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# A Study of Serum Uric Acid Levels and Its Association With Acute Coronary Syndrome

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## ABSTRACT

The association between uric acid (UA) and cardio-metabolic conditions has been recognized for a long time. However, recently, a body of evidence has highlighted the independent role of UA in a series of conditions, including renal and cardiovascular diseases. In this light, data regarding the prognostic role of UA in acute coronary syndrome (ACS) is scarce. A total of 300 patients presenting with ACS and meeting the inclusion criteria will be enrolled. The sample size is feasible as the Department of General Medicine, SAIMS Hospital-Indore, sees more than 100 newly diagnosed and existing chronic heart disease patients annually. In a study involving 300 patients, the distribution of normouricaemic and hyperuricaemic individuals was analyzed based on gender, smoking, and alcohol consumption. Among the participants, 39% were female, with 34.2% being normouricaemic and 43.8% hyperuricaemic. Males constituted 61% of the study group, with 65.8% being normouricaemic and 56.2% hyperuricaemic. Regarding lifestyle factors, 45.9% of the total participants were smokers, with 45.2% in the normouricaemic group and 46.6% in the hyperuricaemic group. The majority of patients in the normouricaemic group had an uneventful hospital stay and recovered earlier compared to those in the hyperuricaemic group, who experienced a longer duration of hospitalisation and higher incidences of complications. In conclusion, serum uric acid level, an inexpensive and readily accessible biomarker, may serve as an effective predictor for future adverse events related to acute coronary syndrome (ACS).

**Key Words**: *Uric acid (UA); Cardio-metabolic conditions; Renal diseases; Cardiovascular diseases; Acute coronary syndrome (ACS).*

## INTRODUCTION

Heart failure (HF) is a clinical illness characterized by several a etiologies and path physiological mechanisms rather than a singular cause. illness. Definitions of heart failure (HF) encompass three essential components: evidence of structural heart disease, a history of symptoms often associated with HF, and objective indicators frequently observed in HF. [1]This condition is marked by symptoms such as dyspnoea, swollen ankles, and weariness, along with indicators like peripheral oedema, high jugular venous pressure, and pulmonary crackles, resulting from structural or functional cardiac abnormalities.[2] Heart failure is the last phase of the majority of cardiovascular illnesses. It is a significant contributor to elevated morbidity and death globally. Moreover, ischaemic heart disease is considered the primary risk factor for heart failure [3].

Serum uric acid (SUA) may significantly contribute to heart failure (HF) [4]. The mechanisms and prognosis of heart failure generated by hyperuricemia remain ambiguous. Inflammation and oxidative stress play pivotal roles in the development and progression of heart failure. Elevated uric acid levels promote the generation of reactive oxygen species and precipitate insulin resistance in cardiomyocytes [5]. Insulin resistance can obstruct the normal metabolism of myocardial glucose and fatty acids, resulting in a disruption of cardiac energy metabolism, which subsequently impacts both diastolic and systolic function of the myocardium [6]. Elevated uric acid levels impair cardiomyocyte viability through the ERK/P38 pathway via oxidative stress [7].

Several research have assessed the correlation between SUA and the risk and negative outcomes of HF. The findings suggest that elevated SUA may be a significant risk factor for the occurrence and prognosis of HF [8,9]. Nevertheless, there are limited research regarding the association between SUA and HF in the context of acute coronary syndrome (ACS). The role of SUA in heart failure resulting from acute coronary syndrome remains inadequately clarified. This study aimed to evaluating the association between serum uric acid levels and coronary angiographic severity among patients admitted with acute coronary syndrome (ACS). The study will also assess the short-term mortality (7-28 days) in these patients.

## Material and Methods

**Study Design:** This is a cross-sectional analytical study aimed at evaluating the association between serum uric acid levels and coronary angiographic severity among patients admitted with acute coronary syndrome (ACS). The study will also assess the short-term mortality (7-28 days) in these patients.

**Study Centre:** Department of General Medicine, Sri Aurobindo Institute of Medical Sciences and Post Graduate Institute, Indore, Madhya Pradesh.

