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To Study Serum Uric Acid Level in St Elevated Myocardial Infarction Patients and its Correlation with Age and Triglyceride Levels

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Abstract: ***Cardiovascular diseases (CVD) have been the leading cause of morbidity and mortality in India. Recent trends indicate that this group of diseases have escalated to younger age groups also. In India, cardiovascular diseases are significantly increasing in males and females in both urban and rural population[1]. There is evidence that high uric acid is a negative prognostic factor in patients with mild to severe heart failure[3] although the development of hyperuricemia is almost always associated with worsening of renal failure in these patients[4]. Therefore, it is difficult to dissect the roles played by reduced renal function and high uric acid in affecting prognosis in these patients. Some evidences suggest that uric acid mayexert a negative effect on cardiovascular disease by stimulating inflammation, which is clearly involved in the pathogenesis of cardiovascular disease.[5,] A prospective study was carried out in 100 patients of Acute Myocardial Infarction. Patients with normal uric acid level served as control and the others with elevated uric acid level constituted the study subjects. The complications and short term outcomes were compared in the two groups.The proportion of hyperuricemics in the study population was 59%. Out of the 8patients who succumbed to death following an acute myocardial infarction, all of them were hyperuricemic at presentation. This establishes a strong significantassociation between elevated serum uric acid levels and mortality rates in acutecoronary syndrome.In our study out of 100 STEMI patients 70 male and 30 female patientswith a mean age of 54.85 ± 12.78years90% of patients had hypertriglyceridemia, 51% had elevated serum uric acid (>7.0 mg/dl). Mean serum uric acid level was7.15±2.38. Overall in-hospital mortality was 8%; in all of whom serum uric acid levels were >7mg/dl (p=0.02).We concluded that serum uric acid levels were elevated in patients with acute myocardial infarction.There is a strong correlation between serum uric acid levels at the time of admission and in-hospital and short-term mortality in patients with acute myocardial infarction. Patients with elevated SUA levels had higher Killip class in STEMI, higher mortality rates and major adverse cardiovascular outcomes.Patients with elevated serum uric acid had lower ejection fraction. Uric acid may be considered as a reliable, non-invasive, easily available and cheap independent prognostic marker in predicting the severity of myocardial infarction along with short term outcome.***

Keywords: Serum uric acid (SUA), Myocardial Infarction (MI), Hypertriglyceridemia, BMI

1. Introduction

Cardiovascular diseases (CVD) have been the leading cause of morbidity and mortality in India. Recent trends indicate that this group of diseases has escalated to younger age groups also. In India, cardiovascular diseases are significantly increasing in males and females in both urban and rural population[1]

Following myocardial infarction (MI) some proteins and enzymes labeled as cardiac markers (CPK, MB/ Troponin T & I) are released into the blood in large quantity from necrotic heart muscle. These markers viz. CPK-MB, Troponin-T, Troponin-I and myoglobin, have specific temporal profile in relation to MI; with Troponin- T having prognostic significance also. Epidemiological studies have recently shown that uric acid may be a risk factor for cardiovascular diseases and a negative prognostic marker for mortality in subjects with pre-existing heart failure. Elevated serum uric acid is highly predictive of mortality in patients with heart failure or coronary artery disease and of cardiovascular events in patients.[2]There is evidence that high uric acid is a negative prognostic factor in patients with mild to severe heart failure[3] although the development of hyperuricaemia is almost always associated with worsening of renal failure in these patients.[4] Therefore, it is difficult to dissect the roles played by reduced renal function and high uric acid in affecting prognosis of these patients. Some evidences suggest that uric acid may exert a negative effect on cardiovascular disease by stimulating inflammation, which is clearly involved in the pathogenesis of cardiovascular disease.[5,6]

There is uncertainty whether uric acid level could be used as a prognostic marker in acute ST elevation myocardial infarction (STEMI) patients. Furthermore, there is a need to find a simple, less expensive but accurate marker that could be used in rural areas where fibrinolytic treatment is the first choice of acute reperfusion therapy. We studied the association of uric acid levels on cardiovascular event in patients with STEMI receiving fibrinolytic treatment.

2. Material and Methods

Study Population:
This study was conducted in the Department of Medicine and Department of Cardiology of Hindu Rao Hospital, Delhi.

