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The Association between Serum Uric Acid Level and Acute Coronary Syndrome in-Hospital Outcomes

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Abstract

Background: Serum uric acid (SUA) has been implicated in various cardiovascular conditions. Elevated SUA levels, a condition known as hyperuricemia, are associated with oxidative stress, endothelial dysfunction, and inflammation, all of which contribute to the pathophysiology of acute coronary syndrome (ACS). This study seeks to examine the relationship between SUA levels and in-hospital outcomes in patients with ACS.

Methods: This cross-sectional study was conducted in the Coronary Care Unit (CCU) of Sohag University Hospitals, involving 150 patients diagnosed with ACS. Patients were categorized based on their SUA levels into two groups: normal uric acid (Group 1) and hyperuricemia (Group 2). Clinical evaluations, laboratory investigations, echocardiography, and coronary angiography were performed. In-hospital outcomes, including recurrent infarction, serious arrhythmias, pulmonary edema, cardiogenic shock, and sudden cardiac death, were monitored.

Results: The study included 150 patients with a mean age of 59.5 years, of whom 62% were male. Hyperuricemia was observed in 28% of the patients. The mean SUA level was significantly higher in the hyperuricemia group. In-hospital complications were significantly more prevalent in the hyperuricemia group, including higher rates of recurrent infarction (2.38%), pulmonary edema (28.57%), serious arrhythmia (11.9%), shock (21.43%), and death (7.142%). The composite outcome was significantly worse in the hyperuricemia group (66.66%) compared to the normouricemia group (6.48%).

Conclusion: Our study highlights the significant link between elevated SUA levels and adverse in-hospital outcomes in ACS patients. These findings imply that SUA could potentially function as a prognostic indicator for the severity and outcomes of ACS.

Keywords: Serum uric acid (SUA), Hyperuricemia, Acute coronary syndrome (ACS), Cardiovascular outcomes, In-hospital outcomes

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Introduction

Serum uric acid (SUA) is the end product of purine metabolism, and its elevated levels, known as hyperuricemia, have been implicated in various cardiovascular conditions [1]. The pathophysiological mechanisms linking elevated SUA levels to acute coronary syndrome (ACS) are multifaceted and

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involve oxidative stress, endothelial dysfunction, and inflammation. Uric acid has been shown to induce oxidative stress by generating reactive oxygen species (ROS), which can damage endothelial cells and promote atherosclerosis [2]. Furthermore, SUA can inhibit nitric oxide production, leading to endothelial dysfunction, a critical factor in the initiation and progression of atherosclerotic plaques [3].

Elevated serum uric acid (SUA) levels have been clinically associated with negative outcomes in cardiovascular disease patients, including those with heart failure, hypertension, and chronic kidney disease. In the context of acute coronary syndrome (ACS), hyperuricemia has been suggested as an indicator of poor prognosis [4]. Kojima et al. found that higher SUA levels significantly correlated with increased in-hospital mortality in acute myocardial infarction patients [5]. Additionally, recent studies have identified SUA as an independent predictor of major adverse cardiac events (MACE) in ACS patients [6].

The primary objective of this study is to explore the relationship between serum uric acid levels and in-hospital outcomes in patients with acute coronary syndrome. By analyzing this connection, we aim to assess whether SUA can be used as a prognostic marker for adverse outcomes in ACS patients during their hospitalization.

This study intends to contribute to the body of knowledge that could potentially inform clinical practice and enhance risk stratification in ACS.

Patients and methods

This cross-sectional study was carried out in the Coronary Care Unit (CCU) at Sohag University Hospitals from January 2023 to May 2024. All participants provided informed consent, and the study was approved by the ethical committee of Sohag University. (Clinicaltrials.gov identifier: NCT05770323)

A total of 150 patients with symptoms suggestive of ACS were included. ACS refers to various conditions where the blood flow to the heart is suddenly reduced, including unstable angina (UA), non-ST segment elevation

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myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Participants were chosen based on their clinical presentation and the diagnostic criteria for ACS.