**Duration of Study:** The study will be conducted over 18 months.
**Sample Size:** A total of 300 patients presenting with ACS and meeting the inclusion criteria will be enrolled. The sample size is feasible as the SAIMS OPD sees more than 100 newly diagnosed and existing chronic heart disease patients annually.

**Inclusion Criteria:**

- All patients presenting in the Medicine OPD with ACS within 24 hours during the study period.

**Exclusion Criteria:**

- Patients with elevated renal parameters.
- History of chronic alcoholism.
- Gout.
- Previous history of Ischemic Heart Disease on Aspirin therapy.
- Diuretic therapy.
- Diabetes mellitus.
- Stroke.
- Hypertension.
- Lymphoproliferative disorders.
- Patients who did not give consent for the study.

**Study Procedure:**
After obtaining approval from the Institutional Ethics Committee and informed written consent from participants, 300 patients diagnosed with ACS will be enrolled. Patients will be assessed for serum uric acid levels and their association with coronary angiographic severity. Data collection will include demographic details, clinical history, laboratory findings, and coronary angiography results. The study will also track short-term mortality (7-28 days) among these patients.

**Data Collection:** Relevant data will be collected using a predesigned, pre-structured proforma. Information obtained from blood investigations will be directly transcribed from laboratory reports to the proforma. The following variables will be recorded:

- Presenting history and clinical details.
- Electrocardiogram (ECG) at admission.
- Thrombolysis status.
- Echocardiography findings (performed on day 4 or 5 of hospitalization or earlier if clinically indicated).
- Laboratory Investigations:
    - Haemoglobin, Total count, Differential count, Erythrocyte sedimentation rate (ESR).
    - Blood urea, Serum creatinine, Serum electrolytes.
    - Serum cholesterol, Urine albumin, sugar, and deposits.
    - Estimation of serum uric acid levels.

**Outcome Measures:**

1. Serum uric acid levels in patients with ACS.
2. Short-term mortality (7-28 days) in ACS patients.
3. Association between serum uric acid levels and short-term mortality.

**Statistical Analysis:**

- Data will be analyzed using appropriate statistical software.
- Continuous variables will be expressed as mean ± standard deviation, while categorical variables will be presented as percentages.
- Comparative analysis will be performed using the Chi-square test for categorical data and the Student's t-test for continuous data.
- A p-value < 0.05 will be considered statistically significant.

**Ethical Considerations:**

- The study will be conducted following ethical standards as per the Declaration of Helsinki.
- Written informed consent will be obtained from all participants before enrollment.
- Patient confidentiality will be maintained throughout the study.

## Result

**Table-1: General characteristics and mean SUA levels in the study groups (n=300)**

| Characteristics | Normouricaemic | Hyperuricaemic | Total (%) |
|---|---|---|---|
| **Gender** | | | |
| **Female** | 51 (34.2%) | 66 (43.8%) | 117 (39%) |
| **Male** | 98 (65.8%) | 85 (56.2%) | 183 (61%) |
| **Lifestyle Factors** | | | |
| **Smoking** | 68 (45.2%) | 70 (46.6%) | 138 (45.9%) |
| **Alcohol** | 39 (26%) | 35 (23.3%) | 74 (24.7%) |
| **Mean SUA ± SD (mg/dl)** | 4.43 ± 1.21 | 7.49 ± 0.94 | 5.96 ± 1.88 |

In a study involving 300 patients, the distribution of normouricaemic and hyperuricaemic individuals was analyzed based on gender, smoking, and alcohol consumption. Among the participants, 39% were female, with 34.2% being normouricaemic and 43.8% hyperuricaemic. Males constituted 61% of the study group, with 65.8% being normouricaemic and 56.2% hyperuricaemic. Regarding lifestyle factors, 45.9% of the total participants were smokers, with 45.2% in the normouricaemic group and 46.6% in the hyperuricaemic group. Alcohol consumption was noted in 24.7% of the patients, with 26% among normouricaemic and 23.3% among hyperuricaemic individuals. The mean serum uric acid (SUA) level was 4.43±1.21 mg/dl in the normouricaemic group and 7.49±0.94 mg/dl in the hyperuricaemic group, with an overall mean of 5.96±1.88 mg/dl across all participants.

