

## Association of Serum Uric Acid Level with Short Term In-Hospital Mortality In St-Elevation Myocardial Infarction

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### ABSTRACT

**Objective:** To determine the relationship between elevated blood uric acid levels and short-term in-hospital mortality in myocardial infarction with ST-elevation.

**Study Design:** Quasi-experimental.

**Place and Duration of Study:** Combined Military Hospital (CMH), Hyderabad, Pakistan from Aug to Dec 2023.

**Methodology:** A total of 378 (189 in each group) patients were enrolled, and serum uric acid sample was sent for analysis, patients were monitored for seven days after admission. Patients were split into two groups based on their serum uric acid levels: Group A (exposed) and Group B (non-exposed), identical treatment was given to both groups. Baseline investigations were carried out on admission including ECG, blood complete picture, coagulation profile, cardiac enzymes, lipid profile, chest X-ray, renal and liver function tests and troponins.

**Results:** Group A (high serum uric acid, 10%) had a greater mortality rate than Group B (low serum uric acid, 3%) and significant categories with higher death rates were patients with history of smoking (75.0%,  $p = 0.029$ ), hypertension (77.8%,  $p = 0.010$ ), BMI  $\leq 25$  kg/m<sup>2</sup> (78.6%,  $p = 0.033$ ), and men (76.5%,  $p = 0.026$ ). Results point to serum uric acid as a prognostic biomarker, highlighting its function in risk assessment for treatment of ST-Segment Elevation Myocardial Infarction (STEMI).

**Conclusions:** Elevated serum uric acid level was noted to be linked to a higher in-hospital death rate among patients with ST elevation myocardial infarction.

**Keywords:** In-hospital mortality, Serum uric acid level, ST elevation myocardial infarction.

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### INTRODUCTION

Acute myocardial infarction is a leading cause of death and significant efforts have been made to identify cardiovascular risk and prognostic markers.<sup>1</sup> Serum uric acid (SUA) is associated with metabolic syndrome, diabetes, and hypertension while ST-segment elevation myocardial infarction (STEMI) and coronary artery disease (CAD) have been linked to it as an independent risk factor.<sup>2</sup> Ischemic heart disease (IHD) affects 6.25% of Pakistanis over the age of 203 while 56.5 million fatalities occurred worldwide, with CADs accounting for 32.9% of those deaths.<sup>4</sup> Recent research has linked cardiovascular disease to increased serum uric acid, which is frequently connected to dyslipidemia, diabetes mellitus, hypertension and smoking with ischemic heart disease causing 12.7% fatalities worldwide.<sup>5</sup> Among the various acute coronary syndromes, ST-elevation myocardial infarction (STEMI) is important since it

causes significant in-hospital deaths so early identification of risk in patients with STEMI can help achieve better clinical outcomes.<sup>6</sup> Hyperuricemia is linked to several factors that make atherosclerosis and ischemic injury worse such as oxidative stress, LDL cholesterol oxidation, lipid peroxidation, inflammation and platelet aggregation which result in coronary thrombosis and worsen STEMI.<sup>7,8</sup> Some studies have shown that high uric acid in the blood is linked to a greater risk of death during a STEMI yet other studies have been inconclusive, thus, this inconsistency shows that more research is needed.<sup>9</sup> Given the lack of medical treatment in Pakistan, finding affordable and non-invasive biomarkers is urgently needed and a blood test for serum uric acid may help patients with STEMI achieve better health outcomes.<sup>10</sup> The aim of this study was to understand how elevated serum uric acid levels might be related to in-hospital mortality among patients with STEMI in Pakistan as the knowledge gained from this study could help manage and improve outcomes especially in areas with limited resources.

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## METHODOLOGY

This quasi-experimental study was conducted at Combined Military Hospital (CMH) Hyderabad, Pakistan from August to December 2023, over a period of 6 months, following approval by the Institutional Ethics Review, via approval number ERC 516-2023. The sample size was calculated using the World Health Organization (WHO) sample size calculator, setting the level of significance at 5% and the power of the test at 80%, with an anticipated population proportion of 9.26% in the high uric acid group (Group A) and 2.5% in the normal uric acid group (Group B) <sup>11</sup>, the required sample size was calculated to be 189 participants per group, making a total of 378 participants, which was enrolled using non-probability consecutive sampling technique.

**Inclusion Criteria:** Patients, both male and female, treated with fibrinolytic therapy, between the ages of 35 and 65 years, within 12-hours of onset of ischemic symptoms, having ST-elevation myocardial infarction on arrival to hospital, were included.

