doi.org/10.36721/PJPS.2026.39.9.255.1

Evaluating the impact of antioxidant enzymes on cardiometabolic health markers among methamphetamine users compared with healthy participants

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Abstract: **Background**: Methamphetamine (MA) use induces oxidative stress and metabolic dysregulation. **Objectives**: This study is to compare and explore the association between oxidative stress markers and cardio metabolic risk factors in order to elucidate potential mechanisms linking MA use with metabolic and cardiovascular complications. **Methods**: A comparative cross-sectional study was conducted and a total of 70 males aged 18 years and above were enrolled from Mamajee Welfare Trust: 35 healthy controls (Group A) and 35 MA users (Group B) confirmed via drug panel testing. Sociodemographic characteristics, substance use patterns, lifestyle behaviors and anthropometric indices were recorded through structured questionnaires. Fasting blood samples were analyzed for lipid profile, fasting plasma glucose, Troponin-I and antioxidant enzyme activities using standardized assays. Data analysis was performed using statistical packages for social sciences (SPSS) software (version 20). **Results**: MA users reported significantly higher smoking, alcohol intake and physical inactivity. Body mass index (BMI) and systolic blood pressure were also significantly elevated ($p<0.01$). MA users exhibited pronounced dyslipidemia with increased lipid variables. Antioxidant enzyme activity was significantly lower in MA users, with higher catalase (5.31 ± 0.15 vs. 4.89 ± 0.32 ng/mL; $p=0.047$) and superoxide dismutase (SOD) levels (127 ± 43.1 vs. 109 ± 23.4 pg/mL; $p=0.003$) in healthy controls vs. MA users, respectively. In methamphetamine users, catalase correlated positively with BMI, cholesterol, triglycerides and low-density lipoprotein (LDL). While SOD in this group showed a significant positive association with blood pressure, lipid markers and very low density lipoprotein (VLDL), with a near-significant trend for Troponin-I. A significant interrelationship between catalase and SOD ($r=0.381$, $p=0.003$) in MA users was also observed. In multivariable analysis, MA use and antioxidant enzyme levels (catalase, SOD) were independently associated with BMI, blood pressure and lipid abnormalities. **Conclusion**: MA use is associated with considerable cardiometabolic disturbances and compromised antioxidant defenses, highlighting the need for early screening and preventive interventions.

Keywords: Antioxidant biomarkers; Catalase; Cardio metabolic risk; Dyslipidemia; Healthy controls; Methamphetamine; Oxidative stress; Superoxide dismutase

Submitted on 20-11-2025 – Revised on 29-12-2025 – Accepted on 07-01-2026

INTRODUCTION

Methamphetamine (MA), a potent psychostimulant within the amphetamine-type stimulant (ATS) class, has become a major global and regional public health concern due to its strong addictive potential, neurotoxicity and high relapse rates among chronic users (Chen *et al*., 2022). MA is derived from a phenethylamine backbone with a methyl substitution on the amine group, a modification that enhances lipophilicity and enables rapid crossing of the blood brain barrier, resulting in intense central nervous system stimulation (Pauly *et al*., 2023).

Globally, MA dependence contributes substantially to morbidity and mortality, with the World Health Organization (WHO) reporting disproportionately high drug- induced mortality rates in low- and middle-income settings (Jaafari-Sheybani *et al.*, 2021). The growing global use of ATS (Hemphill *et al*., 2024), including the estimated 17.4 million users reported by the United Nations Office on Drugs and Crime (UNODC) (Jayanthi *et al*. 2021), highlights expanding public health risks. High-burden regions such as East and Southeast Asia, North America and Oceania continue to experience large-scale illicit production of MA (Wahab *et al*., 2021). In 2023, record seizures exceeding 190 metric tons, including over one billion MA tablets, were reported across Asia (Pisarski 2021). Much of this supply originates from the Golden

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Triangle region, which remains a major global ATS manufacturing hub despite intensified enforcement (Chen *et al*., 2022, Asia TLRHS, 2023). Pakistan has also experienced a sharp rise in MA availability and use over the past decade. Earlier UNODC reports estimated approximately 19,000 MA users in 2013 (Moszczynska 2021), but more recent trends, including dramatic increases in drug seizures, indicate a substantially larger current burden. National records show MA confiscations rising from 4.4 tons in 2022 to 11.4 tons in 2023, including a 580% increase in crystalline MA seizures (Jan, *et al*. 2021).

