Original Article

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Role of Serum Uric Acid Level in Predicting Outcome in Acute Myocardial Infarction

Internal Medicine Section

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ABSTRACT

Introduction: Acute myocardial infarction (AMI) is one of the leading causes of mortality and morbidity. Various prognostic markers have been used in AMI some of which are expensive and/or not easily available.

Aim: To determine the role of serum uric acid levels in predicting short-term outcome in AMI.

Materials and Methods: A hospital-based prospective, analytical observational study, in 102 consecutive AMI patients (WHO criteria), ≥ 18 years of age, admitted to the Departments of Medicine and Cardiology. Patients with recurrent myocardial infarction (MI), with additional confounding factors likely to alter serum uric acid levels were excluded. Serum uric acid was measured by using VITROS Uric acid slide method.

Statistical Analysis: Unpaired 't' test was used to study association of serum uric acid levels with individual parameters. Unadjusted multivariate logistic regression analysis was used for comparison of variables against in-hospital mortality. A 'p-value' <0.05 was considered statistically significant

Results: There was a male preponderance (Male:Female = 1.83:1.0) with a mean age of 58.09±13.40 years. Chest pain (73.53%) was the commonest symptom. Anterior-wall was the commonest site (66.67%) and ST-segment elevation MI (STEMI) was the commonest type (55.9%) of MI. One-third (33.3%) of patients had dyslipidemia and over half (57.84%) were hypertensive. Over one-fourth (27.45%) had elevated serum uric acid (>7.0 mg/dL); mean serum uric acid levels were maximum in patients ≥80 years (7.38mg/dL). Mean serum uric acid level was higher in NSTEMI compared to STEMI (5.78mg/dl vs. 5.59mg/dL; p=0.60). Mean serum uric acid was higher in higher Killip classes (6.58 and 7.38 mg/dL in classes III, IV respectively) compared to lower classes (3.80 & 4.58mg/dL in classes I, II respectively). Higher serum uric acid levels were associated with longer hospital stay (6 days for serum uric acid <4 mg/dL vs 9 days for serum uric acid >7 mg/dL). Overall in-hospital mortality was 9.8%; of which the highest number (70%) had serum uric acid level >7mg/dL (p=0.03).

Conclusion: In AMI, patients with a higher Killip class, signifying severe disease, were found to have a higher serum uric acid level. Further, patients with higher serum uric acid had longer hospital stay and significantly higher in-hospital mortality. Serum uric acid may be used as a cheap and effective prognostic indicator in AMI.

Keywords: Acute coronary syndrome, Biochemical marker, In-hospital mortality

INTRODUCTION

Acute myocardial infarction (AMI) is one of the leading causes of mortality and morbidity globally [1]. Certain markers have been evaluated which indicate unfavourable prognosis in AMI [2]. Uric acid is one such marker that has been evaluated to assess the prognosis in patients with AMI. Previous studies have reported positive associations of increased serum uric acid levels with a greater risk of ischemic heart disease, higher blood pressure, and an overall adverse cardiovascular risk profile [3,4]. Various mechanisms have been postulated for the deleterious effects of hyperuricemia with adverse cardiovascular outcomes, which includes endothelial dysfunction, oxidative metabolism, platelet adhesiveness and aggregation, intracellular stress and inflammation leading to endothelial injury and enhancement of vasoconstrictor effects [5,6].

Out of the various prognostic markers for AMI, like brain natriuretic peptides, C-reactive protein, cell free DNA levels, serum uric acid level is relatively cheap and easily available [7]. However, data on the prognostic implication of serum uric acid on outcome in AMI is limited especially from India. With this background the present study was undertaken in a tertiary care teaching hospital in north east India, to determine the role of serum uric acid levels in predicting in-hospital outcome in AMI.

MATERIALS AND METHODS

This study was a hospital-based prospective, analytical observational study, carried out between July 2012 and June 2013, in consecutive patients with AMI admitted to the Departments of General Medicine and Cardiology, Gauhati Medical College & Hospital, Gauhati, a Tertiary Care Hospital

in Northeast India catering to several Northeastern states of the country. A total of 102 patients with AMI were included by the process of consecutive sampling. AMI was defined as per the following WHO criteria [8] which require at least two of the following three elements to be present:

1. A history of ischemic-type of chest pain.
2. Evolutionary change on serially obtained ECG tracings.
3. A rise and fall in cardiac markers.

Inclusion Criteria

1. Any patient >18 years admitted to the General Medicine and Cardiology Departments with the diagnosis of AMI as per WHO criteria [8].