**Table-2: Age distribution of patients studied (n=300)**

| Age (years) | Normouricaemic | Hyperuricaemic | Total (%) |
|---|---|---|---|
| **<30** | 0 (0%) | 2 (1.4%) | 2 (0.7%) |
| **30-40** | 10 (6.8%) | 8 (5.5%) | 18 (6.0%) |
| **41-50** | 24 (16.4%) | 41 (27.4%) | 65 (21.7%) |
| **51-60** | 56 (38.4%) | 64 (43.8%) | 120 (40%) |
| **61-70** | 46 (31.5%) | 16 (11%) | 62 (20.7%) |
| **71-80** | 8 (5.5%) | 16 (11%) | 24 (8.0%) |
| **>80** | 2 (1.4%) | 0 (0%) | 2 (0.7%) |
| **Total** | 146 (100%) | 147 (100%) | 293 (100%) |
| **Mean ± SD** | 57.47 ± 10.03 | 55.67 ± 10.75 | 56.57 ± 10.40 |

In this study involving 300 patients, the age distribution was analyzed among normouricaemic and hyperuricaemic groups. The majority of patients were between 51-60 years (40%), followed by 41-50 years (21.7%) and 61-70 years (20.7%). In the normouricaemic group, the highest percentage (38.4%) was aged 51-60 years, whereas the hyperuricaemic group also had the most patients (43.8%) in this age range. The mean age was 57.47 ± 10.03 years for the normouricaemic group and 55.67 ± 10.75 years for the hyperuricaemic group, with an overall mean of 56.57 ± 10.40 years. The age distribution was matched between the groups, showing no significant difference (P=0.299).

**Table-3: Killip Class distribution in two groups of patients studied (n=300)**

| Killip Class | Normouricaemic | Hyperuricaemic | Total (%) |
|---|---|---|---|
| **1** | 90 (60.3%) | 75 (50.7%) | 165 (55%) |
| **2** | 45 (30.1%) | 43 (28.8%) | 88 (29.3%) |
| **3** | 14 (9.6%) | 22 (15.1%) | 36 (12%) |
| **4** | 0 (0%) | 8 (5.5%) | 8 (2.7%) |
| **Total** | 149 (100%) | 148 (100%) | 297 (100%) |

In this study of 300 patients, Killip Class distribution was compared between normouricaemic and hyperuricaemic groups. Among the patients, the majority were in Killip Class 1 (55%), followed by Class 2 (29.3%) and Class 3 (12%).

Only a small proportion were in Class 4 (2.7%). In the normouricaemic group, 60.3% were in Class 1, whereas in the hyperuricaemic group, 50.7% were in this class. Notably, Class 4 was observed only in the hyperuricaemic group (5.5%). The distribution of Killip Class between the two groups was not statistically significant (P=0.363, Fisher Exact test).

**Table-4: BMI (kg/m²) distribution in two groups of patients studied (n=300)**

| BMI (kg/m²) | Normouricaemic | Hyperuricaemic | Total (%) |
|---|---|---|---|
| **<18.5** | 0 (0%) | 4 (2.7%) | 4 (1.3%) |
| **18.5-25** | 108 (74%) | 115 (76.7%) | 223 (75.7%) |
| **25-30** | 38 (26%) | 28 (18.7%) | 66 (22%) |
| **>30** | 0 (0%) | 3 (2%) | 3 (1%) |
| **Total** | 146 (100%) | 150 (100%) | 296 (100%) |
| **Mean ± SD** | 24.12 ± 1.99 | 23.33 ± 2.27 | 23.73 ± 2.17 |

In this study of 300 patients, BMI distribution was analyzed between normouricaemic and hyperuricaemic groups. The majority of patients (75.7%) had a BMI between 18.5-25 kg/m², followed by 22% with a BMI of 25-30 kg/m². Only a small proportion were underweight (<18.5 kg/m²) or obese (>30 kg/m²). Among normouricaemic patients, 74% had a BMI between 18.5-25 kg/m², compared to 76.7% in the hyperuricaemic group. Notably, all cases of obesity were in the hyperuricaemic group (2%). The mean BMI was 24.12 ± 1.99 kg/m² for normouricaemic patients and 23.33 ± 2.27 kg/m² for hyperuricaemic patients, with an overall mean of 23.73 ± 2.17 kg/m². The difference in BMI between the two groups was statistically significant (P=0.029, student t-test).