**Exclusion Criteria:** Patients having cardiac failure, congestive heart failure, impaired hepatic function and renal insufficiency, physical or mental impairment, gout, history of head injury, severe respiratory, gastrointestinal, pancreatic, or hematological diseases, cancer, Body Mass Index (BMI) >30, and those using diuretics, angiotensin II receptor blockers (ARBs), vitamin C, or fenofibrate were excluded.

Based on their serum uric acid levels, the patients were split into two groups, where Group A, also known as the exposed group, had serum uric acid levels higher than 8 mg/dL for males and 7.5 mg/dL for females, while Group B, the non-exposed group, had serum uric acid levels of 8 mg/dL or less for males and 7.5 mg/dL for females. The same treatment had been given to both groups. At reception, baseline investigations such as ECG, blood complete picture, liver function tests, renal function tests, lipid profile, chest X-ray, coagulation profile, and sample for cardiac enzymes were done, along with assessments for medical history, physical examination, vital signs, body weight, and baseline investigations while monitoring was continued for another seven days. Data entry and analysis were done using Statistical Package for the Social Sciences (SPSS). Both qualitative and quantitative variables were subjected to descriptive statistics. Shapiro-Wilk Test was applied to check the normality of data. For numerical variables, such as age, median and IQR were calculated. For

categorical variables, such as gender, smoking status, ischemic heart disease, diabetes mellitus, hypertension, hyperlipidemia, stroke, ECG results, and hospital mortality, frequency and percentage were calculated. Discharge and death rates were compared between groups using the chi-square test where a *p*-value ≤ 0.05 was deemed significant and calculation of relative risk was made.

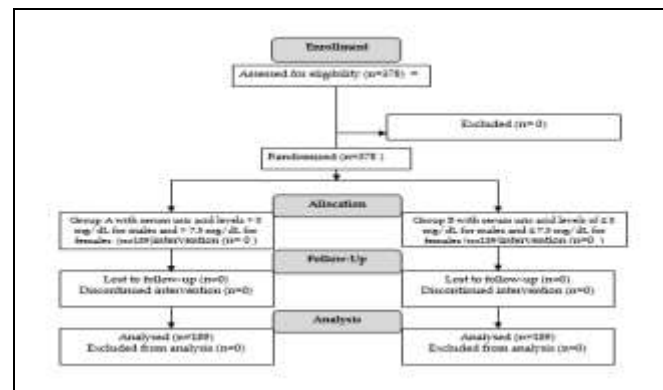


Figure: Patient Flow Diagram (n=378)

## RESULTS

This study involved 378 participants in total with 189 in each group, having a median age of 56.0(49.0-61.0) years while 252(66.7%) participants were male with the median age of 58.0(56.0-63.0) years, and 126(33.3%) were female, with a median age of 49.5(43.0-53.0) years as shown in Table-I, along with other demographic characteristics.

Table-I: Demographic Characteristics (n=378)

Variables		n (%)
Age Groups	35-45 years	50 (13.2%)
	46-55 years	122 (32.3%)
	56-65 years	206 (54.5%)
Gender	Male	252 (66.7%)
	Female	126 (33.3%)
BMI	≤ 25 kg/m <sup>2</sup>	213 (56.3%)
	> 25 kg/m <sup>2</sup>	165 (43.7%)
Diabetes	Yes	182 (48.1%)
	No	196 (51.9%)
Smoking	Yes	234 (61.9%)
	No	144 (38.1%)
Ischemic Heart Disease	Yes	136 (36.0%)
	No	242 (64.0%)
Hypertension	Yes	278 (73.5%)
	No	100 (26.5%)
Hyperlipidemia	Yes	204 (54.0%)
	No	174 (46.0%)
Stroke	Yes	126 (33.3%)
	No	252 (66.7%)
Mortality	Yes	25 (6.6%)
	No	353 (93.4%)

BMI: Body Mass Index

# Association of Serum Uric Acid Level

**Table-II: Stratification of In-Hospital Mortality by Age, Gender, BMI, and Clinical Variables in STEMI Patients (n=378)**