MA disrupts monoaminergic neurotransmission by increasing the release and blocking the reuptake of dopamine, norepinephrine and serotonin, resulting in prolonged synaptic monoamine elevation (Li *et al*., 2021). These effects also contribute to anxiety, depression, aggression and psychosis, often resembling primary psychotic disorders (Koohsar *et al*., 2022). Beyond its neuropsychiatric effects, MA use is strongly associated with systemic metabolic and cardiovascular abnormalities. Chronic users frequently exhibit elevated blood pressure, dyslipidemia, insulin resistance and impaired glucose regulation (Schwarzbach, *et al*. 2020). Experimental studies demonstrate MA-induced mitochondrial dysfunction, oxidative stress and altered lipid metabolism (Ajayi and Okoro 2024), while human data highlight complex interactions between MA exposure, body mass index (BMI) and metabolic risk (Panchal 2020). Cardiovascular complications such as arrhythmias, myocardial-infarction and sudden death due to heart are well-documented outcomes of long-term use (Obolski *et al*., 2022). MA's thermogenic and autonomic effects further destabilize metabolic homeostasis (Jaafari-Sheybani *et al*., 2021). Epidemiological studies consistently show increased risk of stroke and cardiovascular hospitalization among MA users (Huang *et al*., 2016).

Oxidative stress plays a central mechanistic role in MA toxicity. When reactive oxygen species (ROS) accumulate excessively, they exceed the ability of endogenous antioxidant mechanisms, including superoxide dismutase (SOD) and catalase (CAT), resulting in lipid peroxidation, protein damage and mitochondrial dysfunction (Hajam *et al*., 2022; Rajput *et al*., 2021). Although oxidative stress is recognized as a major contributor to MA-related neurotoxicity and metabolic disturbance, its relationship with cardiometabolic health remains insufficiently explored within the Pakistani population. Given increasing MA use in Pakistan and the lack of biochemical data on antioxidant enzyme alterations, this study aimed to compare catalase and SOD activity and examine their associations with cardiometabolic markers in MA users and healthy controls.

MATERIALS AND METHODS

This comparative cross-sectional study was conducted from October 2024 to September 2025. Informed consent in written form was obtained from all individuals who took part in the study. A convenient sampling approach was used to recruit 70 male adults, aged 18 years and above comprising 35 MA users confirmed by drug panel testing from Mamajee Adicare and Welfare Trust and 35 healthy non-users enrolled as controls.

Participant information, including demographic characteristics, socioeconomic background, medical and family history, physical activity and detailed drug-use patterns, was collected using a structured questionnaire. Following an overnight fast of at least 8 to 12 hours, 6 cc of venous blood was drawn from each participant; plasma samples were collected in gray-top sodium fluoride/potassium oxalate tubes, while serum samples were collected in yellow gel-separator tubes. Anthropometric parameters included weight, height (converted to meters) and body mass index calculated as weight (kg)/height (m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a standard mercurial sphygmomanometer after 5 min of seated rest and the mean of two right-arm readings was recorded.

Biochemical parameters were assessed using standardized enzymatic procedures. Fasting plasma glucose (FPG) was measured with the glucose oxidase–peroxidase technique, total cholesterol with the cholesterol oxidase–phenol 4-aminoantipyrine–peroxidase method and triglycerides using the glycerol phosphate oxidase–p-aminophenazone assay. High-density lipoprotein (HDL) cholesterol was determined through a homogeneous enzymatic colorimetric method, and low-density lipoprotein (LDL) cholesterol via the direct method. Cardiac Troponin-I concentrations were quantified using an immunofluorescence assay kit (catalogue IF1001). Antioxidant enzyme activity in serum was assessed using ELISA kits: CAT using the catalog number SEC418Hu (detection range 0.312–20 ng/mL) and SOD using the SES134Hu kit (detection range 62.5–4,000 pg/mL). The sample size was determined using OpenEpi version 3. All laboratory analyses adhered to standardized quality control protocols to ensure reliability and reproducibility.