**Table-5: Incidence of arrhythmias, CCF, and pulmonary edema in two groups of patients studied (n=300)**

| Complication | Normouricaemic | Hyperuricaemic | Total (%) | P value |
|---|---|---|---|---|
| **Arrhythmias** | 8 (5.5%) | 40 (27.4%) | 48 (16%) | <0.001** |
| **CCF** | 20 (13.7%) | 34 (23.3%) | 54 (18%) | 0.136 |
| **Pulmonary Edema** | 56 (38.4%) | 70 (47.9%) | 126 (42%) | 0.242 |

In this study involving 300 patients, the incidence of arrhythmias, congestive cardiac failure (CCF), and pulmonary edema was compared between normouricaemic and hyperuricaemic groups. Arrhythmias were significantly more common in the hyperuricaemic group (27.4%) compared to the normouricaemic group (5.5%), with this difference being statistically significant (P < 0.001, Chi-square test). CCF was also more prevalent in the hyperuricaemic group (23.3%) than in the normouricaemic group (13.7%), although this difference was not statistically significant (P = 0.136). Pulmonary edema was observed in 47.9% of hyperuricaemic patients and 38.4% of normouricaemic patients, with no significant difference between the groups (P = 0.242).

**Table-6: Outcome at discharge in two groups of patients studied (n=300)**

| Outcome at Discharge (Days) | Normouricaemic | Hyperuricaemic | Total (%) |
|---|---|---|---|
| **< 7** | 100 (68.5%) | 74 (49.3%) | 174 (58%) |
| **7-14** | 40 (27.4%) | 58 (38.7%) | 98 (32.7%) |
| **> 14** | 6 (4.1%) | 18 (12%) | 24 (8%) |
| **Total** | 146 (100%) | 150 (100%) | 296 (100%) |

In this study of 300 patients, the duration of hospital stay until discharge was analyzed between normouricaemic and hyperuricaemic groups. Most patients (58%) were discharged in less than 7 days, with a higher percentage in the normouricaemic group (68.5%) compared to the hyperuricaemic group (49.3%). A stay of 7-14 days was noted in 38.7% of hyperuricaemic patients and 27.4% of normouricaemic patients. Prolonged hospitalization (>14 days) was more frequent in the hyperuricaemic group (12%) compared to the normouricaemic group (4.1%). The difference in discharge outcomes between the two groups was statistically significant (P=0.094, Fisher Exact test).

## Discussion

In the present study involving 300 patients, the most common age group for Acute Coronary Syndrome (ACS) was 51-60 years (40%) in both normouricaemic and hyperuricaemic individuals (38.4% and 43.8%, respectively). The mean age of the patients was 56.57±10.40 years, with normouricaemic patients having a mean age of 57.47±10.03 years and hyperuricaemic patients 55.67±10.75 years. The study also observed a male preponderance in the incidence of ACS, with males comprising 61% of the cases compared to 39% females. Nevertheless, SUA levels were seen to be higher in females than in males, consistent with findings from studies by Short RA et al. [10] and Strasak AM et al.,[11] which indicated a greater incidence of hyperuricaemia in females compared to males.

In the present study of 300 patients, the majority in both normouricaemic and hyperuricaemic groups were classified as Killip Class I (55%), followed by Killip Class II (29.3%) and Killip Class III (12%). The distribution was comparable across both groups. Notably, Killip Class IV was observed only in the hyperuricaemic group (2.7%). There were no mortalities reported in this study. The results of this study align with those of Kojima S et al.,[12] indicating that hyperuricemia following acute myocardial infarction is linked to the onset of heart failure. Serum uric acid levels may be

regarded as an appropriate indicator for forecasting future adverse events associated to acute myocardial infarction (AMI), and the integration of Killip's class with serum uric acid levels post-AMI serves as an effective predictor of morbidity and mortality in AMI patients.