Variables		Mortality	Group A	Group B	p-value (≤0.05)	Relative Risk
Age	35-45 years	Yes	2 (66.7%)	1 (33.3%)	0.439	2.476
		No	21 (44.7%)	26 (55.3%)		
	Total		23 (46.0%)	27 (54.0%)		
	46-55 years	Yes	6 (75.0%)	2 (25.0%)	0.126	3.333
		No	54 (47.4%)	60 (52.6%)		
	Total		60 (49.2%)	62 (50.8%)		
	56-65 years	Yes	11 (78.6%)	3 (21.4%)	0.032	3.744
		No	95 (49.5%)	97 (50.5%)		
	Total		106 (51.5%)	100 (48.5%)		
Gender	Male	Yes	13 (76.5%)	4 (23.5%)	0.026	3.334
		No	116 (49.4%)	119 (50.6%)		
	Total		129 (51.2%)	123 (48.8%)		
	Female	Yes	6 (75.0%)	2 (25.0%)	0.108	3.556
		No	54 (45.8%)	64 (54.2%)		
	Total		60 (47.6%)	66 (52.4%)		
BMI	≤ 25 kg/m2	Yes	11 (78.6%)	3 (21.4%)	0.033	3.704
		No	99 (49.7%)	100 (50.3%)		
	Total		110 (51.6%)	103 (48.4%)		
	> 25 kg/m2	Yes	8 (72.7%)	3 (27.3%)	0.081	3.117
		No	71 (46.1%)	83 (53.9%)		
	Total		79 (47.9%)	86 (52.1%)		
Diabetes	Yes	Yes	9 (75.0%)	3 (25.0%)	0.057	3.375
		No	80 (47.1%)	90 (52.9%)		
	Total		89 (48.9%)	93 (51.1%)		
	No	Yes	10 (76.9%)	3 (23.1%)	0.048	3.444
		No	90 (49.2%)	93 (50.8%)		
	Total		100 (51.0%)	96 (49.0%)		
Smoking	Yes	Yes	12 (75.0%)	4 (25.0%)	0.029	3.350
		No	103 (47.2%)	115 (52.8%)		
	Total		115 (49.1%)	119 (50.9%)		
	No	Yes	7 (77.8%)	2 (22.2%)	0.097	3.552
		No	67 (49.6%)	68 (50.4%)		
	Total		74 (51.4%)	70 (48.6%)		
Ischemic Heart Disease	Yes	Yes	9 (81.8%)	2 (18.2%)	0.022	5.368
		No	57 (45.6%)	68 (54.5%)		
	Total		66 (48.5%)	70 (51.5%)		
	No	Yes	10 (71.4%)	4 (28.6%)	0.094	2.544
		No	113 (49.6%)	115 (50.4%)		
	Total		123 (50.8%)	119 (49.2%)		
Hypertension	Yes	Yes	14 (77.8%)	4 (22.2%)	0.010	3.959
		No	122 (46.9%)	138 (53.1%)		
	Total		136 (48.9%)	142 (51.1%)		
	No	Yes	5 (71.4%)	2 (28.6%)	0.271	2.344
		No	48 (51.6%)	45 (48.4%)		
	Total		53 (53.0%)	47 (47.0%)		
Hyperlipidemia	Yes	Yes	10 (76.9%)	3 (23.1%)	0.035	3.741
		No	90 (47.1%)	101 (52.9%)		
	Total		100 (49.0%)	104 (51.0%)		
	No	Yes	9 (75.0%)	3 (25.0%)	0.077	3.075
		No	80 (49.4%)	82 (50.6%)		
	Total		89 (51.1%)	85 (48.9%)		
Stroke	Yes	Yes	6 (75.0%)	2 (25.0%)	0.108	3.556
		No	54 (45.8%)	64 (54.2%)		
	Total		60 (47.6%)	66 (52.4%)		
	No	Yes	13 (76.5%)	4 (23.5%)	0.026	3.334
		No	116 (49.4%)	119 (50.6%)		
	Total		129 (51.2%)	123 (48.8%)		