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 20. Continuous variables were summarized as mean ± standard deviation (SD), whereas categorical variables were reported as frequencies and percentages. Data distribution was evaluated using the Shapiro–Wilk test for normality. Group comparisons for continuous variables were performed using the independent samples t-test, while categorical variables were assessed using the chi-square test or Fisher's exact test when appropriate. Pearson's correlation coefficient (r) was employed to assess relationships between variables, with $r < 0.3$ interpreted as a weak correlation, 0.3–0.7 as moderate and >0.7 as strong. Multivariable linear regression was used to examine

associations of MA use, catalase and SOD with cardiometabolic outcomes in all participants (n = 70), adjusting for age, BMI (except when BMI was the outcome), smoking, alcohol use, physical inactivity and ethnicity. MA use was coded 0 = non-users (reference) and 1 = users. Standardized β coefficients, 95% confidence intervals and p-values were reported.

RESULTS

A total of 70 male participants were enrolled, with 35 in each group. Table 1 presents the baseline characteristics of study participants. Mean age was comparable between groups (27.38 ± 3.11 vs. 26.81 ± 2.38 years; p = 0.620). Most individuals in both groups were married. Occupational status differed, though not significantly (p = 0.402); labor work was more common in Group A (51.4%), whereas Group B had a higher proportion engaged in private business (31.4%) or unemployed (25.7%). Ethnicity was found significant different between the groups (p = 0.007), with Pashto participants predominating in both groups. However, the mean difference of Pashto participants was found to be higher in Group A (60%) compared with Group B (46%).

Comparison of addiction status, physical activity level, and medical history between Group A and Group B was presented in table 2. Smoking and alcohol use differed significantly between groups (p = 0.001 and p < 0.001). All participants in Group A were nonsmokers and abstained from alcohol, while most in Group B were current smokers (83 percent) and reported occasional to daily alcohol use. Physical activity was lower in Group B, with 83 percent inactive, compared with more regular activity in Group A (p = 0.003). MA users had higher rates of hypertension (25.7 percent) and dyslipidemia (8.6 percent) than controls (p < 0.001). Over the past year, Group B reported more metabolic-related symptoms such as frequent urination, fatigue, increased thirst, weight loss and blurred vision, whereas 91.4 percent of Group A reported no symptoms (p < 0.001).

In Group B (MA users), the mean duration of MA use was 43±2.41 months, with an average frequency of 5±1.63 episodes per week. The mean time since the last reported use was approximately 27±2.93 hours prior to data collection. No such history was present in Group A (Fig 1).

Lipid profile parameters differed significantly between groups (table 3). Total cholesterol was higher in Group B (211 ± 3.12 mg/dl) than in Group A (186 ± 2.51 mg/dl; p = 0.032) and triglycerides were substantially elevated (196 ± 0.76 vs. 159 ± 0.83 mg/dl; p = 0.002). HDL levels were lower in Group B (36 ± 0.92 mg/dl) relative to Group A (43 ± 1.07 mg/dl; p = 0.043), while LDL concentrations were higher (175 ± 2.91 vs. 135 ± 3.71 mg/dl; p = 0.021). VLDL also differed significantly, with Group B showing elevated levels (29.3 ± 0.83 mg/dl) compared with Group A (21.8 ± 0.51 mg/dl; p = 0.001).

Fasting blood sugar did not differ significantly between groups and Troponin-I concentrations remained comparable (0.027 ± 0.01 vs. 0.021 ± 0.001 ng/mL; p = 0.371), indicating no acute myocardial injury. Antioxidant enzyme levels were notably reduced in MA users. Catalase activity was significantly lower in Group B (4.89 ± 0.318 ng/mL) compared with Group A (5.31 ± 0.153 ng/mL; p = 0.047). Similarly, SOD activity showed a significant decline in Group B (109 ± 23.4 pg/mL) relative to Group A (127 ± 43.1 pg/mL; p = 0.003).

Table 4 outlines the correlations between catalase activity and clinical variables in Group A and Group B. Among healthy participants (Group A), catalase showed a moderate positive association with BMI (r=0.321, p=0.043), suggesting higher enzyme activity at increased body mass. Other parameters, including systolic blood pressure, total cholesterol, triglycerides, LDL and SOD demonstrated weak, non-significant relationships.