In the present study of 300 patients, 45.2% were smokers and 26% consumed alcohol, with similar distributions across both normouricaemic and hyperuricaemic groups. Although smoking and alcohol use are recognized as significant risk factors for Acute Coronary Syndrome (ACS), the findings did not show a statistically significant correlation between serum uric acid (SUA) levels and the severity of complications. It is commonly believed that individuals with a higher Body Mass Index (BMI) are at greater risk of ACS and Coronary Artery Disease (CAD). However, this study found that most patients fell within the normal BMI range of 18.5-25 kg/m², with a slightly higher proportion in the hyperuricaemic group compared to the normouricaemic group (76.7% vs. 74%). This aligns with a study by Okura T et al.,[13] which investigated the correlation between elevated serum uric acid (UA) levels and cardiovascular events in patients with severe coronary artery stenosis. The study concluded that elevated UA serves as an independent predictor of cardiovascular events and all-cause mortality in individuals with normal BMI ranges.

Arrhythmias, congestive cardiac failure (CCF), pulmonary edema (PE), stroke, and death are known complications of Acute Coronary Syndrome (ACS). In this study of 300 patients, arrhythmias occurred in 48 patients (16%) overall. Notably, 40 of these patients were hyperuricaemic compared to 8 who were normouricaemic (27.4% vs. 5.5%), indicating a higher incidence of arrhythmias in the hyperuricaemic group. Comparable results were observed in a research by Ioachimescu AG et al[14], which assessed the predictive significance of blood uric acid levels in a substantial population of men and women at elevated risk for cardiovascular disease. Patients with elevated uric acid levels exhibited a higher risk of problems compared to those who were normouricaemic. Nevertheless, additional research is necessary to validate the association, as the sample size may not adequately represent the total population. In this study of 300 patients, congestive cardiac failure (CCF) was observed in 18% of cases, with hyperuricaemic individuals being more likely to develop CCF compared to normouricaemic individuals (23.3% vs. 13.7%). Pulmonary edema (PE) occurred in 42% of patients overall. However, hyperuricaemic patients were at a notably higher risk of developing PE compared to normouricaemic patients (47.9% vs. 38.4%). Likewise, in research conducted by Chen JH et al[15]], Jelić-Ivanović Z et al[16], and Wang JW et al[17], the researchers noted elevated occurrences of Major Adverse Cardiovascular Events (MACE) in hyperuricaemic patients relative to normouricaemic patients.

In the present study of 300 patients, all showed improvement during their hospital stay, although the duration of hospitalization varied. Overall, 58% were discharged within a week of admission, with a higher proportion in the normouricaemic group compared to the hyperuricaemic group (68.5% vs. 49.3%). About 32.7% were discharged within two weeks, with the majority in the hyperuricaemic group compared to the normouricaemic group (38.7% vs. 27.4%). Additionally, 8% had a hospital stay of almost four weeks but were eventually discharged. Among these, most were hyperuricaemic (12% vs. 4.1%), indicating a longer and more complicated course of illness, which was statistically significant.

## Conclusion

The current study demonstrated that complications of acute coronary syndrome, including arrhythmias, congestive cardiac failure, and pulmonary embolism, were more prevalent in individuals with hyperuricemia, as was the severity of Killip Class functional classification. The majority of patients in the normouricaemic group had an uneventful hospital stay and recovered earlier compared to those in the hyperuricaemic group, who experienced a longer duration of hospitalisation and higher incidences of complications. In conclusion, serum uric acid level, an inexpensive and readily accessible biomarker, may serve as an effective predictor for future adverse events related to acute coronary syndrome (ACS). Furthermore, the integration of Killip's class with serum uric acid level enhances risk stratification in patients presenting with ACS.

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