Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/43qjwm11

SERUM URIC ACID LEVELS AND THEIR ASSOCIATION WITH MYOCARDIAL INFARCTION OUTCOMES

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ABSTRACT

Clinical and epidemiological studies have proved that serum uric acid (SUA) is significantly correlated with cardiovascular disease. The present study has been undertaken with the following High uric acid level is a negative prognostic factor in patients with myocardial infarction. In myocardial infarction higher the uric acid level increases the risk of mortality rate. There is uncertainty about the role. This prospective study evaluated the relationship between serum uric acid (SUA) levels and clinical outcomes in 100 patients with acute myocardial infarction (MI). SUA levels were measured on admission, and patients were monitored for heart failure, arrhythmias, ejection fraction, and mortality. The mean SUA level was 5.9 mg/dl, with males having higher levels than females. Patients with SUA levels above 7 mg/dl had significantly lower ejection fractions and poorer Killip classifications. Among patients in Killip class IV, 12 out of 15 had SUA levels above 7 mg/dl, and 4 died from arrhythmias and hypotension. Additionally, patients with ventricular tachycardia (VT) had SUA levels exceeding 7 mg/dl and experienced in-hospital mortality. No significant differences in SUA levels were found between diabetic and non-diabetic patients. The study concludes that elevated SUA at admission is a strong, independent predictor of short-term adverse outcomes, including mortality, in MI patients. SUA measurement can be a cost-effective tool for early risk stratification and guiding treatment strategies.f uric acid in acute coronary syndrome and whether it could be used as a prognostic marker in MI patients. The role of serum uric acid in cardiovascular and renal diseases has been intensively investigated. High serum uric acid has been indicated as a risk factor for CAD and as an independent prognostic factor of poorer outcomes in patients with verified CAD. Study was done in one hundred patients of myocardial infarction at Sri Venkateshwaraa Medical College Hospital and Research Centre, Pondicherry.Detailed history and clinical examination done. Uric acid was estimated. The relationship of uric acid with severity of Myocardial infarction, treatment response, ejection fraction, arrhythmia and hypotension were studied. A total of 100 patients were recruited to the study. The mean age and mean uric acid level of the study sample was 56 years and 5.9mg/dl respectively. There were 65(65%) males and 35(35%) females. Males had higher uric acid level than females. ($p<0.05$). Those who had SUA >7mg/dl (n= 17) had low ejection fraction which was statistically significant p value ,0.03. Among the 15 patients belonging to KILLIP IV, 12 had SUA values more than 7 mg/dL.(, $p <0.05$.). Measuring serum uric acid level at admission for acute Myocardial infarction patients we can stratify them and can treat effectively. Uric acid is a strong risk factor for myocardial infarction and stroke.

KEY WORDS: Coronary artery disease,Serum uric acid, Cardiovascular events, Vasodilator, Xanthine Oxidase, Myocardial Infarction.

INTRODUCTION

Elevated serum uric acid (SUA) levels are associated with an increased risk of myocardial infarction (MI) and overall mortality, with the timing of SUA accumulation playing a crucial role. Early rises in SUA contribute more significantly to MI risk and mortality than later accumulations, highlighting the importance of managing SUA levels from a young age. In humans, uric acid is the final byproduct of purine metabolism. Its levels in the blood, regulated by production in the liver and elimination through the kidneys, are influenced by genetic factors, demographics (such as sex, gonadal function in women, and obesity), lifestyle habits (such as diet rich in purines, fructose, and alcohol), medical conditions (e.g., heart failure, kidney disease, cancer), and medications like diuretics and chemotherapy. The relationship between SUA and cardiovascular or kidney diseases has been well-studied (Picard, J. et al., 2012; Alderman M. et al., 2004). High SUA levels are a strong predictor of mortality in patients with heart failure and coronary artery disease (Cicoira M. et al., 2002). On a molecular level, uric acid has both protective and harmful effects. As a major plasma antioxidant, it counteracts oxidative damage, but at excessive levels, it promotes oxidative stress, endothelial dysfunction, smooth muscle cell proliferation, platelet aggregation, and microinflammation. Uric acid rises shortly after vascular blockage due to local adenosine degradation, a process meant to protect tissues. However, excessive accumulation leads to its conversion into a pro-oxidant, worsening tissue damage from free radicals (Olexa P. et al., 2002; Bickel C. et al., 2002). Several studies have associated elevated SUA with diabetes, metabolic syndrome, chronic kidney disease, and poorer outcomes in acute stroke and cardiovascular events (Ochiai ME et al., 2005). In myocardial infarction (MI)—a severe manifestation of coronary artery disease—xanthine oxidase activity and uric acid production increase under ischemic conditions. Adenosine, produced in heart tissue, degrades into uric acid and rapidly exits the cells due to low intracellular pH and negative membrane potential. This results in elevated SUA, which may signal underlying ischemia. Though the exact mechanism linking SUA to cardiovascular diseases remains uncertain, hyperuricemia is strongly correlated with endothelial dysfunction, oxidative stress, and platelet aggregation—factors that worsen heart failure outcomes (Kroll K. et al., 1992). High SUA levels also stimulate inflammation, a key factor in cardiovascular disease development. Researchers have recognized SUA as an independent biomarker and risk factor for coronary heart disease (CHD). Elevated SUA indicates increased xanthine oxidase activity, a key enzyme in converting ATP byproducts into uric acid under ischemic conditions. Hyperuricemia from impaired xanthine oxidase activity contributes to oxidative damage and vascular dysfunction. Several studies, including one by Castelli P. et al. (1995), have reported a link between hyperuricemia and MI development. In patients with coronary artery disease (CAD), high SUA levels are associated with worse outcomes. A retrospective Japanese study (Kogure K. et al., 1999) found that elevated SUA within 48 hours of MI symptoms correlated with higher 30-day mortality. Elevated SUA at admission acts as a negative prognostic marker, helping identify patients at risk of short-term mortality, poor long-term survival, and complications post-percutaneous coronary intervention (PCI) (Anker SD. et al., 2003; Johnson RJ. et al., 2005). This study aims to evaluate SUA levels in patients with acute myocardial infarction and investigate possible correlations between SUA levels and outcomes such as heart failure, short-term mortality, arrhythmias, and ejection fraction.