In MA users (Group B), catalase displayed stronger associations with several cardio-metabolic markers, showing moderate positive correlations with BMI (r=0.389, p=0.039), total cholesterol (r=0.316, p=0.043), triglycerides (r=0.418, p=0.003) and LDL (r=0.341, p=0.049). A weak but significant negative correlation with systolic blood pressure (r=−0.328, p=0.041) was also observed, suggesting altered vascular redox regulation in chronic MA exposure.

Table 5 summarizes the correlations between SOD levels and clinical parameters in Group A and Group B. In Group A, SOD showed weak positive correlations with age (r=0.246, p=0.322), BMI (r=0.281, p=0.209) and diastolic blood pressure (r=0.252, p=0.162), none of which were statistically significant. Lipid markers also showed modest associations total cholesterol (r=0.310, p=0.178), triglycerides (r=0.308, p=0.190), HDL (r=0.330, p=0.029) and LDL (r=0.326, p=0.248) with only HDL reaching significance (p=0.029).

In Group B, SOD demonstrated clinically meaningful correlations. A moderate negative association with BMI (r=−0.312, p=0.028) indicated declining SOD activity with greater adiposity. Significant positive correlations were also noted for systolic blood pressure (r=0.369, p=0.038), total cholesterol (r=0.311, p=0.034), triglycerides (r=0.379, p=0.012), HDL (r=0.351, p=0.011) and VLDL (r=0.317, p=0.022). Troponin-I showed a near-significant correlation (r=0.329, p=0.051). The relationship between catalase and SOD was weak and non-significant in Group A (r=0.211, p=0.251), whereas Group B showed a significant positive correlation (r=0.381, p=0.003).

In multivariable regression analyses including all participants, MA use was significantly associated with BMI (β = 0.29, 95% CI 0.08–0.51, p = 0.007), elevated

systolic blood pressure (β = 0.31, 95% CI 1.9–8.2, p = 0.004) and worsened lipid profiles, including total cholesterol (β = 0.34, 95% CI 9.1–27.6, p = 0.001), triglycerides (β = 0.36, 95% CI 14.2–39.8, p < 0.001) and LDL cholesterol (β = 0.33, 95% CI 11.3–31.4, p = 0.002). Catalase levels were positively linked to BMI and lipid markers, while SOD was inversely associated with BMI (β = −0.24, p = 0.014) but positively associated with systolic blood pressure and lipid profiles.

Multivariable linear regression was performed using all participants (n = 70). MA use was coded as 0 = non-users (reference) and 1 = users. Standardized β coefficients are presented. Models were adjusted for age, BMI (except when BMI was the outcome), smoking, alcohol use, physical inactivity and ethnicity (table 6).

DISCUSSION

The interplay between oxidative stress and cardiometabolic risk in MA users was investigated relative to healthy individuals. MA users showed significantly higher BMI and systolic blood pressure, with pronounced dyslipidemia characterized by elevated total cholesterol, triglycerides, LDL and VLDL, accompanied by reduced HDL. CAT and SOD activities were significantly reduced in MA users. Correlation analyses revealed weak associations of antioxidant enzymes with metabolic parameters in healthy controls, whereas in MA users, both CAT and SOD correlated moderately with adverse lipid markers, blood pressure and BMI. Notably, CAT and SOD were positively inter-correlated in MA users, suggesting coordinated regulation of antioxidant defenses under chronic oxidative stress. Multivariable analysis indicates that MA use was independently associated with higher BMI, blood pressure, and adverse lipid profiles, even after adjusting for confounders. CAT and SOD levels were also linked to cardiometabolic markers, suggesting a role of oxidative stress. These findings also highlight the combined impact of substance use and antioxidant imbalance on cardiometabolic health.

The results of this study are consistent with experimental and clinical evidence demonstrating that MA induces oxidative stress through multiple mechanisms, including mitochondrial dysfunction, dopamine auto-oxidation and activation of NADPH oxidase, which collectively increase ROS production (Kolluru *et al*., 2022). Elevated ROS promotes lipid peroxidation, endothelial dysfunction and impaired vascular homeostasis, thereby increasing cardiometabolic risk (Akhigbe, Ajayi 2021). Experimental studies in rodent models have shown that chronic MA administration results in downregulation of SOD and CAT activity, alongside elevated malondialdehyde (MDA) and lipid abnormalities, supporting the notion that oxidative stress is associated to MA-induced metabolic disturbances (Ajayi and Okoro 2024, McDonnell-Dowling and Kelly 2017). In contrast, some studies have reported compensatory upregulation of CAT and glutathione (GSH) as an adaptive response to ROS overload (Viola *et al*., 2023), which aligns partially with our observation of positive inter-correlation between CAT and SOD in MA users (Viola *et al*., 2023). These discrepancies likely reflect differences in exposure duration, tissue-specific oxidative burden and measurement methods.

