

Biochemical and Hematological Markers of Methamphetamine-Induced Systemic Toxicity

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ABSTRACT

In this work, the hematological and hormonal changes in 50 chronic methamphetamine (MA) male abusers in comparison to normal controls, showing that systemic dysregulation occurs outside of neurotoxicity. The major findings in hematology were the gradual and substantial accumulation of neutrophils (up to 72.4% on day 22) indicating ongoing neutrophilic inflammatory response, a drastic decrease in the number of erythrocytes (to 2.3 million/ μ L), and hematocrit, which confirmed the development of anemia. It has been supported by an increase in osmotic fragility that is significant indicating erythrocyte membrane oxidative damage. The number of platelets also changed non-significantly with a possible risk of thrombocytopenia. Hormonal analyses showed a deep endocrine dysfunction, with a testosterone level of 2.5 ng/mL and a cortisol level of 27 μ g/dl, which indicated hypothalamic-pituitary-gonadal (HPG) axis suppression and hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis respectively. These occurrences show that persistent MA use causes simultaneous hematological issues and hormonal derangements hence the need to carry out thorough physiological monitoring in the management of addiction.

Keywords: Methamphetamine; hematological alterations; endocrine dysfunction; oxidative stress; anemia; testosterone; cortisol; drug addiction

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INTRODUCTION

Methamphetamine was discovered in 1893 commonly called crystal meth, is widely used. Methamphetamine is available in variety of morphs like as a pure crystalline hydrochloride salt or in tablets form. Paths of administration are sniffing, respiratory inhalation, intravenous administration and oral ingestion. The effects of methamphetamine use include euphoria; these effects may last much longer [1].

Addiction is a treatable, chronic medical disease involving complex interactions of brain circulatory, genetics, environment, and an individual's life experiences. Patients with addiction have identifiable, characteristic signs and symptoms, the very serious issue in the cosmopolitan society of Pakistan [2-4].

Methamphetamine addiction is the prevailing abusing drug in most regions of the world like Europe, Australia, Asia and United States as World drug report 2020 states that,

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about 27 million people are addicted to methamphetamine globally [5, 6].

A questionnaire-based study was conducted regarding the awareness of Meth Addiction 142 persons were included in the study with male 55% and 45% female in Karachi Pakistan who know the possible implications of MA however 38% male and 14% female were still using methamphetamine for addiction; therefore, it is important for drugs controlling authorities and public health to combat the alarming addiction ration among teenagers and adults in Pakistan [7-11].

Methamphetamine addiction is a chronic public health concerns having mostly physical psychological and social implications. The consumption of methamphetamine compound is very common in Pakistan. Methamphetamine addiction is the panic issue of the globe that have hazardous consequences of health and society as well, it is widely used illicit drug worldwide and its misuse has been increased in the recent years with higher mortality rate in present more specifically in Europe [12-15].

Factors for the abuse of amphetamines addiction are euphoria, mood swings, and loss of appetite, ease of availability, illegal trafficking, and the affordability of illicit amphetamines as compared to other illicit drugs [17].

Methamphetamine addiction has elevated levels of liver enzymes (ALT, AST, alkaline phosphatase), white blood cells (WBCs), and platelets, while showing decreased hemoglobin, hematocrit, and albumin levels compared to healthy individuals. These changes suggest increased inflammation and a higher risk of liver disease and anemia among abusers [18-22]. Methamphetamine abusers had decreased fasting blood glucose levels, alongside increased serum levels of creatinine and creatine kinase, further highlighting metabolic disturbances associated with the drug [23-26]. Addiction or substance abuse have serious public health related hazards [27].