MATERIALS AND METHODS:

This study, conducted at Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, (July 2021 to July 2024), aimed to assess serum uric acid (SUA) levels in patients diagnosed with acute myocardial infarction (MI) and to explore the association between SUA levels and clinical outcomes, including heart failure, short-term mortality, arrhythmias, and ejection fraction. The research proposed that elevated SUA levels at the time of hospital admission could serve as a negative prognostic marker, predicting poor outcomes and an increased risk of major adverse cardiovascular events (MACE) in patients experiencing MI (Tuomilehto J, et al., 1988). The study employed a

prospective, descriptive, and analytical design, providing a comprehensive evaluation of the relationship between SUA levels and MI prognosis.

Study setting:
The study was carried out at Sri Venkateshwaraa Medical College Hospital and Research Centre, Pondicherry, spanning from July 2020 to December 2020.

Study population:
The study included patients admitted to Sri Venkateshwaraa Medical College Hospital and Research Centre, Pondicherry, presenting with a history and clinical signs of myocardial infarction.

Inclusion Criteria:
Inclusion Criteria:
Participants were individuals aged above 18 years, of both genders, diagnosed with myocardial infarction (MI). Diagnosis was confirmed based on a history suggestive of MI, clinical examination findings, electrocardiogram (ECG) changes indicating either ST-elevation MI (STEMI) or non-ST-elevation MI (NSTEMI), and elevated CK-MB levels.Exclusion Criteria: The following patients were excluded from the study: Individuals with a history of previous myocardial infarction. Patients diagnosed with chronic kidney disease. Individuals with a history or clinical signs of gout. Patients with hematological malignancies. Individuals with a history of using medications such as thiazide diuretics or antitubercular therapy (ATT). Patients with a history of cerebrovascular accidents (CVA). Sample Size: A total of approximately 100 patients were enrolled during the specified study period.

Study Procedure:
A pre-structured proforma was utilized to gather demographic and clinical information from the patients. Comprehensive clinical examinations were performed for all participants. An electrocardiogram (ECG) covering all six leads was recorded for each patient promptly, within 15 minutes of hospital admission. Serial ECGs were conducted daily throughout the patient's hospitalization period. Serum uric acid levels were measured upon admission, and an echocardiogram was performed on subsequent days. Uric acid analysis was conducted using non-hemolyzed serum samples. Ethical Considerations:
The study received ethical clearance from the Ethics Committee of Sri Venkateshwaraa Medical College Hospital and Research Centre. Informed consent was obtained from all participants prior to their inclusion in the study.