Study Design:
The study was a prospective study. It aimed to assess the prognostic role of serum Uric acid level following Acute Myocardial Infarction and correlating the levels with short term complications. The study included 100 patients of Acute Myocardial Infarction of which patients with who normal Uric acid level were taken as control and the others

with elevated uric acid level were taken as study population. In both groups the complications and short term outcome were compared.

Inclusion Criteria:
Patients with a diagnosis of Acute ST Elevation Myocardial Infarction were included into the study. A definite diagnosis of Acute ST Elevation Myocardial Infarction was made if the patients satisfied the following criteria:

1) A History of typical retrosternal compressive chest pain lasting for more than 30 minutes, not relieved by rest or nitrates.
2) Typical ECG changes of Acute ST Elevation Myocardial Infarction (ST-T changes in two contiguous leads).
3) Elevated enzymes (CPK-MB or TROPONIN-T or both).

Exclusion Criteria

1) Patients with elevated renal parameters.
2) Patients with Gout.
3) Patients with History of chronic alcoholism.
4) Patients with previous History of Ischemic Heart Disease and on Aspirin therapy
5) Patients on Diuretic therapy.
6) Late presentations of patients i.e. more than 72 hours.

Variables recorded during the study
Routine History, physical examination, routine laboratory investigations in all the study subjects.

1) Presenting History
   a) Duration of chest discomfort
   b) Associated symptoms like sweating, palpitations, dyspnoea
   c) Time of onset of symptoms.
2) Killip's classification on admission
3) Admission Electrocardiogram (ECG) :
   a) Site of infarction: Anterior, Inferior, Lateral, Right ventricular, Global.
   b) No. of leads with Q waves or ST Elevation.
4) Laboratory Investigations :
   a) Complete Blood count
   b) Blood Sugar, Blood Urea, Serum creatinine, Serum Electrolytes.
   c) Serum Uric acid level on admission.
   d) Urine Albumin, Sugar, Deposits.
   e) Serum Cholestrol

Qualifying patients received thrombolytic therapy with 1.5 million units of Streptokinase followed by Heparin for 5 – 7 days. Assessment of left ventricular ejection fraction by Echocardiography was performed either on day 4 or 5 of hospitalisation in most patients or earlier if clinically indicated.

Uric Acid Estimation:
Immediately after admission blood sample of 3cc was drawn by venepuncture and transferred to dry plain bottle and taken tobiochemistry laboratory. The method used for analysis was enzymatic method (Uricase method) by using Auto analyser.In our laboratory, values taken as normal range[51]

Males: 3.4 - 7.0 mg/dl. Females:

2.1 Methodology

Methods using URICASE, the enzyme that catalyzes theoxidation of uric acid to allantoin are most specific.[52] The simplest of these methods measures the differential absorption of uric acid andallantoin at 293 nm.[53] The difference in absorbance before and after incubation with URICASE is proportional to the uric acid concentration.This method has been proposed as candidate reference method.[54]This method was adopted in our study. This is the most specific method.

All the patients were followed up for a period of 7 days. During follow up any changes in killip's classification, or any complications were recorded. Daily ECG was taken and additional investigations carried out if necessary. Patients were discharged oncethey stabilized. Those who with hyperuricemia were counselled and advised for further management of hyperuricemiaFramingham criteria for Heart failure like JVP elevation , Basal Rales, Acute pulmonary edema, S3 gallop, Tachycardia (>120/mt), Lower extremity edema were used in this study for making a diagnosis of CCF.[55]

All patients were subjected to continuous cardiac monitoring for arrhythemias. In this study the incidence of arrhythmias like atrial fibrillation, atrial flutter, Paroxysmal Supra Ventricular Tachycardia, Sustained and ill sustained Ventricular Tachycardia and Ventricular fibrillation were noted in both group of patients. Patients presented with benign ventricular premature beats were not included into the arrhythmias category.

3. Observation and Results

This was a prospective, observational and non-interventional study. The studypopulation had 100 subjects.

1) Age Distribution
The average age of the study group was 54.85 years. 31% of the patients belonged to the age group between 51 to 60 years. The age of the subjects ranged from as low as 27 years to as high as 89 years.

