



THE ROLE OF SERUM URIC ACID LEVELS IN PATIENTS OF ACUTE MYOCARDIAL INFARCTION AND ITS CORRELATION WITH THE SEVERITY AND OUTCOME IN TERTIARY CARE CENTER

Medicine

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ABSTRACT

Introduction- Acute Myocardial Infarction, the most important form of Cardio Vascular Disease (CVD) continues to be the leading cause of death in the industrialized countries. Increased serum uric acid levels are observed in patients with Myocardial Infarction. Clinical studies have proved that serum uric acid (SUA) is significantly associated with cardiovascular disease.¹⁻³ Uric acid is an independent predictor of major adverse cardiovascular events (MACE) in patients with coronary artery disease.^{4,5} High serum uric acid causes increasing platelet reactivity mediating inflammation and stimulation of smooth muscle cell proliferation which probably worsens acute thrombosis.⁶⁻¹¹ The aim of the study is to estimate the serum uric acid levels in patients of acute myocardial infarction, and to evaluate the associations of raised uric acid with severity and outcome in tertiary care centre. **Methodology:-** Prospective Case Control Study with duration of study was 18 Months. After obtaining written informed consent, all patients were subjected to detailed history taking, detailed general examination, systemic examination of cardiovascular, neuromuscular, gastrointestinal, respiratory & genitourinary system, ECG in all leads and blood investigations viz., Hb %, TLC, DC, ESR, S. Urea, S. Creatinine, Fasting/RBS, urine, serum uric acid and biochemical markers like troponin I & CPK-MB. Evaluation of the patient was done using Killip classification on the day of admission D0, D3, D7.1. **Inclusion Criteria.** -1. Patient brought to hospital with history of chest pain and diagnosed as acute myocardial infarction (both STEMI and NSTEMI). 2. Diagnosis confirmed by ECG findings, biochemical markers like troponin T, creatinine kinase CK-MB, CPK.

Exclusion Criteria- 1. Any patient condition known to elevate uric acid levels, for example chronic liver disease, gout, haematological malignancy etc.

2. Patients taking drugs that increase serum uric acid level like salicylates etc. Venous blood sample was collected from all the subjects. Serum CK-MB and uric acid were estimated in cases and serum uric acid in controls. Unpaired t test and Pearson's correlation coefficient were employed to analyse the results.

Results: The mean $\pm$ SD of serum uric acid among cases and controls were 7.10 ± 0.9 and 5.62 ± 0.58 respectively displaying a highly significant statistical difference ($p < 0.001$). The mean CK-MB among the cases was 48.2 ± 3.4 IU/ L. Serum uric acid showed positive correlation with CK-MB in subjects with Myocardial Infarction with 'r' and 'p' value being +0.38 and 0.007 respectively. **Conclusion:** This study concludes that serum uric acid levels were high and had a positive correlation with CK-MB in patients with Myocardial Infarction.

KEYWORDS

Myocardial Infarction (MI), Uric Acid.

INTRODUCTION

Acute myocardial infarction the most important of Cardio Vascular Disease (CVD) continues to be the leading cause of death in industrialized countries and India.³ Uric acid is an independent predictor of major adverse cardiovascular events (MACE) in patients with coronary artery disease.^{4,5}

High serum uric acid causes increasing platelet reactivity mediating inflammation and stimulation of smooth muscle cell proliferation which probably worsens acute thrombosis.^{6,7} Following myocardial infarction (MI) some proteins and enzymes labeled as cardiac markers (CPK-MB / Troponin T) are released in large quantity from necrotic heart muscle into the circulation. In this study, we wanted to determine the role of serum uric acid levels in acute myocardial infarction and prognostic significance of serum uric acid concentration in acute myocardial infarction to correlate severity and outcome. Epidemiological studies have shown that uric acid may be a risk factor for cardiovascular diseases. Uric acid is a general marker of cell death and elevated serum uric acid is linked with obesity, dyslipidemia, hypertension, insulin resistance, male gender, aging, menopause, excessive alcohol intake and diuretic use. Although uric acid can act as an antioxidant, excess serum accumulation is often associated with cardiovascular disease. Hyperuricemia has always been presumed to be a consequence of insulin resistance. Studies have shown that high serum uric acid is associated with higher risk of type 2 diabetes, independent of obesity, dyslipidemia, and hypertension.⁹

METHODOLOGY

AIM- The aim of the study is to estimate the serum uric acid levels in patients of acute myocardial infarction, and to evaluate the associations of raised uric acid with severity and outcome in tertiary care centre.