The dyslipidemia observed in this cohort parallels findings from both clinical and preclinical studies. Elevated triglycerides, LDL and VLDL with reduced HDL have been reported in chronic MA users and in animal models exposed to high-dose MA, supporting the role of catecholamine-mediated lipolysis, hepatic VLDL overproduction and impaired lipid oxidation in metabolic derangements (Mbugua *et al*., 2022). Conversely, some experimental studies have noted that short-term MA exposure may transiently reduce lipid levels due to anorexigenic effects, highlighting the impact of exposure duration on metabolic outcomes (Stăcescu *et al*., 2019; Pergolizzi *et al*., 2020).

BMI and blood pressure elevations in MA users contrast with the classical view of MA as an anorexigenic agent, but are consistent with reports showing that chronic exposure and withdrawal can promote adiposity and insulin resistance, mediated by oxidative stress, sympathetic dysregulation and reduced physical activity (Algahtani *et al*., 2025). Correlation analyses revealed a positive relationship between CAT activity and lipid markers but a paradoxical negative association with systolic blood pressure. This may reflect maladaptive antioxidant responses, as excessive CAT activity can reduce hydrogen peroxide availability required for endothelium-dependent vasodilation (Mbugua *et al*., 2022). Similarly, SOD activity negatively correlated with BMI but positively with lipid markers and blood pressure, suggesting enzyme-specific dysregulation under chronic oxidative stress (Lei *et al*., 2016).

Interestingly, a near-significant association was observed between SOD and Troponin-I in MA users. This suggests that lower SOD activity may track with subclinical myocardial injury, reinforcing the hypothesis that oxidative stress is associated with MA-associated cardiotoxicity. According to Tobolski *et al*. (2022) MA is known to induce cardiomyopathy, arrhythmias and ischemic injury through catecholamine toxicity and oxidative damage to myocardial tissue. In this study, low Troponin-I levels were observed; however, low SOD in individuals with higher Troponin-I may reflect an attempt to counteract ROS-driven cardiac injury. This observation, though preliminary, highlights the potential utility of SOD as a biomarker linking oxidative stress with cardiovascular injury in drug-using populations.

Table 1: Baseline demographic characteristics of study participants in Group A (healthy controls) and Group B (methamphetamine users)

Baseline Characteristics	Group A (n=35)	Group B (n=35)	p-value
Gender			
Male	35 (100%)	35 (100%)	–
Marital Status			
Married	28 (80%)	25 (71.4%)	0.344
Unmarried	7 (20%)	10 (28.6%)	
Occupation			
Govt. Servant	4 (11.4%)	4 (11.4%)	
Labour	18 (51.4%)	5 (14.3%)	
Own Business	4 (11.4%)	11 (31.4%)	0.402
Student	8 (22.8%)	6 (17.1%)	
Unemployed	1 (2.8%)	9 (25.7%)	
Ethnicity			
Sindhi	2 (5.7%)	3 (8.6%)	
Punjabi	2 (5.7%)	7 (20%)	
Balochi	3 (8.6%)	1 (2.8%)	0.007
Pashto	21 (60%)	16 (46%)	
Muhajir	6 (17.1%)	6 (17.1%)	
Others	1 (2.8%)	2 (5.7%)	
Age (years)	27.38 ± 3.11	26.81 ± 2.38	0.620

Data are presented as mean ± SD for continuous variables and n (%) for categorical variables. Comparisons were made using the independent sample t-test for continuous variables and the chi-square test or Fisher's Exact test for categorical variables. A p-value < 0.05 was considered statistically significant.

