of abuse	N	Mean	Std. Deviation	P .value
ALP IU/L	Up to 2 years	17	145.6	28.6	0.4
	More than 2 years	32	138.4	31.8	
ALT IU/L	Up to 2 years	18	57.2	25.5	0.03
	More than 2 years	31	75.52	30.5	
AST IU/L	Up to 2 years	18	72.0	16.3	0.08
	More than 2 years	32	80.6	17.0	
GGT IU/L	Up to 2 years	17	29.2	13.8	0.8
	More than 2 years	31	29.9	15.1	
NH3	Up to 2 years	17	39.2	6.6	0.0001
	More than 2 years	32	49.1	2.8	

Table-5: Comparison of Enzymes Levels Means Between Categories of Usage Frequency Among Ice Crystal Abusers

	Usage times	N	Mean	Std. Deviation	P .value
ALP IU/L	Every day	34	142.1	33.2	0.6
	Once every 2 to 3 weeks	15	138.01	24.7	
ALT IU/L	Every day	34	71.5	30.8	0.3
	Once every 2 to 3 weeks	15	62.7	27.6	
AST IU/L	Every day	35	78.6	17.4	0.4
	Once every 2 to 3 weeks	15	74.8	16.7	
GGT IU/L	Every day	33	29.7	14.4	0.9
	Once every 2 to 3 weeks	15	29.6	15.0	
NH3	Every day	35	49.0	2.8	0.0001
	Once every 2 to 3 weeks	14	37.4	5.9	

V. DISCUSSION

This study aimed to evaluate the impact of Ice Crystal (Shabu) use on liver function and ammonia metabolism by analyzing liver enzyme activity and ammonia levels in amphetamine users compared to non-users. The findings reveal significant alterations in these biochemical markers among amphetamine users, highlighting the potential hepatotoxic and metabolic effects of methamphetamine abuse.

The significantly elevated levels of liver enzymes, including ALT, AST, ALP, and GGT, observed in the case group indicate potential hepatocellular damage and cholestatic effects caused by methamphetamine use. Elevated ALT and AST levels are well-recognized markers of liver injury, particularly when associated with substance abuse, which induces oxidative stress and mitochondrial dysfunction in hepatocytes (19,20). Similarly, the rise in ALP and GGT levels points to possible cholestasis or bile duct injury, corroborating previous studies linking amphetamine use to hepatic dysfunction (21).

The increased ammonia levels in the case group further suggest impaired nitrogen metabolism, potentially resulting from methamphetamine's toxic effects on the liver's urea cycle. Hyperammonemia has been reported as a consequence of hepatocyte dysfunction, leading to an accumulation of ammonia in the blood (4). This condition can have severe neurological implications, including hepatic encephalopathy, as suggested by prior research on methamphetamine-induced hepatic stress (22).

Correlation analysis revealed a significant association between AST levels and age among amphetamine users, which aligns with existing evidence that age-related physiological changes may exacerbate the hepatotoxic effects of methamphetamine (23). However, other liver enzymes and ammonia levels showed no statistically significant correlations with age, gender, or usage patterns, suggesting that individual physiological responses to methamphetamine vary widely.

The findings underscore the need for heightened clinical awareness of methamphetamine's adverse effects on liver function and metabolic health. Public health interventions focusing on prevention, early detection, and management of liver dysfunction in amphetamine users are essential to mitigate these risks. Future studies should explore the underlying mechanisms of methamphetamine-induced hepatotoxicity and investigate potential therapeutic interventions.

A study conducted by Halpin and Yamamoto (2012) investigated the biochemical disruptions caused by methamphetamine (METH). The study tested plasma ammonia levels and liver enzymes (AST and ALT). They found a significant increase in both ammonia and liver enzymes in the subjects. These results are highly consistent with our findings in Khartoum State, where we also observed a significant elevation in ammonia and liver enzymes among the "Ice Crystal" test group. This agreement reinforces the evidence that methamphetamine acts as a potent hepatotoxic agent that disrupts nitrogen metabolism (24).

Regarding liver function, Al-huseini *et al* (2018) are tested ALT and AST levels in methamphetamine addicts and they found a significant increase in ALT and AST levels with (p-value < 0.05). This finding aligns with the current study results, which also observed a significant elevation in liver enzyme activity (ALT, AST) with a (p-value of 0.005), confirming that the drug induces substantial hepatocyte damage⁽²⁵⁾.

A study done by Basu *et al* (2020), focused on ammonia testing in substance abusers are reported a significant elevation in ammonia level with a (p-value of 0.008). This finding is agree with the current study result (P = 0.001). Both studies suggest that methamphetamine use impairs the hepatic urea cycle, leading to the accumulation of ammonia in the blood⁽²⁶⁾.

VI. CONCLUSION

This study demonstrates that Ice Crystal (Shabu) use significantly elevates liver enzyme and ammonia levels, indicating potential hepatotoxicity and impaired nitrogen metabolism. The findings highlight the severe impact of methamphetamine on liver function and metabolic processes, with AST showing a notable correlation with age among users.

These results emphasize the urgent need for healthcare providers to monitor liver function in amphetamine users and to develop targeted interventions for early diagnosis and treatment of methamphetamine-induced liver damage. Public health strategies aimed at reducing methamphetamine use and educating at-risk populations about its harmful effects are critical.

Further research is recommended to explore the underlying mechanisms of hepatotoxicity in methamphetamine users and to identify potential therapeutic approaches to mitigate these adverse effects.

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