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Original Research Article

SERUM URIC ACID LEVEL AS AN EARLY PROGNOSTIC INDICATOR IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Abstract

Background: Cardiovascular disease (CVD) is a leading cause of death globally, with 80% of cases occurring in low and middle-income countries. The study aims to implicate the elevation of serum uric acid in acute coronary syndrome and to assess the prognostic significance of serum uric acid in patients with acute coronary syndrome. **Materials and Methods:** This prospective observational study was conducted for six months at Rajiv Gandhi Government General Hospital (RGGGH), Chennai. One hundred patients were selected based on inclusion and exclusion criteria, informed consent and ethical approval obtained, detailed history taking and clinical examination, ECG recording, serum levels of cardiac biomarkers, Killip Class of all patients, and serum levels of Uric acid. **Results:** Most cases were in the 51-60 age group (48%) and least represented by those between 71 and 80 years. There is no significant difference in gender, age, hypertension, and diabetes between groups. Serum uric acid level at day 0 was significantly higher in cases than in controls. The correlation between SUA levels on day 0 and Killip Class on day 5 is significant, but not between Killip Class on day 0 and Killip Class on day 5. The mean serum uric acid values on admission were 6.8 ± 2.68, with 23 patients of Killip Class 1. On day five, the mean serum uric acid level was 5.6 ± 1.2 for Killip Class 1. **Conclusion:** Serum uric acid is an inexpensive risk factor and prognostic marker for assessing short-term adverse outcomes in patients with ACS.

INTRODUCTION

Cardiovascular disease (CVD) is a condition that affects the heart and blood vessels and is responsible for a significant number of deaths globally.[1] The disease has been studied extensively by researchers, who have identified various risk factors that contribute to the development of CVD. These risk factors include high blood pressure, smoking, high cholesterol levels, obesity, and diabetes. While the mortality rate for CVD has decreased in developed countries, it is still a leading cause of death in people over 35.[2] Moreover, low and middle-income countries bear the brunt of the burden of CVD, with 80% of cases occurring in these countries.[3] CVD has become the leading cause of mortality in India, affecting people a decade earlier than those of European ancestry. Case fatality rates for CVD in low-income countries, including India, are also higher than in middle and high-income countries.[4]

Researchers have studied various biomarkers in patients with acute coronary syndrome (ACS), a type of CVD. However, no single marker has been found to provide definitive prognostic information during the disease. Recent studies have suggested that hyperuricemia, or high levels of uric acid in the blood, may be a novel prognostic marker for CVD.[5,6] Uric acid is a by-product of purine metabolism; the kidneys usually excrete it. Still, when uric acid levels in the blood exceed a certain threshold, it can lead to hyperuricemia. Epidemiological studies have shown that uric acid may be a risk factor for CVD and a prognostic marker for mortality in subjects with heart failure and coronary artery disease.[7] While multiple factors contribute to the development of CVD,

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hyperuricemia may play a significant role in predicting outcomes for patients with ACS.[8]

Studies have found that hyperuricemia is associated with an increased risk of adverse outcomes in patients with ACS, such as recurrent myocardial infarction, heart failure, and death.[9] However, the exact mechanism by which hyperuricemia contributes to the development of CVD is not yet fully understood. It is thought that uric acid may cause oxidative stress and inflammation, which can damage the endothelium, the inner lining of blood vessels. This damage can lead to the formation of atherosclerotic plaques, which can ultimately result in an ACS event. Therefore, the study aims to implicate the elevation of Serum Uric acid in acute coronary syndrome and to assess the prognostic significance of Serum Uric acid in patients with acute coronary syndrome.

MATERIALS AND METHODS

This prospective observational study was conducted for six months at the Institute of Internal Medicine, Rajiv Gandhi Government General Hospital (RGGGH), Madras Medical College, Chennai.

Inclusion Criteria

Patient >18 years admitted with the diagnosis of acute coronary syndrome as per WHO criteria which require at least two of the following three elements to be present as a history of ischemic-type of chest pain, evolutionary change on serially obtained ECG tracings, and a rise and fall in cardiac markers were included.

Exclusion Criteria

Chronic kidney disease, gout, malignancy, hypothyroidism, patients on hypo/hyperuricemic medications, chronic alcoholics, and recurrent myocardial infarction were excluded.

Patients were selected as per the inclusion and exclusion criteria. Informed consent and ethical approval were obtained before the study started.

Detailed history taking and clinical examination was made. ECG recording as per ACC guidelines and serum levels of cardiac biomarkers were estimated. Killip Class of all the patients were estimated on the day of admission and day five following admission. Serum levels of Uric acid were estimated on the day of admission and day five following admission for these patients.