BMI: Body Mass Index

Table-II summarizes the association between mortality and key variables (age, gender, BMI, diabetes, smoking, ischemic heart disease, hypertension, hyperlipidemia, and stroke) in Group A (Exposed: serum uric acid > 8 mg/dl for males, > 7.5 mg/dl for females) and Group B (Unexposed: serum uric acid ≤ 8 mg/dl for males, ≤ 7.5 mg/dl for females). Mortality was significantly higher in Group A among participants aged 56–65 years (78.6% vs. 21.4%,  $p = 0.032$ , RR = 3.744), indicating that Group A individuals in this age group had 3.74 times higher risk of mortality compared to the Group B. Other age groups showed a non-significant trend, such as RR = 2.476 in the 35–45 age group, suggesting a 2.5-fold increase in risk, although this was not statistically significant ( $p = 0.439$ ). Male mortality was significantly higher in Group A (76.5% vs. 23.5%,  $p = 0.026$ , RR = 3.334), meaning males with elevated serum uric acid had a 3.3 times higher risk of mortality compared to those with normal levels. In females, the trend was similar (RR = 3.556) but not statistically significant ( $p = 0.108$ ). Participants with BMI ≤ 25 kg/m<sup>2</sup> in Group A had significantly higher mortality (78.6% vs. 21.4%,  $p = 0.033$ , RR = 3.704), indicating they were 3.7 times more likely to die compared to their unexposed counterparts. For BMI > 25 kg/m<sup>2</sup>, the RR was 3.117, implying a threefold increased risk, though not statistically significant ( $p = 0.081$ ). Among diabetics, those in Group A had a higher mortality risk (75.0% vs. 25.0%,  $p = 0.057$ , RR = 3.375), suggesting a 3.4 times higher risk of death, nearing statistical significance. Similar findings were seen in non-diabetics (RR = 3.444,  $p = 0.048$ ), where elevated uric acid was also associated with a significantly increased mortality risk. Smokers in Group A had significantly higher mortality (75.0% vs. 25.0%,  $p = 0.029$ , RR = 3.350), indicating a 3.35 times higher risk compared to non-exposed smokers. Similarly, among patients with ischemic heart disease, Group A had a markedly higher mortality (81.8% vs. 18.2%,  $p = 0.022$ , RR = 5.368), which means exposed individuals were more than five times as likely to die compared to unexposed individuals with IHD. Participants with hypertension in Group A had significantly elevated mortality (77.8% vs. 22.2%,  $p = 0.010$ , RR = 3.959), indicating a nearly fourfold increased risk of death compared to those in Group B. Mortality was also significantly higher in those with hyperlipidemia in Group A (76.9% vs. 23.1%,  $p = 0.035$ , RR = 3.741), reflecting a 3.7 times greater risk.

## DISCUSSION

The relationship between SUA levels and acute myocardial infarction (AMI) has been debated in recent years, with limited research available on older individuals<sup>12</sup> and while some studies have presented SUA as an independent risk factor for AMI, others have taken a different stance with literature reporting that in patients with acute coronary syndrome (ACS), elevated SUA admission levels were independently linked to poor outcomes in-hospital and elevated mortality.<sup>12-15</sup> According to one study, there is a U-shaped correlation between SUA and negative outcomes related to CVD, and both low and high SUA levels are linked to higher mortality from CVD.<sup>13</sup> High blood uric acid (SUA) levels have been identified as a distinct risk factor for older patients suffering from STEMI which implies that having a higher SUA alone raises the likelihood of negative outcomes, independent of other medical conditions like diabetes or high blood pressure.<sup>14</sup> The findings of our study are consistent with regional and international research where hyperuricemia was strongly linked to all-cause and cardiovascular mortality in males, smokers, and individuals with renal insufficiency.<sup>16</sup> The predictive importance of hyperuricemia in patients with ACS with regard to medium- to long-term outcomes following hospital discharge was evaluated and majority of patients (74.2%) were male, and the average patient age was  $68.1 \pm 12.9$  years with smoking (30.6%), diabetes mellitus (34.9%), and hypertension (67.1%) being frequent.<sup>17</sup> High serum uric acid (HSUA) levels were discovered to significantly increase mortality in individuals with AMI and higher mid/long-term mortality (RR = 2.32) and short-term mortality (RR = 3.09) linked to HSUA, which additionally increased mid/long-term mortality (RR = 2.33) and greater risk of short-term mortality (RR = 6.70 for lower HSUA cut-off levels) in patients receiving percutaneous coronary intervention (PCI).<sup>18</sup> Raised SUA level can also identify individuals at a higher risk of hemorrhage and renal failure, independently predicting one-year mortality in STEMI patients.<sup>19</sup> One author assessed 20 years of monitoring patients with hypertension, and reported that the SUA thresholds linked to the risk of cardiovascular and all-cause deaths were much lower than those used in clinical practice to detect hyperuricemia<sup>20</sup> while another study reported that on admission and during hospital stay, STEMI patients with Killip Classes I and II had lower uric acid levels than patients with Classes III and IV, making them a



reliable indicator of the degree of heart failure and the short-term mortality that followed STEMI.21

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## LIMITATIONS OF STUDY

The study's single-center design, small sample size, possible confounders, lack of long-term follow-up, and scant investigation of underlying mechanisms are some of its limitations that impact the findings' accuracy and generalizability.

## CONCLUSION

A high level of uric acid in the blood was noted to be linked to a higher rate of death among patients with ST-elevation myocardial infarction in this study.

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**Funding Source:** None.

## Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MI & AM: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZA & IMJ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SFUH & MN: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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