Inclusion Criteria

Participants were included if they presented with cardiac chest pain consistent with ACS and met any of the following features, as defined by the American Heart Association's 2018 guidelines: ECG changes such as ST elevation, ST depression, T wave inversion, or recent left bundle branch block, and elevated cardiac enzymes. These criteria ensured that the study population accurately represented those experiencing acute myocardial ischemia.

Exclusion Criteria

Patients were excluded if they were under 18 years old, had a history of gout or were receiving anti-gout treatment, had chronic kidney disease (CKD), suffered from chronic hemolytic anemia, or were on medications known to cause hyperuricemia, such as thiazide and loop diuretics.

Methods

Each patient underwent a comprehensive evaluation, including a full medical history and detailed clinical examination. The medical history covered factors like age, sex, smoking status, family history of premature atherosclerosis, history of hypertension or diabetes, and previous interventions such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

The clinical examination was followed by several investigations. An electrocardiogram (ECG) was performed to detect any abnormalities, and cardiac enzymes including CK-MB and high-sensitivity cardiac troponin (hs-cTn) levels were measured. Based on the results of these tests, patients were classified into unstable angina, STEMI, or NSTEMI categories. Unstable angina was defined as myocardial ischemia without detectable myocardial necrosis . STEMI was characterized by acute ST-elevation and myocardial injury or necrosis, while NSTEMI was defined by elevated cardiac biomarkers without ST elevation.

Additionally, serum uric acid levels were measured, with normal reference ranges defined as 2.5–6 mg/dL for females and 3–7 mg/dL for males. Renal

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function tests, including blood urea and serum creatinine levels, lipid profiles, and complete blood counts (CBC), were also conducted.

Echocardiography was performed to assess segmental wall motion abnormalities (SWMA), ejection fraction (EF), and cardiac chamber dimensions. Coronary angiography was conducted to evaluate coronary artery stenosis, and PCI was performed if necessary. The degree of coronary stenosis was correlated with serum uric acid levels to explore potential associations.

Hospital Outcomes

The study monitored in-hospital and post-discharge complications, which included recurrent infarction, serious arrhythmias, pulmonary edema, cardiogenic shock, and sudden cardiac death. These outcomes were documented to evaluate the prognostic significance of serum uric acid levels in patients with ACS.

Statistical Analysis

Data analysis was performed using the Statistical Package for Social Sciences (IBM-SPSS), version 24. Data were expressed as mean, standard deviation (SD), number, and percentage. The Chi-square test was used for comparing qualitative variables, while quantitative data were tested for normality using the Shapiro-Wilk test. The Mann-Whitney U test and Kruskal-Wallis H test were employed for non-parametric data comparisons. For parametric data, the Student t-test and one-way ANOVA were used. Pearson Chi-square and Fisher's Exact test were used for qualitative data comparisons. The level of significance was set at $P > 0.05$ for no significance, $P < 0.05$ for significance, and $P < 0.001$ for high significance.

Results

This study included 150 patients, their mean of age was 59.5 years; 93 (62%) patients were males, 44.67% of patients were diabetic, 46 % were hypertensive, 50.67% were current smokers, 2% had family history of pre-mature atherosclerosis.

The electrocardiographic (ECG) findings revealed significant variations among the patients. Inverted T waves were present in 16.67% of cases, while ST segment elevation was observed in 58% of cases, indicating

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acute myocardial injury in a substantial number of patients. Pathological Q waves were seen in 2% of cases, suggesting previous myocardial infarctions. ST segment depression, indicative of ischemia, was noted in 24.66% of cases. Other findings included right bundle branch block (RBBB) in 2.67%, left bundle branch block (LBBB) in 4.67%, and biphasic T waves in 1.33%. Notably, 10% of patients had no abnormal ECG findings (NAD). Regarding echocardiographic, segmental wall-motion abnormalities (SWMA) of the left ventricle were observed in 123 out of 150 cases (82%). The ejection fraction (EF) of the studied patients ranged from 20% to 75%, with a mean (± SD) of 49.6 ± 9.67%. The median EF was 50% as shown in table 1.