OBJECTIVES- 1. To find the prevalence of raised serum uric acid level in the patients with acute myocardial infarction

2. To find difference in uric acid level based on severity of myocardial infarction.

3. To compare the trend of uric acid level in patients over a period of seven days and the outcomes of patients

Definition Of The Various Outcome Indicators: Short-term Outcome Indicators:

Outcome indicators that occur within 30 days of diagnosis of MI and admission to treatment, including: death within 30 days, including in-hospital and cardiac death Other adverse indicators occurring within 30 days, including atrial fibrillation (AF), acute kidney injury (AKI), myocardial infarction recurrence (RMI), complete atrioventricular (AV) block, coronary artery disease (CAD), coronary prevalence (CP), cardiogenic shock (CS), heart failure (HF), impaired renal function (IRF), major bleeding, renal failure (RF), target vessel revascularization (TVR), ventricular arrhythmia (VR) and Angina pectoris (AP).

Long-term Outcome Indicators:

Indicators of adverse outcomes occurring more than 30 days after diagnosis of MI and admission to follow-up, including.

Location of study: - Tertiary Care Centre.

Study design: - Prospective Case Control Study

Duration of study: - 18 Months.

Source of study: - The present study will be carried out in tertiary care centre. After Ethics Committee approval patients will be selected as per inclusion and exclusion criteria. Consent of the patient will be taken for the study or consent of legally acceptable relative (LAR) will be taken if patients is unconscious or his sensorium is altered and re-consent will be taken once patient gains consciousness. After obtaining written informed consent, all patients were subjected to detailed

history taking, detailed general examination, systemic examination of cardiovascular, neuromuscular, gastrointestinal, respiratory & genitourinary system, ECG in all leads and blood investigations viz., Hb %, TLC, DC, ESR, S. Urea, S. Creatinine, Fasting/RBS, urine, serum uric acid and biochemical markers like troponin I & CPK-MB. Evaluation of the patient was done using Killip classification on the day of admission D0, D3, D7.

Inclusion Criteria

1. Patient brought to hospital with history of chest pain and diagnosed as acute myocardial infarction (both STEMI and NSTEMI)
2. Diagnosis confirmed by ECG findings, biochemical markers like troponin T, creatinine kinase CK-MB, CPK.

Exclusion Criteria

1. Any patient condition known to elevate uric acid levels, for example chronic liver disease, gout, haematological malignancy etc.
2. Patients taking drugs that increase serum uric acid level like salicylates, ethambutol, amiloride, bumetide, chlorthalidone, cisplatin, cyclophosphamide, cyclosporin, ethacrynic acid, thiazide diuretics, furosemide, indapamide, vitamin C, levodopa etc.
3. pts with CKD, Gout, Hypothyroidism, stroke, hematological malignancies will be excluded from the study.

Statistical Analysis

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means $\pm$ SD and as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Shapiro-Wilk test. The following statistical tests were applied for the results: The association of the variables which were quantitative in nature were analysed using Independent t test (for two groups) and ANOVA (for more than two groups). The association of the variables which were qualitative in nature were analyzed using Chi-Square test. The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

Table 1:- Association Of Uric Acid With Killip Grading.

Uric acid (mg/dL)	I (n=74)	II (n=73)	III (n=64)	IV (n=69)	Total	P value
At day 0						
Mean $\pm$ SD	5.76 $\pm$ 1.36	5.77 $\pm$ 1.44	5.75 $\pm$ 1.46	5.89 $\pm$ 1.59	5.79 $\pm$ 1.46	0.936 [*]
Median(25 th - 75 th percentile)	5.38(4.888-6.195)	5.72(4.71- 6.13)	5.38(4.755- 6.1)	5.64(4.6-6.35)	5.48(4.72- 6.2)	
Range	4.07-9.5	4-9.95	4.04-9.98	4.08-9.76	4-9.98	
At day 3						
Mean $\pm$ SD	5.55 $\pm$ 1.58	5.69 $\pm$ 1.71	5.33 $\pm$ 1.56	5.66 $\pm$ 1.72	5.56 $\pm$ 1.64	0.588 [*]
Median(25 th - 75 th percentile)	5.04(4.232- 6.265)	5.47(4.28- 6.27)	4.93(4.168- 6.028)	5.49(4.08- 7)	5.26 (4.2- 6.27)	
Range	3.52-9.05	3.16-9.6	3.24-9.27	3.34-9.33	3.16-9.6	
At day 7						
Mean $\pm$ SD	4.94 $\pm$ 1.63	5.06 $\pm$ 1.71	4.74 $\pm$ 1.61	5.03 $\pm$ 1.69	4.95 $\pm$ 1.66	0.672 [*]
Median(25 th - 75 th percentile)	4.54(3.577- 5.8)	4.79(3.85- 5.74)	4.44(3.405- 5.512)	4.84(3.5- 6.01)	4.7(3.56- 5.78)	
Range	2.55-8.44	2.48-9.26	2.43-9	2.57-8.74	2.43-9.26	