Table 2: Comparison of addiction status, physical activity level, and medical history between Group A (healthy controls) and Group B (methamphetamine users)

Characteristic	Group A n (%)	Group B n (%)	p-value
N	35	35	
Smoking status			
Current smoker	0 (0%)	29 (83.0%)	
Former smoker	0 (0%)	6 (17.1%)	0.001
Non-smoker	35 (100%)	0 (0%)	
Alcohol use			
Daily	0 (0%)	2 (5.7%)	
Weekly	0 (0%)	4 (11.4%)	<0.001
Rare	0 (0%)	29 (83.0%)	
Never	35 (100%)	0 (0%)	
Physical activity			
Daily	12 (34.3%)	0 (0%)	
Weekly	14 (40.0%)	1 (2.8%)	
Monthly	2 (5.7%)	1 (2.8%)	0.003
Rare	3 (8.6%)	4 (11.4%)	
Never	4 (11.4%)	29 (83.0%)	
Medical history			
Hypertension	1 (2.8%)	9 (25.7%)	
Diabetes	1 (2.8%)	1 (2.8%)	<0.001
Dyslipidemia	0 (0%)	3 (8.6%)	
Cardiovascular disease	0 (0%)	0 (0%)	
Symptoms (past year)			
Frequent urination	0 (0%)	8 (22.8%)	
Increased thirst	0 (0%)	3 (8.6%)	
Unexplained weight loss	0 (0%)	2 (5.7%)	<0.001
Fatigue	3 (8.6%)	5 (14.3%)	
Blurred vision	0 (0%)	2 (5.7%)	
None	32 (91.4%)	15 (42.8%)	

Data are expressed as n (%). The Chi-square test or Fisher's Exact test was used as appropriate. A p-value < 0.05 was considered statistically significant.

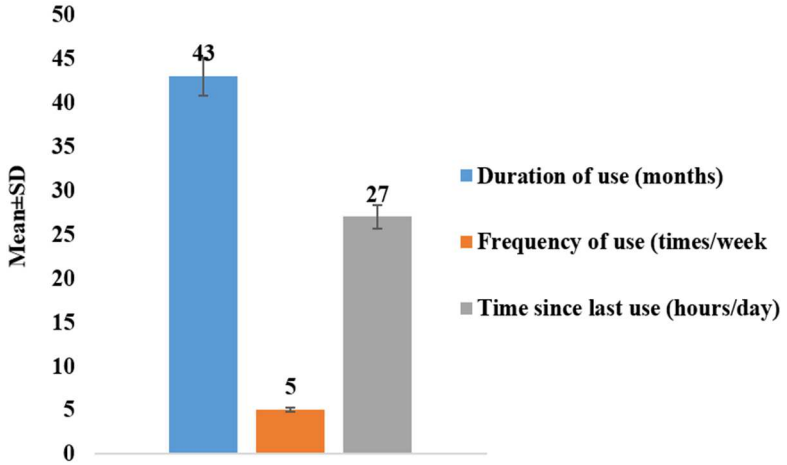

Fig. 1: Duration, frequency and time since last use of methamphetamine in methamphetamine users (Group B).

Group B showed a significantly higher mean BMI (27.01 ± 1.05 kg/m²) than Group A (24.22 ± 0.95 kg/m²; p = 0.004). Systolic blood pressure was also markedly elevated in Group B (126 ± 2.64 mmHg) compared with Group A (120 ± 1.83 mmHg; p = 0.003). Although diastolic pressure was slightly greater in Group B (83 ± 1.43 mmHg) than in Group A (80 ± 1.33 mmHg), this difference was not statistically significant (p = 0.073).

Table 3: Comparison of anthropometric parameters and cardio-metabolic risk markers between healthy controls (Group A) and methamphetamine users (Group B)

Variables	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
N	35	35	–
Body-mass- index (kg/m²)	24.22 ± 0.95	27.01 ± 1.05	0.004
Systolic- blood- pressure (mmHg)	120 ± 1.83	126 ± 2.64	0.003
Diastolic- blood- pressure (mmHg)	80 ± 1.33	83 ± 1.43	0.073
Total- cholesterol (mg/dl)	186 ± 2.51	211 ± 3.12	0.032
Triglycerides (TG) (mg/dl)	159 ± 0.83	196 ± 0.76	0.002
High- density- lipoprotein (mg/dl)	43 ± 1.07	36 ± 0.92	0.043
Low- density- lipoprotein (mg/dl)	135 ± 3.71	175 ± 2.91	0.021
Very low-density- lipoprotein (mg/dl)	21.8 ± 0.51	29.3 ± 0.83	0.001
Fasting- blood sugar (mg/dl)	87.5 ± 0.75	89.3 ± 0.39	0.542
Troponin-I (ng/mL)	0.021 ± 0.001	0.027 ± 0.01	0.371
Catalase (ng/mL)	5.31 ± 0.153	4.89 ± 0.318	0.047
Superoxide- dismutase (SOD) (pg/mL)	127 ± 43.1	109 ± 23.4	0.003