Exclusion Criteria

1. Chronic kidney disease
2. Gout
3. Malignancy
4. Hypothyroidism
5. Patients on hypo/hyper uricemic medications
6. Chronic alcoholics
7. Diabetes Mellitus
8. Recurrent Myocardial infarction.

Detailed history, clinical examination and laboratory tests were done in all cases. Serum uric acid was measured by using The VITROS uric acid slide method using the VITROS URIC SLIDES and the VITROS Chemistry products calibrator kit 1 on VITROS 250/350/950 and 5,1, FS chemistry systems and the vitros 5600 integrated system. Data with respect to demographic characteristics, laboratory investigations and clinical profile of the patient was collected and recorded.

Prior to initiation of the study ethical clearance from Institutional Ethical Committee was obtained. Informed consent was taken from all patients who were enrolled in the study.

STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package for Social Survey (SPSS) for Windows version 17.0. A comparison between serum uric acid level and patients admitted with AMI was made. Unpaired 't' test were used to study association of serum uric acid levels with parameters like sex, type of MI, hypertension etc. Unadjusted multivariate logistic regression analysis was used for comparison of variables against in-hospital mortality.

RESULTS

A total of 102 patients were included (Male =66, Female =36) with a male to female ratio of 1.83:1. Maximum numbers of patients were in the age group of 50-59 years irrespective of sex with an overall mean age of 58.09±13.40 years. The age and sex distributions of the study population are shown in [Table/Fig-1].

Age Group (years)	Male (%)	Female (%)	Total (%)
18-29	0(0.0)	0(0.0)	0(0)
30-39	2(3.03)	0(0.0)	2(1.95)
40-49	9(13.64)	6(16.67)	15(14.71)
50-59	32(48.48)	12(33.33)	44(43.14)
60-69	13(19.70)	8(22.22)	21(20.59)
70-79	8(12.12)	7(19.44)	25(24.51)
>80	2(3.03)	3(8.33)	5(4.9)
Total	66(100.00)	36(100)	102

[Table/Fig-1]: Age and sex distributions of acute myocardial infarction patients.

The predominating presenting symptom was chest pain (73.53%). Three-fifths (55.9 %) of patients had ST-Segment elevation MI (STEMI) while rest had non-STEMI. Anterior wall MI was the commonest site for AMI (66.67%). Nearly three-fifths of the patients were hypertensive and one-third had abnormal lipid profile. The clinical presentations and biochemical profile of the patients is shown in [Table/Fig-2].

Among the patients studied 22.55% had serum uric acid level < 4 mg/dL, 28.43% had uric acid between 4.1-5.5 mg/dL, 21.57% had serum uric acid between 5.6-7.0 mg/dL and 27.45% had serum uric acid >7.0 mg/dL. Levels of serum uric acid in patients with MI are shown in [Table/

Characteristics	Male (n=66)	Female (n=36)	Total (n=102)
Chest Pain	50 (75.76%)	25 (69.44%)	75 (73.53%)
Atypical presentation	16 (24.24%)	11 (30.56%)	27 (26.47%)
STEMI*	37 (56.07%)	20 (55.56%)	57 (55.9%)
Anterior wall STEMI	26 (70.27%)	12 (60%)	38 (66.67)
Inferior wall STEMI	11 (29.73%)	8 (40%)	19 (33.33)
NSTEMI†	29 (43.93%)	16 (44.44%)	45 (44.1%)
Hypertensive	37 (56.06%)	22 (61.11%)	59 (57.84%)
Normotensive	29 (43.94%)	14 (38.89%)	43 (42.16%)
Dyslipidemia	18 (27.27%)	16 (44.44%)	34 (33.3%)
Normal Lipid Profile	48 (72.73%)	20 (55.56%)	68 (66.7%)

[Table/Fig-2]: Clinical and biochemical characteristics of acute myocardial infarction patients.
*ST segment elevation myocardial infarction; †non-ST segment elevation myocardial infarction.

Serum Uric Acid Level (mg/dl)	Number of Patients (%) (n=102)
<4 mg/dl	23 (22.55%)
4.1-5.5 mg/dl	29 (28.43%)
5.6-7.0 mg/dl	22 (21.57%)
>7.0 mg/dl	28 (27.45%)

[Table/Fig-3]: Levels of serum uric acid in patients with acute myocardial infarction.

Fig-3]. Mean serum uric acid for males and females were 5.66mg/dL and 5.68mg/dL respectively. The mean serum uric acid was maximum in the age group greater than 80 years (7.38mg/dL) followed by those aged between 30-39 years (7.15mg/dL). The levels of serum uric acid according to age distributions are shown in [Table/Fig-4].