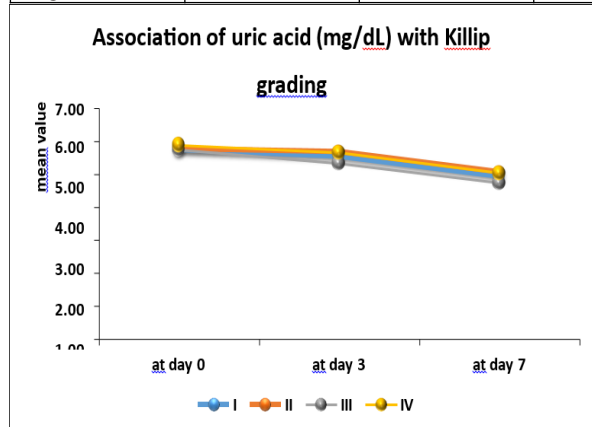


Figure 1 Association of uric acid (mg/dL) with Killip grading

RESULTS AND OBSERVATIONS

The study was conducted in Department of medicine, Tertiary care Hospital. 280 patients brought to hospital with history of chest pain and diagnosed as acute myocardial infarction (both STEMI and NSTEMI) were included in the study. Serum uric acid levels in patients of acute myocardial infarction were estimated and results are as follows. Mean age of the study subjects was 40.2 ± 12.4 years, with median (25th-75th percentile) of 40 (29.75-51) years. Mean values of hemoglobin, TLC and platelet count among the study subjects were 13.43 ± 2.04 g/dL, 8208.3 ± 2250.85 cells/ μ L and 305107.66 ± 89298.1 cells/ μ L respectively, with medians (25th-75th percentile) of 13.25 (11.817-15.042) g/dL, 8230.5 (6317-10117.5). Distribution of hyperuricemia among the cases was as follows: 214 (76.43%) cases did not have hyperuricemia and 66 (23.57%) cases had hyperuricemia cells/ μ L and 311325.5 (229106.75-379583.75) cells/ μ L.

Mean values of uric acid at day 0, day 3 and day 7 among the study subjects were 5.79 ± 1.46 mg/dL, 5.56 ± 1.64 mg/dL and 4.95 ± 1.7 mg/dL, respectively. Medians (25th-75th percentile) were 5.48 (4.72-6.2) mg/dL at day 0, 5.26 (4.2-6.27) mg/dL at day 3 and 4.7 (3.56-5.78) mg/dL at day 7.

Mean value of troponin I among the study subjects was 5.17 ± 3.01 ng/mL, with median (25th-75th percentile) of 5.13 (2.675-7.892) ng/mL.

Mean value of CPK-MB among the study subjects was 103.69 ± 55.5 ng/mL, with median (25th-75th percentile) of 105.04 (58.418-149.038) ng/mL (Table 12, Figure 1). Distribution of Killip grading among the cases was as follows: 74 (26.43%) cases had grade I, 73 (26.07%) cases had grade II, 69 (24.64%) cases had grade IV and 64 (22.86%) cases had grade III (Table 13, Figure 13).

Association Of Killip Grading With Hyperuricemia.

Compared to patients without hyperuricemia, patients with hyperuricemia had comparable distribution of Killip grades: Grade I (27.27% in patients with hyperuricemia vs. 26.17% in patients without hyperuricemia), Grade II (27.27% vs. 25.70%), Grade III (18.18% vs. 24.30%) and Grade IV (27.27% vs. 23.83%) (p value = 0.768) (Table 1, Figure 1).

No significant association was seen in uric acid levels at day 0 (p value = 0.936), day 3 (p value = 0.588) or day 7 (p value = 0.672) with Killip grading. Mean $\pm$ SD of uric acid at day 0, day 3 and day 7 in Grade I was 5.76 ± 1.36 mg/dL, 5.55 ± 1.58 mg/dL and 4.94 ± 1.63 mg/dL; in Grade II was 5.77 ± 1.44 mg/dL, 5.69 ± 1.71 mg/dL and 5.06 ± 1.71 mg/dL; in Grade III was 5.75 ± 1.46 mg/dL, 5.33 ± 1.56 mg/dL and 4.74 ± 1.61 mg/dL and in Grade IV was 5.89 ± 1.59 mg/dL, 5.66 ± 1.72 mg/dL and 5.03 ± 1.69 mg/dL, respectively, with no significant association between them.