Methamphetamine, once used for medical purposes, is now a popular street drug with dangerous effects. In small doses, it boosts alertness, but higher doses or long-term use harm learning, decision-making, and motor skills. Withdrawal can cause depression and psychosis. This review highlights how methamphetamine affects cognition, risk-taking, and driving performance, stressing that using it without medical supervision increases these risks [28-32]. Nevertheless, in the last decade, new regions emerged as the meth main producers and suppliers: Southeast and East Asia. While experts say the meth epidemic trimmed around 2000-2001, meth use and trafficking abounds in some corners of the Mekong. Cambodia, Indonesia, Malaysia, and the Philippines are among those countries with a meth production issue. In order to slow the continued penetration of meth into these locations more effort has to be applied [33-38]. Methamphetamine (MA) is a powerful stimulant and addictive drug that has excessively used in North America in the past, the drug that is toxic to the brain; therefore,

any abusive use is likely to cause excessive neural deterioration. This damage commonly makes learners experience dementia touching on elements such as attention, memory as well as capability of reasoning. This review examine the impact of MA use and considers MA-induced psychosis [39-43].

In the a study, the participants were examined in relation to blood and biochemical factors influenced by methamphetamine abuse. A total of 60 methamphetamine addicts showed increased liver enzymes, white blood cells, platelets and creatinine level, and reduced hemoglobin and albumin level comparing with 60 normal subjects. These investigations declare possible elevated morbidity from liver disease, inflammation, and anemia [44-47]

Methamphetamine (MA) addictions in young aged persons elevate public health related issues. A meta synthesis of 47 papers showed that MA use was significantly related to psychiatric disorders such as depression, psychosis and suicidal behaviors. Young MA users are also likely to die from overdose and suicide [48].

Methamphetamine is a stimulant, which has been associated with increased sexual risk taking, HIV/AIDS positive status, violence and socially undesirable conducts. The number of women seeking meth use disorder treatment is surpassing the number of men seeking the same. Today's treatment programs may not address the specifics related to women adequately. Meth's versatility and effects are studied in this article focusing on the effect on women and overall treatment and prevention reflections [49].

Methamphetamine (MA) use among young people is linked to serious mental health issues like depression, psychosis, and suicidal thoughts, with overdose and suicide being major causes of death. The evidence connecting MA to infections and dental problems is weak. Public health efforts should focus on well-documented mental health risks, while further research explores other possible harms [50]

Southeast and East Asia have emerged as global centers for methamphetamine production and trafficking over the past decade. This paper examines the rise of methamphetamine supply and the extent of its use in the region. Data from the Drug Abuse Information Network for Asia and the Pacific (DAINAP) shows that the methamphetamine epidemic peaked in 2000–2001 but continues to grow in parts of the Mekong region. Large-scale production is evident in countries like Cambodia, Indonesia, Malaysia, and the Philippines. Although smoking and ingestion are common, drug injection also occurs. Continued focus is needed to control the drug's spread [51].

Methamphetamine Addiction changed the monthly cycle of the female where bleeding level were deviated from the normal range. Irregularities of sex hormones was observed in 73.3% of participants during asceticism. The most common patterns were simple anovular menstruation,

which was caused mainly by a hypothalamic deregulation and pituitary suppression with or without ovarian suppression. Normal hormone levels were observed more frequently in participants abstinent for more than 10 months (39.5%) than in participants who were abstinent for less than 10 months (18.6%) [52, 53].

MATERIALS AND METHODS

A total of 50 male subjects addicted to narcotic drug Methamphetamine (NDM, $N = 50$) were enrolled. Only single-drug users were included; individuals with co-morbid infections (HIV, hepatitis, syphilis), contagious diseases, or dermatological syndromes were excluded. The experimental group (ET) consisted of methamphetamine abusers, while a healthy control group was included for comparison.

Participants were recruited from the Hematological Research Unit 1, Federal Urdu University of Arts, Science and Technology (FUUAST), Karachi, with approval from Prof. Dr. M.J. Haider. Venous blood (3 mL) was collected from the cubital vein using sterile techniques and transferred to EDTA tubes. Sampling occurred between 7:00 AM and 8:00 PM. Hematological parameters analyzed included segmented and band neutrophils (%), eosinophils (%), basophils (%), platelet count ($\times 10^3/\mu\text{L}$), erythrocyte count ($\times 10^6/\mu\text{L}$), hemoglobin (g/dL), hematocrit (%), osmotic fragility (%), and RBC reduction (%). Data were analyzed using SPSS version 2009 to determine statistical significance between experimental and control groups.