RESULTS:
A total of 100 patients participated in the study, with their serum uric acid (SUA) levels analyzed across various categories (Table 1). The average age of the study population was 56 years, and the mean SUA level was 5.9 mg/dl. A trend of increasing uric acid levels with advancing age was observed. Among the participants, 65 (65%) were male, and 35 (35%) were female. The average SUA level was higher in males (5.8 mg/dl) than in females (5.2 mg/dl). Among the male participants, 67% had SUA levels within the range of 5.9 ± 0.6 mg/dl, and 20% recorded levels above 7 mg/dl. In comparison, 57% of females had levels within the normal range (5.9 ± 0.6 mg/dl), while 14% had values exceeding 7 mg/dl. Statistically, males exhibited significantly higher uric acid levels than females ($p < 0.05$). Out of the 100 patients, 57 had hypertension in addition to myocardial infarction (MI), while 43% were non-hypertensive. Among the hypertensive group, 71% (n=41) had normal SUA levels, and 12% (n=7) had levels above 7 mg/dl. Among non-hypertensive individuals, 53% (n=23) had normal SUA levels, while 23% recorded levels above 7 mg/dl. Additionally, patients with SUA levels below 5 mg/dl (n=19) had a higher ejection fraction (61–70%) post-MI. In contrast, those with SUA levels above 7 mg/dl (n=17) had significantly lower ejection fractions, with those exceeding 7 mg/dl showing an ejection fraction below 40%. This relationship was statistically significant ($p = 0.03$). (Refer to Table 2). Regarding diabetes status, 52 patients were diagnosed with

type 2 diabetes. Among these, 12 had SUA levels above 7 mg/dl, and 9 had levels below 5 mg/dl. Among the 48 non-diabetic patients, 5 recorded SUA levels above 7 mg/dl, and 10 had levels below 5 mg/dl. In terms of MI classification, 83 patients presented with ST-elevation myocardial infarction (STEMI), and 17 had non-ST-elevation myocardial infarction (NSTEMI). Among the STEMI group, 16 patients had SUA levels exceeding 7 mg/dl, and 14 had levels below 5 mg/dl. Arrhythmias were observed in only 7 patients, with 3 experiencing ventricular tachycardia (VT) and 4 developing ventricular premature complexes (VPC). All three patients with VT had SUA levels above 7 mg/dl and died during their hospital stay. Additionally, 18 patients experienced hypotension, of whom 15 had SUA levels exceeding 7 mg/dl. One patient with resistant hypotension and high SUA levels also passed away during hospitalization. Patients were classified according to the Killip classification system upon admission. The distribution was as follows: 36 patients in Killip Class I, 33 in Class II, 6 in Class III, and 15 in Class IV. Among those in Killip Class IV, 12 had SUA levels above 7 mg/dl, a significantly higher proportion compared to those in Classes I to III ($p < 0.05$) (Refer to Table 3). On the fifth day of hospitalization, the Killip classification was reassessed. At that time, 70 patients were in Class I, 10 in Class II, 6 in Class III, and 10 in Class IV. Notably, 4 patients from Killip Class IV, all of whom had SUA levels exceeding 7 mg/dl on admission, died due to arrhythmias and hypotension during their hospital stay. The findings from this study demonstrate that elevated serum uric acid levels are associated with a poorer prognosis in patients with myocardial infarction ($p < 0.05$). Higher SUA levels were linked to an increased risk of complications, such as arrhythmias and hypotension, and were predictive of worse long-term outcomes and increased morbidity.

Table 1: Different levels of Serum Uric acid among the MI patients, age, ex,Hypertension, Diabetes wise and presence of Arrhythmia

Age in years	SUA < 5	SUA 5 to 7	SUA > 7
< 40 (6)	1	4	1
41 - 50 (19)	6	12	1
51 - 60 (36)	5	27	4
61 - 70 (35)	6	21	8
> 70 (4)	1	0	3
Total	19	64	17
Sex			
Male (65)	9	44	13
Female (35)	10	20	5
Total	19	64	17
HT			
Yes (57)	9	41	7
No (43)	10	23	10
Total	19	64	17
DM			
YES (52)	9	31	12
NO(48)	10	33	5
TOTAL	19	64	17
TYPE OF MI			
STEMI (83)	14	53	16
NSTEMI (17)	5	11	1
TOTAL	19	64	17
Arrhythmia			
Yes (7)	0	4	3
No (93)	19	60	15
Total	19	64	17

Table 2: Comparison of Uric acid level with the Ejection Fraction by Echocardiogram

EF	Uric Acid level < 5	Uric Acid level > 7	
< 50 (16)	0	13	
> 50 (84)	19	4	
0/19 vs 13/17		0.003 Sig	