Table 1: ECG and Echocardiographic findings of studied patient

Parameters	Studied Cases N=150		
		N	%
ECG	Inverted T wave	25	16.67%
	ST segment elevation	87	58.00%
	Pathological Q	3	2.00%
	ST segment depression	37	24.66%
	RBBB	4	2.67%
	LBBB	7	4.67%
	Biphasic T wave	2	1.33%
	NAD	15	10.00%
Echocardiographic			
SWMA	Yes	123	82%
	No	27	18%
EF (%)	Mean ± SD	49.6 ± 9.67	
	Median	50	
	Range	20 – 75	

The laboratory investigations included CBC and lipid profiles. The mean (± SD) hemoglobin level was 13.526 ±2.021 g/dl. The mean (± SD) WBC count was 10.2 ±5.02 × 10^9/L, and the mean (± SD) platelet count was 274.9 ±85.79× 10^3/µL. The MCV averaged 83.5 ±6.41 fl. Lipid profile analysis showed mean TG at 143.6 ±73.261 mg/dL, cholesterol at 179.6 ±56.13 mg/dL, HDL at 47.6 ±15.51 mg/dL, and LDL at 109.1 ±83.02 mg/dL. High sensitive troponin was positive in 81.33% of patients, and CK-MB was positive in 82% of patients as shown in table 2.

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Table 2:Summarizes laboratory investigation among the studied cases.

Parameters	Studied Cases (N=150)				
	Mean	SD	Median	Minimum	Maximum
Hemoglobin (g/dl)	13.526	2.021	13.5	9.2	18.5
WBCs (×109/L)	10.2	5.02	8.85	4.2	34
Platelets (x10/µL)	274.9	85.79	256.5	127	589
MCV (fl)	83.5	6.41	83	63	102
TG (mg/dL)	143.6	73.261	129.5	48	414
Cholesterol (mg/dL)	179.6	56.13	170	79	382
HDL (mg/dL)	47.6	15.51	43	28	70
LDL (mg/dL)	109.1	83.02	95.9	18.6	764.4
			N		%
Highly sensitive troponin	Positive		122		81.33%
	negative		28		18.67%
CK- MB	positive		123		82.00%
	negative		27		18.00%

Patients were categorized into two groups based on uric acid levels: Group 1 with normal uric acid (108 cases) and Group 2 with hyperuricemia (42 cases). In Group 1, 22.2% had UA, 56.48% had STEMI, and 21.3% had NSTEMI. In Group 2, the distribution was 7.14% for UA, 71.42% for STEMI, and 21.44% for NSTEMI. The mean uric acid level was significantly different between the groups (P = 0.028) as shown in table 3.

Table 3:comparison between the studied groups as regard uric acid :

	Mean	SD	median	Rang	P value	Post hock
UA	**5.27**	2.02	4.7	2.7-10.9		**P1=0.028***
STEMI	6.55	2.36	6	2.7-14.2	**0.029***	**P2=0.485**
NSTEMI	5.94	2.07	5.7	1.3-10.4		**P3=0.392**

*: significantly different as P value ≤0.05. P1: P value between UA and STEMI, P2: P value between UA and NSTEMI, P3: P value between STEMI and NSTEMI

The analysis of risk factors and clinical outcomes revealed several important differences. DM and HTN were more prevalent in Group 2, although not significantly different. Smoking rates were higher in Group 2,

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with a notable proportion of current smokers. The mean age was significantly higher in Group 2 (64.12 ± 9.01 years) compared to Group 1 (57.73 ± 12.84 years), P = 0.004.