Data are expressed as Mean ± SD. A two-tailed independent samples t-test was used for group comparisons, with $p < 0.05$ considered statistically significant.

Table 4: Correlation of catalase with baseline and clinical parameters between Group A (healthy participants) and group B (methamphetamine users)

Variables	Group A (r)	Group A (p-value)	Group B (r)	Group B (p-value)
Age (years)	-0.251	0.297	0.241	0.386
Body- mass- index (kg/m²)	0.321	0.043	0.389	0.039
Systolic- blood- pressure (mmHg)	0.130	0.205	-0.328	0.041
Diastolic- blood- pressure (mmHg)	0.149	0.546	0.149	0.156
Total- cholesterol (mg/dl)	0.259	0.356	0.316	0.043
Triglycerides (TG) (mg/dl)	0.263	0.392	0.418	0.003
High- density- lipoprotein (mg/dl)	-0.186	0.751	0.238	0.061
Low- density- lipoprotein (mg/dl)	0.325	0.084	0.541	0.049
Very- low-density- lipoprotein (mg/dl)	0.281	0.176	0.253	0.286
Fasting- blood- sugar (mg/dl)	0.114	0.962	0.223	0.716
Troponin-I (ng/mL)	0.254	0.184	0.267	0.149

Pearson's correlation coefficient (r) was used to assess the strength of associations, with a p-value < 0.05 regarded as statistically significant. Correlations with r values < 0.3 were interpreted as weak, those between 0.3 and 0.7 as moderate, and values exceeding 0.7 as indicative of a strong relationship

Table 5: Correlation of superoxide dismutase (SOD) with baseline and clinical parameters between Group A (healthy participants), Group B (methamphetamine users)

Variables	Group A (r)	Group A (p-value)	Group B (r)	Group B (p-value)
Age (years)	0.246	0.322	0.219	0.252
Body- mass- index (kg/m²)	0.281	0.209	-0.312	0.028
Systolic- blood- pressure (mmHg)	0.194	0.073	0.369	0.038
Diastolic- blood- pressure (mmHg)	0.252	0.162	0.274	0.531
Total- cholesterol (mg/dl)	0.310	0.178	0.311	0.034
Triglycerides (TG) (mg/dl)	0.308	0.190	0.379	0.012
High- density- lipoprotein (mg/dl)	0.230	0.029	0.351	0.011
Low- density- lipoprotein (mg/dl)	0.326	0.248	0.452	0.148
Very- low-density- lipoprotein (mg/dl)	0.026	0.920	0.317	0.022
Fasting- blood- sugar (mg/dl)	0.241	0.187	0.259	0.273
Troponin-I (ng/mL)	0.232	0.604	0.329	0.051
Catalase (ng/mL)	0.211	0.251	0.381	0.003

Pearson's correlation coefficient (r) was used to assess the strength of associations, with a p-value < 0.05 regarded as statistically significant. Correlations with r values < 0.3 were interpreted as weak, those between 0.3 and 0.7 as moderate, and values exceeding 0.7 as indicative of a strong relationship.