Table 1: Showing Age Distribution in the Study Population

Age	Frequency	Percentage
1)<=40	11	11.00%
2)41-50	27	27.00%
3)51-60	31	31.00%
4)61-70	22	22.00%
5)>70	9	9.00%
Total	100	100.00%

Table 2: Serum Uric Acid with Age

Age	uric acid		Total	P value
	Normal	Raised		
1)<=40	6 (14.63%)	5 (8.47%)	11 (11.00%)	0.109
2)41-50	15 (36.59%)	12 (20.34%)	27 (27.00%)	
3)51-60	13 (31.71%)	18 (30.51%)	31 (31.00%)	
4)61-70	5 (12.20%)	17 (28.81%)	22 (22.00%)	
5)>70	2 (4.88%)	7 (11.86%)	9 (9.00%)	
Total	41 (100.00%)	59 (100.00%)	100 (100.00%)	

2) Gender Distribution

Among the 100 subjects, there were 70 males and 30 females

Table 3: Gender Distribution of the Study Population

Sex	Frequency	Percentage
F	30	30.00%
M	70	70.00%
Total	100	100.00%

Table 4: Serum triglycerides: 90 out of the 100 patients had hypertriglyceridemia, 56 out of the 90 hypertriglyceridemiasubgroup had Hyperuricemia (62.22) but the association is not statistically significant. (p value 0.086)

		uric acid		Total	P value
		Normal	Raised		
TG	Abnormal	34 (82.93%)	56 (94.92%)	90 (90.00%)	0.086
	Normal	7 (17.07%)	3 (5.08%)	10 (10.00%)	
Total		41 (100.00%)	59 (100.00%)	100 (100.00%)	

Table 5: EF with Uric Acid

		uric acid		Total	P value
		1)<=7	2)>7		
EF	1)<=45	18 (36.73%)	51 (100.00%)	69 (69.00%)	<.0001
	2)>45	31 (63.27%)	0 (0.00%)	31 (31.00%)	
Total		49 (100.00%)	51 (100.00%)	100 (100.00%)	

Table 6: Age Distribution with Mortality

	Mortality		Total	P value
	N	Y		
1)<=40	11 (100.00%)	0 (0.00%)	11 (11.00%)	0.292
2)41-50	26 (96.30%)	1 (3.70%)	27 (27.00%)	
3)51-60	29 (93.55%)	2 (6.45%)	31 (31.00%)	
4)61-70	18 (81.82%)	4 (18.18%)	22 (22.00%)	
5)>70	8 (88.89%)	1 (11.11%)	9 (9.00%)	
Total	92 (92.00%)	8 (8.00%)	100(100.00%)	

Table 7: Ejection fraction with Mortality

		Mortality		Total	P value
		N	Y		
EF	1)<=45	61 (88.41%)	8 (11.59%)	69 (100.00%)	0.055
	2)>45	31 (100.00%)	0 (0.00%)	31 (100.00%)	
Total		92 (92.00%)	8 (8.00%)	100 (100.00%)	

Table 8: CK-MB with mortality

		Mortality		Total	P value
		N	Y		
CK – MB	1)<=25	8 (100.00%)	0 (0.00%)	8 (100.00%)	1.000
	2)>25	84 (91.30%)	8 (8.70%)	92 (100.00%)	
Total		92 (92.00%)	8 (8.00%)	100 (100.00%)	

Table 9: BMI with serum uric acid

		Uric acid		Total	P value
		Normal	Raised		
BMI	1)<=25	39 (95.12%)	57 (96.61%)	96 (96.00%)	1.000
	2)>25	2 (4.88%)	2 (3.39%)	4 (4.00%)	
Total		41 (100.00%)	59 (100.00%)	100 (100.00%)	

4. Discussion

Age Distribution

The average age of the subjectsin the study was 54.85years, which truly reflects thestatement that AMI occurs 5-10 years earlier in Indian population than in the westernpopulation. The age ranged from 27 years to 89 years. Majority of patientsbelonged to the age group 51-60 years.Study in a Japanese group by M Kuzuya et al showed a decline in uric acid levels between 30-70 years in males, but a rise in uric acid levels after about 45 years in females[7]. In our study majority of the subjects with hyperuricemia were in the age group 51-70 years.