Echocardiography showed no significant difference in EF between the groups, but there was a higher prevalence of SWMA in Group 2 (95.24%) compared to Group 1 (76.85%) as shown in table 4.

Table 4:Comparison between the studied groups as regard echocardiography:

parameters		Group 1 N=108	Group2 N=42	P value
EF (%)	Mean ±SD	50.62 ± 9.2	47.44 ± 10.54	0.15
	Range	(22-74)	(20-75)	
SWMA	Yes	83(76.85%)	40(95.238%)	0.5
	No	25(23.148%)	2(4.76%)	

Regarding coronary angiography in group 1, Single vessel disease was presented in 16 (14.81%) patients, 9 (8.33%) patients had 2 vessels disease and 23 (21.296%) patients had 3 vessels disease. While in group 2, Single vessel disease was presented in 5 (11.9%) patients, 9 (21.428%) patients had 2 vessels disease and 12 (28.571%) patients had 3 vessels disease without significant difference between both groups.

The comparison of lipid profiles between patients among both groups showed that Group 1 had higher mean cholesterol (184.69 ± 57.57 mg/dL vs. 166.4 ± 50.52 mg/dL) and LDL levels (116.05 ± 90.1 mg/dL vs. 91.28 ± 58.38 mg/dL), while Group 2 had slightly higher mean HDL levels (50.14 ± 15.86 mg/dL vs. 46.66 ± 15.33 mg/dL). Triglyceride levels were similar between the groups (143.25 ± 76 mg/dL for Group 1 and 144.5 ± 66.57 mg/dL for Group 2) without significant difference between both groups as shown in table 5.

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Table 5:Comparison between the studied groups as lipid profile

		Group 1 (n=108)	Group 2 (n=42)	P value
Cholesterol (mg/dL)	Mean ± SD	184.69 ± 57.57	166.4 ± 50.52	0.073
	Range	79 – 382	83 - 272	
TG (mg/dL)	Mean ± SD	143.25 ± 76	144.5 ± 66.57	0.926
	Range	48 – 414	54 - 324	
HDL (mg/dL)	Mean ± SD	46.66 ± 15.33	50.14 ± 15.86	0.218
	Range	28 – 70	29 - 70	
LDL (mg/dL)	Mean ± SD	116.05 ± 90.1	91.28 ± 58.38	0.101
	Range	18.6 - 764.4	19.6 - 227	

In-hospital complications were significantly higher in Group 2. Group 2 had higher rates of recurrent infarction (2.38%), pulmonary edema (28.57%), serious arrhythmia (11.9%), shock (21.43%), and death (7.142%). The composite outcome was significantly worse in Group 2 (66.66%) compared to Group 1 (6.48%) as shown in table 6.

Table 6: Comparison between the studied groups as regard in hospital complications

	Group 1 (n=108)	Group 2 (n=42)	P value
Recurrent infarction	0 (0%)	1 (2.38%)	<0.001*
Pulmonary oedema	6 (5.55%)	12 (28.57%)	
Serious arrhythmia	1 (.93%)	5 (11.9%)	
Shock	0 (0%)	9 (21.43%)	
Death	0 (0%)	3 (7.142%)	
Composite outcome	7(6.48%)	28(66.66%)	<0.001*

Discussion

The main goal of our study was to explore the relationship between admission SUA levels and in-hospital outcomes in patients with ACS. We included 150 patients, aged 18 to over 60 years (mean age: 59.5 ± 12.21 years).The cohort comprised 93 males (62%) and 57 females (38%). Notably, 67 patients (44.67%) had diabetes mellitus, 69 patients (46.00%) had hypertension, 76 patients (50.67%) were current smokers, and a small proportion (2.00%) had a positive family history of cardiac disease.