Table 6: Multivariable linear regression analysis of antioxidant enzymes and methamphetamine use in relation to cardiometabolic health markers (n=70)

Outcome Variable	Predictor	β (standardized)	95% CI	p-value
Body mass index (kg/m²)	Methamphetamine use (yes vs no)	0.29	0.08 to 0.51	0.007
	Catalase (ng/mL)	0.21	0.03 to 0.39	0.021
	SOD (pg/mL)	−0.24	−0.44 to −0.05	0.014
Systolic blood pressure (mmHg)	Methamphetamine use (yes vs no)	0.31	1.9 to 8.2	0.004
	Catalase	−0.19	−0.37 to −0.01	0.038
	SOD	0.26	0.05 to 0.48	0.017
Total cholesterol (mg/dL)	Methamphetamine use (yes vs no)	0.34	9.1 to 27.6	0.001
	Catalase	0.22	1.4 to 9.7	0.026
	SOD	0.25	2.1 to 10.8	0.018
Triglycerides (mg/dL)	Methamphetamine use (yes vs no)	0.36	14.2 to 39.8	<0.001
	Catalase	0.27	3.6 to 12.4	0.009
	SOD	0.31	4.8 to 16.9	0.004
Low-density lipoprotein (mg/dL)	Methamphetamine use (yes vs no)	0.33	11.3 to 31.4	0.002
	Catalase	0.24	2.3 to 10.2	0.019
	SOD	0.28	3.1 to 13.7	0.007

Multivariable linear regression was performed using all participants (n = 70). Methamphetamine use was coded as 0 = non-users (reference) and 1 = users. Standardized β coefficients are presented. Models were adjusted for age, BMI (except when BMI was the outcome), smoking, alcohol use, physical inactivity, and ethnicity.

Lifestyle factors in this cohort, including high rates of smoking, alcohol consumption and physical inactivity, likely compounded oxidative stress and cardiometabolic risk. These findings are supported by epidemiological studies showing co-occurrence of nicotine dependence and stimulant use, with synergistic effects on vascular dysfunction and oxidative damage (Kolluru *et al.,* 2022; Hajam *et al*., 2022; Hassan *et al.,* 2019). These findings indicate that chronic MA use disrupts systemic redox balance, linking oxidative stress to early cardiometabolic abnormalities. The differential regulation of CAT and SOD highlights their potential utility as biomarkers for oxidative stress and cardiometabolic vulnerability in MA dependence, emphasizing the need for integrated clinical management, lifestyle interventions and cardiovascular monitoring in this high-risk population.

Strengths, limitations and future recommendations

A key strength of this study is its integration of cardio metabolic parameters with oxidative stress biomarkers in MA users. The relatively small sample size and recruitment from a single center may limit generalizability to broader populations. The sampling method was convenience sampling, which introduces significant selection bias, and only males were included, which is another limitation. The history of smoking and alcohol use as confounders is more prominent in meth users, and this is also one of our limitations. Larger, more diverse cohorts, including female participants, are needed to improve generalizability. This study is limited to only the ELISA levels technique. Further study for functional enzyme assays along with integration of additional oxidative stress markers, inflammatory mediators and genetic susceptibility profiles with

longitudinal design, could further elucidate underlying mechanisms.

CONCLUSION

Prolonged MA exposure is associated with substantial cardiometabolic alterations and a pronounced reduction in the antioxidant enzymes catalase and superoxide dismutase (SOD). The diminished activities of these enzymes indicate the presence of MA -induced oxidative stress. Furthermore, reduced catalase and SOD levels demonstrated moderate correlations with adverse lipid profiles and increased body mass index. This highlights the dual burden of oxidative and cardiometabolic risk, supporting their potential as biomarkers and therapeutic targets in this population.

Acknowledgments
We would like to express our sincere gratitude to the organizers of Mamajee Adicare and Welfare Trust and Baqai Medical University for research support.

Authors' contributions
IK: Conceived and designed the study, data collection, data analysis and drafted the manuscript; NW: Conceived, designed and supervised the study, interpretation of results, critical review and was responsible for data integrity; MN: Data analysis and revised the manuscript; UA: Interpretation of results and wrote the manuscript; AI: Critical review, edited and approved the final version; UN: Critical review and approved the final version; AF: Critical review and final approval of the manuscript.

Funding
There was no funding.

Data availability statement
All data generated or analysed during this study are included in this published article and its supplementary information files.

Ethical approval
The ethical approval was obtained from the Institutional Review Ethical Board (Ref no. BMU-IREB/10-2024/008) and the Board of Advanced Studies and Research, Baqai Medical University, Karachi. This study was performed in adherence with the STROBE guidelines. See supplementary file for the STROBE checklist.

Conflict of interest
The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Supplementary data
https://www.pjps.pk/uploads/2026/06/SUP1781433552.pdf

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