All the data obtained were entered in the proforma. Data were analysed using the SPSS package and by Chi-square and Independency tests.

RESULTS

Among 100 patients, both cases and controls contained an equal representation of male and female genders. There were 17 cases in the age group of 41-50 years and 19 controls under the same age group. Among the age group of 51-60, there were 24 cases and 22 controls. There were 8 in the age group of 61-70 and 1 in each age group of 71-80.

Most cases were in the age group of 51-60 years (48%) and least represented by those between 71 and 80 years. There is no significant difference in gender and age between groups

Table 1: Demographic data of the study

		Case	Control	**P-value**
Gender	Male	25 (50%)	25 (50%)	1.0
	Female	25 (50%)	25 (50%)	
Age group (Years)	41-50	17 (34%)	19 (38%)	0.978
	51-60	24 (48%)	22 (44%)	
	61-70	8 (16%)	8 (16%)	
	71-80	1 (2%)	1 (2%)	
HTN	Yes	27 (54%)	29 (58%)	0.687
	No	23 (46%)	21 (42%)	
DM	Yes	31 (62%)	29 (58%)	0.683
	No	19 (38%)	21 (42%)	
SUA Day 0		6.8182 ± 2.68382	4.8840 ± 0.73356	<0.001

Twenty-seven individuals were hypertensives among cases and 29 among controls. Among cases, 31 individuals had diabetes; among controls, 29 were diabetics. There is no significant difference in hypertension and diabetes between groups.

The mean serum uric acid level in cases was 6.8 ± 2.6, and in controls was 4.8 ± 0.7. There is a significant difference in serum uric acid level at day 0 between groups (p=<0.001) [Table 1].

Table 2: Assessment of correlation between the SUA levels and Killip class on the day of admission and day five following

Correlations					
		SUA day 0	**SUA day 5**	**Killip day 0**	**Killip day 5**
SUA day 0	Pearson Correlation	1	.905**	.819**	.394**
	Sig. (2-tailed)		.000	.000	.006
	N	100	47	50	47
SUA day 5	Pearson Correlation	.905**	1	.559**	.619**

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	Sig. (2-tailed)	.000		.000	.000
	N	47	47	47	47
Killip day 0	Pearson Correlation	.819**	.559**	1	.081
	Sig. (2-tailed)	.000	.000		.588
	N	50	47	50	47
Killip day 5	Pearson Correlation	.394**	.619**	.081	1
	Sig. (2-tailed)	.006	.000	.588	
	N	47	47	47	47
**. Correlation is significant at the 0.01 level (2-tailed).					

Table 2 shows that there is a significant positive correlation between SUA levels on day 0 and Killip class on day 0 ($r = .819$, $p < .001$), as well as between SUA levels on day five and Killip class on day 5 ($r = .619$, $p < .001$). A significant positive correlation exists between SUA levels on day 0 and SUA levels on day 5 ($r = .905$, $p < .001$). However, there is no significant correlation between Killip class on day 0 and Killip class on day 5 ($r = .081$, $p = .588$) [Table 2].

Table 3: Comparison of serum uric acid levels with Killip class on the day of admission and day five among cases

	Mean and STD		95% Confidence Interval for Mean		Min-Max	P-value
			Lower bound	Upper bound		
SUA day 0	1.00	5.1613 ± 1.33068	4.5859	5.7367	3.50-9.20	<0.001
	2.00	6.5143 ± 1.41957	5.6947	7.3339	4.90-10.60	
	3.00	8.5125 ± 1.87954	6.9412	10.0838	6.70-11.10	
	4.00	12.5800 ± 1.55467	10.6496	14.5104	10.90-14.70	
SUA day 5	1.00	5.6000 ± 1.19971	5.1520	6.0480	4.00-9.90	<0.001
	2.00	6.3364 ± 1.89118	5.0659	7.6069	3.90-10.00	
	3.00	9.2000 ± 1.11893	8.0258	10.3742	3.90-10.00	

Among the cases, the mean serum uric acid values on admission were 6.8 ± 2.68. Twenty-three patients were of Killip Class 1 on the day of admission, while it was 14 under Killip Class 2, 8 under Killip Class 3 and 5 under Killip Class 4. The mean serum uric acid value of patients under Killip Class 1 was 5.16 ± 1.3. Patients under Killip Class 2 had a mean serum uric acid value of 6.5 ± 1.4, those under Killip Class 3 had a value of 8.5 ± 1.8, and those under Killip Class 4 had a value of 12.58 ± 1.5. Most patients belonged to Killip Class 1; the least were under Killip Class 4. The highest serum uric acid level value among the cases was 14.5, with the individual falling under Killip Class 4 (Table 3).