RESULTS

Segmented Neutrophils value showed an increase in its value along with t value from day first (60%) onward up to

day 22nd (72.4%) during increase of the administration of doses NDM an indication for neutropenia may be due to mild bacterial infection or inflammatory response due to bacterial invasion associated with NDM administration.

No significant change has been noted in Band neutrophils (%) and eosinophils (%), which is an indication of lack of microbe's attack. Basophils showed a non-significant elevation on day 22nd. Thrombocyte counts were little devalued from 200,000 to 170,000/ μL , but the changes were non-significant and only show the risk of thrombocytopenia. Osmotic fragility values were significantly elevated than reference value, implications of increased erythrocyte membrane fragility, might be due to oxidative stress.

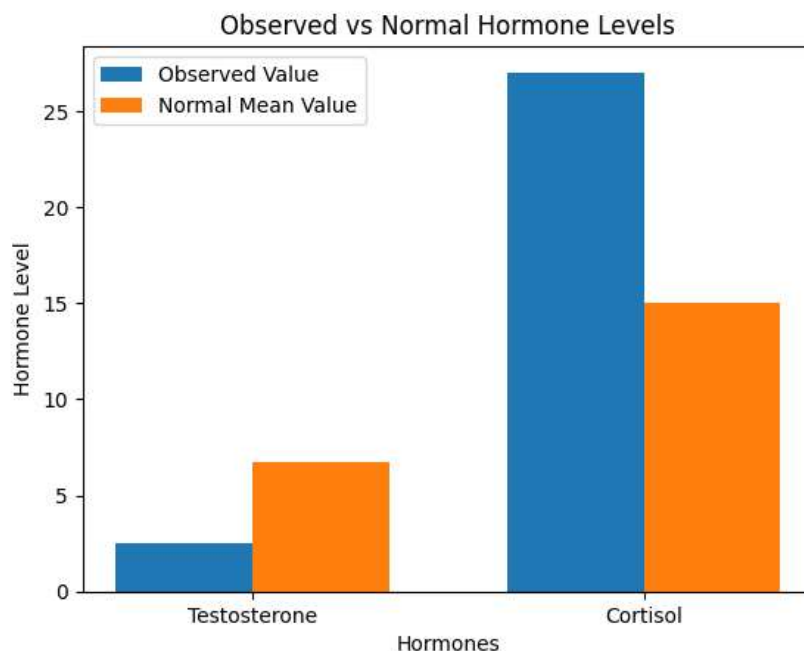
Erythrocyte count devalued from 4.2 to 2.3 million/ μL by day 22, significantly below the normal range, implicating anemia development. Hemoglobin level first dropped and then rose up significantly on day 22nd, which is a reflection of compensatory erythropoietic response. Hematocrit was decreased as compared to the reference value, suggesting diluted blood volume or anemia, aligning with reduced RBC count. Hemolysis may not have been occurred despite of reduction of RBCs % remained largely insignificant, supporting that although erythrocytes reduced numerically. This study indicates that chronic exposure to NDM at ever-increasing doses over 30 days induces hematological alterations, notably neutrophilia, anemia, increased osmotic fragility, and devaluation in hematocrit value. These alterations are statistically significant in key parameters and may reflect a combined effect of altered erythrocyte integrity, bone marrow stress, and mechanism for compensation.