The mean serum uric acid level was higher in NSTEMI (5.78 mg/dL) as compared to STEMI (5.59mg/dL), but difference was not statistically significant (p=0.6042).The mean serum uric acid level was 5.58 mg/dL in patients who had anterior wall MI as compared to 5.59 mg/dL in patients having Inferior wall MI, the difference was statistically not significant (p=0.9879). The co-relation between mean serum uric acid levels and different forms of MI is shown in [Table/Fig-5].

Mean serum uric acid level was 3.8 mg/dL in patients in Killip's class I, 4.58 mg/dL in patients in Killip's class II, 6.58 mg/dl in class III patients while 7.38 mg/dL in class IV patients. Thus, it was seen that patients having higher uric acid level belonged to higher Killip's class [Table/Fig-6].

Mean duration of hospital stay increased in patients having higher uric acid level. Patients having serum uric acid level <4 mg/dL had mean duration of hospital stay of 6 days while patients having uric acid level >7 mg/dL had mean duration of stay of 9.1 days. The co-relation between serum uric acid levels and mean duration of hospital stay is depicted graphically [Table/Fig-7].

Out of the total 102 patients, 10 patients (9.8%) expired. Maximum mortality [i.e. 7 out of 10 (70%)] was seen in patients having serum uric acid level >7mg/dL. Remaining 3 out of 10 patients (30%) had uric acid in the range of 5.6-7.0 mg/dL. However, no mortality was seen in patients having uric acid level between 4.1-5.5 mg/dL and below 4 mg/dL. The results of mortality according to serum uric acid levels are shown in [Table/Fig-8].

Unadjusted multivariate logistic regression analysis of variables with respect to in-hospital mortality showed a significant association with serum uric acid levels [Table/Fig-9]. Though mortality in hospital was higher in patients with comparatively lower ejection fractions we could not show a statistically significant correlation.

Age of Distribution (in years)	No. of Patients (%)	Mean Serum Uric Acid Level (mg/dL)
18-29	0	____
30-39	2 (1.9%)	7.15
40-49	15 (14.7%)	5.53
50-59	44 (43.1%)	5.92
60-69	21 (20.6%)	5.23
70-79	15 (14.7%)	4.91
>80	5 (4.9%)	7.38

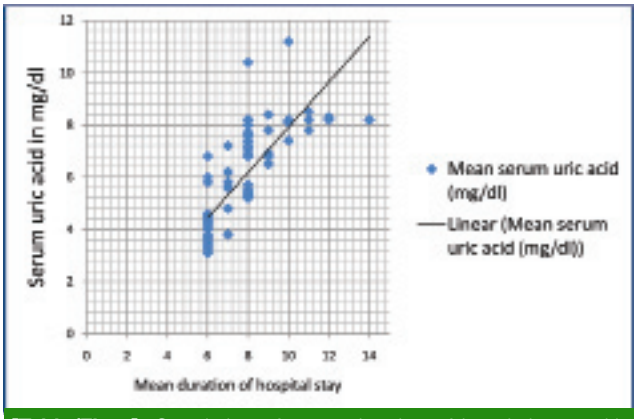
[Table/Fig-4]: Levels of mean serum uric acid according to age distributions.

Type of Myocardial Infarction	Mean Serum Uric Acid (mg/dL)	p-value
STEMI*	5.59	0.6042
NSTEMI†	5.78	
Anterior wall STEMI	5.58	0.9879
Inferior wall STEMI	5.59	

[Table/Fig-5]: Correlation between mean serum uric acid levels and different forms of acute myocardial infarction.
*ST segment elevation myocardial infarction; †non-ST segment elevation myocardial infarction.

Killip's Class	Number of Patients (%)	Mean Serum Uric Acid (mg/dL)
I	16 (15.69 %)	3.80
II	35 (34.31 %)	4.58
III	24 (23.53%)	6.58
IV	27 (26.47 %)	7.39

[Table/Fig-6]: Mean serum uric acid levels according to Killip's classification.



[Table/Fig-7]: Correlation of mean duration of hospital stay with mean serum uric acid (mg/dL).

Uric Acid (mg/dL)	No. of Patients Expired (%) (n=10)	Mean Serum Uric Acid Level (mg/dL)
<4	0	-
4.1-5.5	0	-
5.6-7.0	3 (30%)	6.5
>7	7 (70%)	9.0

[Table/Fig-8]: Mortality and serum uric acid levels in patients with acute myocardial infarction.