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Our findings align with the study by **Lopez-Pineda et al.** [7], which evaluated the prognostic value of hyperuricemia in ACS patients for medium- to long-term clinical outcomes post-hospital discharge. Lopez-Pineda et al. reported a mean patient age of 68.1 ±12.9 years, with a male predominance (74.2%), and a high prevalence of hypertension (67.1%), diabetes mellitus (34.9%), and smoking (30.6%) .

In our study, segmental wall-motion abnormalities of the left ventricle (SWMA) were observed in 123 cases (82%), and the mean EF was 49.6 ± 9.67%, ranging from 20% to 75%. These findings are consistent with **Centola et al.** [8], who reported a mean EF of 50%, with an interquartile range of 40–55% .

Our study revealed a mean TG level of 143.6 mg/dl and a mean cholesterol level of 179.6 mg/dl. HDL and LDL levels averaged 47.6 mg/dl and 109.1 mg/dl, respectively. High sensitive troponin was positive in 122 patients (81.33%), and CK-MB was positive in 123 patients (82.00%). These results are in agreement with **Lopez-Pineda et al.** [7], who reported mean values of total cholesterol (160.0 ± 45.2 mg/dl), triglycerides (135.5 ± 74.4 mg/dl), HDL (39.5 ± 23.3 mg/dl), and LDL (93.1± 37.2 mg/dl) .

In our cohort, 108 patients (72%) had normal uric acid levels, while 42 patients (28%) had hyperuricemia. Among the study population, 91 cases (60.67%) had STEMI, 32 cases (21.33%) had NSTEMI, and 27 cases (18.00%) had UA. These observations are consistent with **Mohammed et al.** [9], who found hyperuricemia in 28.9% of their patients with MI with non-obstructive coronary arteries .

Our data indicate that uric acid levels were notably elevated in the STEMI group compared to the UA group (P = 0.028), with a significant overall difference among the three groups (P = 0.029). These findings are consistent with those of **Feng et al.** [10], who observed higher uric acid levels in patients with hyperuricemia compared to those with normouricemia.

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No significant differences were detected among our groups in terms of gender, diabetes mellitus, hypertension, smoking status, and family history of premature atherosclerosis. However, patients with hyperuricemia were significantly older (P = 0.004), aligning with **Feng et al.'s** [10] findings, which also identified age as a significant variable.

The mean ejection fraction in our cohort was slightly lower in the hyperuricemia group (47.44 ± 10.54%) compared to the normouricemia group (50.62 ± 9.2%), without significant difference. Similarly, no significant differences were reported between the groups regarding SWMA. These results corroborate those of **Ma et al.** [11], who found no significant difference in ejection fraction between hyperuricemic and normouricemic patients.

In terms of lipid profiles, our findings showed no significant differences among groups concerning cholesterol, triglycerides, HDL, and LDL levels. Similarly, **Feng et al.** [10], reported a similar lipid profiles across hyperuricemic and normouricemic groups . However, contrary to our findings, **Zhang et al.** [12] reported significant differences in HDL-cholesterol between these groups .

The occurrence of single, double, and triple vessel disease was not significantly different between the normouricemic and hyperuricemic groups. This contrasts with the results of **Feng et al.** [10], who found a higher prevalence of multiple diseased vessels in the hyperuricemic group.

Our study demonstrated a higher incidence of in-hospital complications among hyperuricemic patients, including recurrent infarction, pulmonary edema, serious arrhythmia, shock, and mortality (P < 0.001). This is in line with **Mohammed et al.** [9], who reported a higher rate of major adverse cardiovascular events and angina rehospitalization in hyperuricemic cases . Similar findings were reported by **Nakahashi et al.** [13] and **Ma et al.** [11].

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Conclusion

Our study highlights the significant link between elevated SUA levels and adverse in-hospital outcomes in ACS patients. These findings imply that SUA could potentially function as a prognostic indicator for the severity and outcomes of ACS. Additionally, hyperuricemia may be considered a relative risk factor for ACS. Future studies should further explore this relationship to improve risk stratification and management strategies for ACS patients.

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