There were 30 patients under Killip Class 1 on day 5, 11 patients under Class 2, 6 patients under Class 3 and 3 cases had decreased. The mean serum uric acid level on day five among individuals under Killip Class 1 was 5.6 ± 1.2, while that for individuals under Killip Class 2 was 6.3 ± 1.9 and for individuals under Class 3 was 9.2 ± 1.1. The highest value of serum uric acid on day five was 10.37, and the individual belonged to Killip Class 3. There were 47 cases on day five, and the mean serum uric acid level among the cases was 6.2 ± 1.8 [Table 3].

DISCUSSION

Elevated serum UA levels have been associated with an increased risk for cardiovascular disease. The potential mechanisms by which serum UA may directly cause cardiovascular risk include enhanced platelet aggregation and inflammatory activation of the endothelium.[10] Previous studies have shown that serum uric acid increases cardiac failure.[11-13] A study by Kojima et al.[14] showed that serum uric acid levels correlated with Killip classification. Combining the Killip class and serum uric acid level after AMI is a good predictor of mortality in patients with AMI.

The present study was conducted on 50 patients of ACS, 25 male and 25 female patients, and all the patients with acute STEMI were thrombolysed. Fifty age and sex-matched healthy controls were also evaluated to compare uric acid levels. There was no significant difference in age, status of systemic hypertension and diabetes mellitus in patients with acute coronary syndrome and healthy controls. Most participants in each group were hypertensives, 27% of cases and 29% of controls. People with diabetes constituted 31% of cases and 29% of controls.

Patients with acute coronary syndrome had statistically significantly higher serum uric acid levels on admission than healthy controls ($P< 0.01$). The mean serum uric acid level on the day of admission was 6.8 ± 2.6 among cases compared to 4.8 ± 0.7 among controls. On the day of admission, most (46%) of patients belonged to Killip Class 1, 28% to Class 2, 16% to Killip Class 3 and only 10% to Killip Class 4. A study by Patil et al.[14] concluded that patients with acute coronary syndrome (ACS) who had elevated serum uric acid levels had a higher Killip classification and were associated with higher mortality rates. Additionally, the study found a significant reduction in serum uric acid levels from day 0 to day seven among the patients with ACS.

In the present study, 15 patients had an SUA level above 7, of which four were in Killip Class 4, 9

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were in Killip Class 3, and the remaining were in Killip Class 2. The mean serum uric acid levels were higher among cases that belonged to the higher Killip Class on the day of admission. Nadkar et al.[15] concluded that SUA levels were higher in patients with higher Killip Class among patients of acute MI.

In our study, on day five following admission, the majority (63%) of patients belonged to Killip Class 1, and 23% to Killip Class 2. The mean serum uric acid levels were higher among cases that belonged to higher Killip Class on day five following admission. It was also observed that patients with a higher SUA level (10.6) and Killip Class 2 on clinical evaluation on admission had exhibited clinical worsening to Killip Class 3 on day 5 with an SUA level of 10.79. It was also noted that there was a significant relationship between SUA levels and mortality. Three patients in Killip Class 4, on the day of admission, had deceased following ACS. All patients who died had an SUA level of > 10 mg/ dL. Thus, there was a significant association between SUA level and mortality. A study by Bhaskar et al.[16] found that patients with acute coronary syndrome (ACS) who had high serum uric acid levels had a significantly higher mortality rate of 80% compared to those with normal levels, who had a mortality rate of 20%. Additionally, the study found a significant association between high serum uric acid levels and higher Killip class (III & IV) of heart failure.

Car S et al.[17] found that higher SUA on admission was associated with higher in-hospital and 30-day mortality and poorer long-term survival after acute MI. Thus, SUA may rise following an ACS, and the converse also holds good; elevated SUA may be associated with coronary artery disease. Kojima et al.[18] noted that hyperuricemia after acute MI was associated with the development of heart failure. Our study found a positive correlation between SUA concentration and Killip classification, both on the day of admission and five days later, suggestive of left ventricular failure. Higher SUA levels on admission were strongly associated with adverse outcomes in patients with acute coronary syndrome.

Limitations

Although conducting this study in a sole institution with a lack of time and resources highlighted the role of serum uric acid in influencing the course of ACS, a more elaborate multi-centric study would have been desirable to establish the role of serum uric acid in ACS precisely. This study has not included the details of the treatment modalities, such as thrombolysis and PCI, which could potentially alter the clinical outcome of patients with ACS.

CONCLUSION

It is concluded from the present study that serum uric acid levels were higher in patients of ACS as compared to healthy controls. Patients with elevated serum uric acid levels belonged to the higher Killip classification and had higher mortality. It can be inferred from this study that serum uric acid can be regarded as an inexpensive independent risk factor and prognostic marker for assessing short-term adverse outcomes in patients with ACS.

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