Variable	Unadjusted Odds Ratio	95% Confidence Interval	p Value
Serum Uric Acid	13.56	1.35-46.11	0.031
LVEF	0.847	0.85-1.15	0.075

[Table/Fig-9]: Effect of serum uric acid and left ventricular ejection fraction (LVEF) on in-hospital mortality using unadjusted multivariate logistic regression analysis.

DISCUSSION

Our study was carried out with the primary aim of evaluation serum uric acid as a prognostic marker for AMI. There was a male preponderance in our study population which is concordant to previous studies which also show a higher male preponderance in patients with AMI [2,5]. Maximum number of patients were elderly (50-59) years irrespective of sex with an overall mean age of 58.09±13.40 years. Previous studies have shown similar mean ages of 58.29±11.31 years and 58±11.7 years respectively [2,5]. The most common presentation was chest pain or chest discomfort, found in around 3/4th of the patients with the rest having atypical presentation, in the form of absence of chest pain, dyspnoea, nausea, sweating etc. Previous studies have shown similar results with the most common presenting feature being chest pain [8]. STEMI was commoner than non-STEMI and among those having STEMI, a majority had an anterior wall infarction, a finding which is in concordance with previous studies [2,9].

In our study, we observed that among the risk factors the incidence of hypertension was 57.84% and dyslipidemia was 33.3%. A previous study had shown a similar incidence of hypertension at 59% [5]. Another study found prevalence of hypertension as 56.36% while dyslipidemia was present as a risk factor in 45.45% [2]

In the present study, a total of 22.55% patients had serum uric acid level < 4 mg/dL, 28.43% between 4.1-5.5 mg/dL, 21.57% between 5.6-7.0 mg/dL and 27.45% had serum uric acid >7.0 mg/dL. A previous study in patients with AMI showed similar results with 35% patients having serum uric acid level <4 mg/dL, 29% between 4.1-5.5 mg/dL, 21% between 5.6-7.0 mg/dL and 15% having uric acid level >7 mg/dL [5]. In present study, we found two separate peaks in serum uric acid levels according to age, one being in the 30-39 years of age group and the others being aged above 80 years. A previous study reported that there is no significant co-relation between the serum uric acid levels and the age distributions in patients with AMI [10].

In our study though the levels of serum uric acid were slightly higher in patients with STEMI than those with NSTEMI we could not find any significant statistical difference. Furthermore, there was no significant statistical difference between the serum uric acid levels and sites of STEMI as anterior or inferior wall infarction. Previous studies too have failed to show any association between serum uric acid and types and sites of AMI [2,11].

In the present study, it was found that patients having higher mean serum uric acid level were in the higher Killip's class. Killip's classification is an indicator of severity of heart failure [12]. Previous studies too have found a co-relation between serum uric acid with severity of the Killip's classification [13,14]. A possible explanation for such an association may be the fact that the failing heart in AMI leads to tissue hypoperfusion and hypoxia, which triggers xanthine oxidase activation and oxidative stress thereby increasing uric acid levels and triggering a vicious cycle [15].

In the present study it was seen that patients with a higher serum uric acid level also had a longer duration of hospital stay suggesting that patients with higher uric acid suffered from increased morbidity, which prolonged their duration of hospital stay. Mortality rate was higher in patients having higher uric acid levels. Out of 102 patients (9.8%) expired, of which three had serum uric acid in the range of 5.6- 7.0 mg/dl while 7 patients had a serum uric acid level >7mg/dl. Thus, higher uric acid level predicts poor prognosis. A previous study which included 683 patients with AMI also concluded that serum uric acid was an independent predictor of all-cause mortality in medium-term follow-up in patients with AMI and has an added value for risk stratification [11]. In another study of 184 patients of STEMI it was observed that uric acid had a prognostic role for in-hospital and short-term (30-day) mortality [2]. However, on the contrary another large study with 2218 patients with AMI observed that uric acid was not an independent prognostic marker in hospital mortality after AMI [16].

LIMITATIONS

The sample size in our study was relatively small due to constraints of time and resources, which is a limitation of the study.

CONCLUSION

In present study, we found that serum uric acid levels correlated with Killip's class; patients in higher Killip's class, and hence a more severe form of MI, had higher serum uric acid levels. Further patients with higher serum uric acid levels had longer duration of hospital stay and increased in-hospital mortality, the latter being statistically significant. However, probably because of the smaller sample size, statistically significant correlations could not be found between serum uric acid level and the other parameters. Thus, serum uric acid can be considered as a cheap and effective prognostic indicator in patients with AMI, although further study in a larger sample would be more conclusive.

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