Table 1: Hematological Parameters Analysis among Methamphetamine Abusers

S.No	Blood Parameters	Values	References Value	T value
1	Segmented Neutrophils %	67.05%	45-75%	1.16
2	Band Neutrophils %	1.35	0-5%	0.55
3	Eosinophils %	3.89	0-8%	1.25
4	Basophil %	0.20	0-3%	1.11
5	Thrombocytes count / μL	185000	200000-500000	1.35
6	Osmotic fragility (%NaCl) 75g/dl (NaCl)	8.00	0.8-9.1	1.54
7	Erythrocytes count M/ μL	2.97	4.4-5.7	1.75
8	Hemoglobin concentration g/dl	15.70	14-17.4	1.70
9	Hematocrit Vol %	35.18	42-52	1.55
10	Reduction of RBCs %	0.43	0.0-0.0	0.00

Table 2: Hormonal Analysis Among Methamphetamine Abusers

S. No	Hormones	Observed Value	Normal Value
1	Testosterone	2.5 ng/ml	2.7-10.7ng/ml
2	cortisol	27 $\mu\text{g/dl}$	5-25 $\mu\text{g/dl}$



DISCUSSION

This study shows that long-term exposure to methamphetamine (NDM) and have observed induced hematological parameters and an imbalance of hormonal level in males. A steady increase in segmented neutrophils from day 1 (60%) to day 22 (72.4%) with a t-value of 1.16 is consistent with a neutrophilic response and perhaps a response to inflammatory reactions or subclinical infections related to NDM use. Band neutrophils and eosinophils were normal, representing no significant microbial or parasitic infections, while a slight though non-significant increase in basophils can be seen as low-grade immune stimulation. Platelet counts decreased slightly but not significantly, indicating a possible risk of thrombocytopenia which may increase with long-term exposure. The results related to the erythrocyte were more significant. A dramatic decrease in the number of RBC from 4.2 to 2.3 million/uL ($t = 1.75$) and hematocrit ($t = 1.55$) suggests the development of anemia, perhaps as a result of bone marrow suppression or oxidative damage. The studies also confirmed by an increase in osmotic fragility ($t = 1.54$) reflecting a loss of erythrocyte membrane integrity, which is presumably due to oxidative stress-a known effect of chronic exposure to stimulants. Interestingly, hemoglobin concentration decreased but subsequently increased markedly by day 22 ($t = 1.70$) indicating a compensatory erythropoietic response. However, the negligible decrease in RBCs percentage ($t = 0.00$) suggests that hemolysis does not seem to be the main mechanism of anemia.

Hormonal examination showed testosterone at 2.5 ng/mL, lower than normal, suggesting suppression of the hypothalamic-pituitary-gonadal (HPG) axis, which in long-term users can cause fatigue, loss of libido, and reproductive problems. Elevated cortisol (27 ug/dL)

reflected HPA axis hyperactivation consistent with chronic physiological stress, immune suppression and mood dysregulation commonly described in methamphetamine users. Our findings demonstrate a systemic effect of methamphetamine abuse beyond neurotoxicity in immune competence and endocrine control.

CONCLUSION

Persistent methamphetamine addiction leads to severe and parallel hematological and endocrine pathophysiology as demonstrated by the emergence of neutrophilic response, anemia and elevated erythrocyte osmotic fragility, and thrombocytopenia tendency. The testosterone inhibition and cortisol increase are the hormonal proofs of the chronic physiological stress and the HPG and HPA axes deregulation. These systemic changes involved are characterized by signs of oxidative stress, inflammatory stimulation, and bone marrow suppression and place the familiar pathology of MA abuse beyond central nervous system toxicity. The results support the fact that regular hematological and hormonal screening should be included in the rehabilitation schedule and state the urgency of the focus on the development of the public health policies, which would cover the holistic burden of physiological consequences of MA dependence to reduce potential harm in the long run and improve the effectiveness of its treatment.

SUGGESTIONS

The elevation in methamphetamine abuse needs to be highlighted immediately through public health interventions at the community level.

The Rehabilitation programs should integrate the routine blood and hormonal screening for the purpose of Pathological harm reduction.

Educating the population should be focused based on physical and psychological health consensus.

A combined effort of healthcare providers, policies makers, public health and rehabilitation centers be used to decrease the long-term biological harm by diagnosing pathological, hematological, hormonal and psychological imbalances in the body.

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