Table 3: Comparison of Uric acid level with the KILLIPS score

KILLIPS D0	<5	5-7	>7	TOTAL
I	19	27	0	36
II	0	32	1	33
III	0	2	4	6
III	0	2	4	6
IV	0	3	12	15
TOTAL	19	64	17	100

DISCUSSION

Research on the role of serum uric acid (SUA) as a risk factor for stroke remains limited. However, studies have established a link between elevated SUA levels and increased stroke risk, particularly in patients with diabetes. Additionally, an association between SUA and fatal strokes has been observed in the general population. One published study on the relationship between SUA and both fatal and nonfatal strokes in the general population found that elevated SUA was an independent risk factor only in individuals not using diuretics. Since diuretic users typically have hypertension, these findings support the view that the association between SUA and stroke is more significant in normotensive individuals (Safi AJ et al., 2004). Previous research has shown that the risk of myocardial infarction (MI) and overall mortality depends on both the level of SUA exposure and the timing of its accumulation. Notably, early exposure to high SUA levels poses a greater risk for MI and mortality than later exposure, even if the total cumulative exposure is the same. This underscores the importance of maintaining optimal SUA levels early in life, as lowering SUA later may not fully reverse the damage caused by elevated levels earlier in life (Pietro Cirillo et al., 2004). Kojima S et al. (2005) concluded that hyperuricemia following acute myocardial infarction is associated with an increased risk of heart failure. Additionally, SUA levels are effective markers for predicting future adverse events related to MI. Combining Killip classification and SUA levels was found to be a reliable predictor of mortality in patients with MI (Nadkar MY et al., 2008; Ersan Tatli et al., 2008). A study conducted by Nadkar et al. in India also demonstrated that patients with higher SUA levels had poorer Killip classification scores and higher short-term mortality rates. Interestingly, while our study observed differences in SUA levels between male and female patients, Nadkar et al. reported no significant difference. However, studies such as those by Kojima et al. found that men typically have higher SUA levels than women. In our study, 52% of the patients were known diabetics, and there was no significant difference in SUA levels between diabetic and non-diabetic patients on day 0. This finding aligns with the study by Hongyu Zhang et al. (2011), which also found no correlation between SUA levels and diabetic status. However, other studies have reported a significant association between hyperuricemia and type 2 diabetes mellitus. Research from Croatia by Vladimir et al. concluded that high SUA levels at admission independently predict poor short- and long-term outcomes after MI. Elevated SUA was linked to increased in-hospital mortality, 30-day mortality, and poorer survival following MI. In our study, patients were followed for five days and monitored for adverse cardiac events. Of the 100 patients, only 7 experienced arrhythmias—3 had ventricular tachycardia (VT), and 4 had ventricular premature complexes (VPC). All three patients with VT had SUA levels above 7 mg/dl and died during hospitalization. Those with VPC had SUA levels between 5–7 mg/dl, exceeding the confidence interval. Other studies have identified an association between

elevated SUA levels and atrial fibrillation (AF), particularly in women. Research by Yuansheng Liu et al. found that high SUA levels increased the risk of future AF in both sexes. Additionally, Filippo Valbusa et al. (2011) concluded that elevated SUA level were strongly associated with a higher incidence of AF in patients with type 2 diabetes, even after adjusting for multiple clinical risk factors. On comparing SUA levels with Killip classification, it was evident that patients with higher SUA levels performed poorly. Four patients with Killip class IV and SUA levels above 7 mg/dl died from arrhythmias and hypotension during hospitalization. These observations suggest that higher SUA levels on admission correlate with worse Killip scores and poor response to treatment. In contrast, patients with lower SUA levels improved significantly with treatment and demonstrated better Killip scores. All four patients who died belonged to Killip class IV and had SUA levels above 7 mg/dl—a finding consistent with Nadkar et al.'s results. Research by Yildiz Alia et al. (2007) established a significant relationship between SUA levels and coronary blood flow, highlighting that elevated SUA could be an independent predictor of slow coronary flow. This may partially explain why elevated SUA levels influence MI outcomes. The exact mechanisms through which SUA affects coronary artery disease (CAD) remain unclear. Current models do not fully explain the pathophysiological relationship. However, studies indicate that soluble uric acid acts as a pro-oxidant, facilitating free radical production. Uric acid can also form monosodium urate crystals, which deposit in tissues and trigger local inflammation. Uric acid has been found in atherosclerotic plaques, suggesting that elevated SUA levels promote thrombus formation through purine metabolism. SUA can also induce oxidative stress, endothelial dysfunction, and vasoconstriction. Additionally, SUA may promote low-density lipoprotein cholesterol (LDL-C) oxidation and lipid peroxidation, which are crucial factors in atherosclerosis progression and CAD development. Despite some sex-based differences in findings, the exact reason for these discrepancies remains unclear, and further research is necessary. Clinical and biochemical studies are required to understand this relationship fully.

CONCLUSION:

Serum uric acid plays a significant role in influencing both short- and long-term morbidity and mortality in patients with myocardial infarction (MI). It also impacts the overall treatment outcomes. Therefore, measuring serum uric acid levels at the time of admission in patients with acute myocardial infarction can help in risk stratification and guide appropriate treatment strategies. This study suggests that serum uric acid can serve as a cost-effective and reliable independent risk factor and prognostic marker for predicting short-term adverse outcomes in MI patients.

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