Gender Distribution

The study included 70% males and 30% females. Male predominance was observed in all the age subgroups included in the study. Our study showed no significant association between gender and mortality. Similarly there is no significant association between elevated uric acid levels and male gender, though the mean uric acid levels were higher in males compared to females. This is in accordance with the studies done by Nadkar[8]et al.

Hyperuricemia and Mortality

The proportion of hyperuricemics in the study population was 59%. Out of the 8patients who succumbed to death following an acute myocardial infarction, all of them were hyperuricemicat presentation. This establishes a strong significantassociation between elevated serum uric acid levels and mortality rates in STEMI. According to Vladimir Trkulja et al, higher serum uric acid on admission was independently associated with thirty day mortality[9]

Uric Acid and Ejection Fraction

LV dysfunction is an important prognostic indicator in myocardial infarction. In our study, there exists an inverse relation between serum uric acid levels and ejection fraction. 69 subjects in the study population had ejection fraction <45%, all of them had serum uric acid> 7mg/dl. The subjects that expired during the study period were included in this subgroup. This is further proof that serum uric acid can be used to predict mortality and severity of left ventricular dysfunction and heart failure. This is supported by the study done by Li Chen[10] et al.

Uric Acid and Killip Class

The mean serum uric acid level has a linear relation with Killip class, indicating that serum uric acid levels correlate with the severity of myocardial infarction as assessed by Killip classification. 59 patients in the study group had uric acid levels more than 7mg/dl out of which 47.46 % belonged to Killip classes 3 and 4. This is a significant association. Similar results were brought out by Li Chen[4] et al in their studies, thereby highlighting the prognostic significance of uric acid in myocardial infarction[4].

Mortality in this study was 8% and all the subjects had serum uric acid >7mg/dl. Nadkar et al reported hyperuricemia in 100% of the dstudy[2.] SUA levels > 7mg/dl was the strongest independent predictor of mortality according to Dharma et al.

Serum Uric Acid with CK-MB

Statistically significant increase in the levels of serum uric acid (P < 0.001) and a highly positive correlation between Serum Uric acid and CKMB levels among cases was observed in our study. Our study is in accordance with the

study done by Nadkar et.al.[2]who found significant increase in the serum uric acid levels in patients with MI and stated that it was a good predictor of mortality in those patients. Sokhanvar S. et.al.[7]concluded that there was a meaningful relation between hyperuricaemia and MI wherein serum uric acid behaved as an independent variable and had no relationship with other risk factors.

Uric Acid and Dyslipidemia

In this study, SUA levels were not correlated positively with serum TG levels (P=0.196). Epidemiologic studies have shown that SUA level is affected by many factors, and it is closely related to the metabolism of lipids. Hyperuricemia is often associated with dyslipidemia, especially hypertriglyceridemia [9,11]. The mechanism of the close relationship between SUA level and lipid metabolism has not been understood completely. Studies done by Li Chen et al showed a positive correlation between triglyceride level and hyperuricemia[4]. They found proportion of hyperuricemics in the dyslipidemic subgroup as 62.2%.

Uric Acid And Ejection Fraction

LV dysfunction is an important prognostic indicator inmyocardial infarction. In our study, there exists an inverse relation between serum uric acid levels and ejection fraction. 69subjects in the study population had ejection fraction <45%,in that 51 patients had serum uric acid> 7mg/dl. 8 patients who died during the study period had serum uric acid >7mg/dl. This is further proof that serum uric acid can be used to predict mortality and severity of left ventricular dysfunction and heart failure. This is supported by the study done by Li Chen[10]et al.

5. Conclusions

1) Serum uric acid levels are elevated in patients with STEMI.
2) Majority of the patients with hyperuricemia were in the age group 51-70 years.
3) There is a strong correlation between serum uric acid levels at the time of admission and in-hospital and short-term mortality in patients with acute myocardial infarction. Patients with elevated SUA levels had higher Killip class in STEMI and higher mortality rates and Major adverse cardiovascular outcomes.
4) Patients with elevated serum uric acid had lower ejection fraction on echocardiographic examination.
5) There was no positive correlation between serum uric acid and serum triglyceride level.
6) Uric acid may be considered as a reliable, non-invasive, easily available and cheap independent prognostic marker in predicting the severity of myocardial infarction along with short term outcome.

6. Financial support and sponsorship

Nil

7. Conflicts of interest

There are no conflicts of interest

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