Association Of Trend Of Uric Acid At Different Time Intervals With Outcome.

No significant association was seen in uric acid levels at day 0 (p value = 0.212), day 3 (p value = 0.361) or day 7 (p value = 0.332) with outcome. Mean $\pm$ SD of uric acid at day 0, day 3 and day 7 in death group was 6.18 ± 1.8 mg/dL, 5.89 ± 1.84 mg/dL, and 5.3 ± 1.86 mg/dL, respectively and in discharge group was 5.76 ± 1.43 mg/dL, 5.54 ± 1.63 mg/dL and 4.92 ± 1.64 mg/dL, respectively, with no significant association between them (Table 18, Figure 18).

Outcome Distribution-

Distribution of outcomes among the cases was as follows: 260 (92.86%) cases were discharged and 20 (7.14%) cases died (Table 2, Figure 2).

Table 2:- Association Of Killip Grading With Hyperuricemia.

Killip grading	Patients with hyperuricemia (n=66)	Patients without hyperuricemia (n=214)	Total	P value
I	18 (27.27%)	56 (26.17%)	74 (26.43%)	0.768 [†]
II	18 (27.27%)	55 (25.70%)	73 (26.07%)	
III	12 (18.18%)	52 (24.30%)	64 (22.86%)	
IV	18 (27.27%)	51 (23.83%)	69 (24.64%)	
Total	66 (100%)	214 (100%)	280 (100%)	

[†]Chi square test

Compared to patients without hyperuricemia, patients with hyperuricemia had comparable distribution of Killip grades: Grade I (27.27% in patients with hyperuricemia vs. 26.17% in patients without hyperuricemia), Grade II (27.27% vs. 25.70%), Grade III (18.18% vs. 24.30%) and Grade IV (27.27% vs. 23.83%) (p value = 0.768)

Association Of Killip Grading With Hyperuricemia.

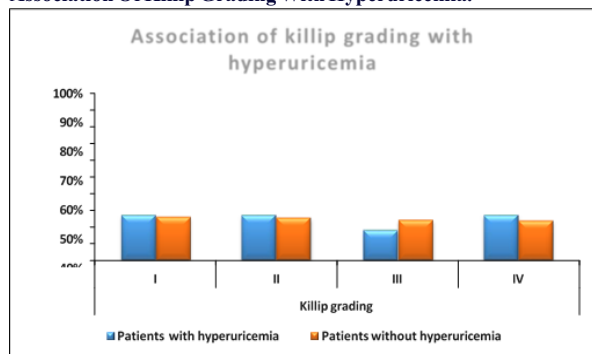


Figure 2 :- Association of trend of uric acid (mg/dL) at different time intervals with Killip grading.

Table 2, Figure 2-Association of trend of uric acid (mg/dL) at different time intervals with Killip grading.

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DISCUSSION

In our study Mean age of the study subjects was 40.2 $\pm$ 12.4 years, with median of 40 years. About 50.71% patients were female and 49.29% patients were male, showing slight female predominance. Mean age of the study subjects was 40.2 $\pm$ 12.4 years, with median of 40 years. About 50.71% patients were female and 49.29% patients were male, showing slight female predominance. 52.14% cases had NSTEMI changes in ECG and 47.86% cases had STEMI changes in ECG. About

23.57% cases had hyperuricemia. Distribution of Killip grading showed that 26.43% cases had grade I, 26.07% cases had grade II, 24.64% cases had grade IV and 22.86% cases had grade III. About 12.12% cases expired in patients with hyperuricemia and 5.61% cases expired in patients without hyperuricemia. No significant association was seen in uric acid levels and Killip Grading. Increased levels of uric acid is associated with increased rate of mortality.

Study done by Kamat A et al.⁵ shows the predominance of male sex affected STEMI which was similar to other studies with regard to male predominance in STEMI. There was significant rise of Uric acid in female patients particularly more than 70 years of age (p=0.031) in contrast to other age groups. Hyperuricemia was defined as a SUA level equal to or greater than 420 μ mol/L (7.0 mg/dL) in males and equal to or greater than 357 μ mol/L (6.0 mg/dL) in females

Uric acid is a general marker of cell death and elevated serum uric acid is linked with obesity, dyslipidemia, hypertension, insulin resistance, male gender, aging, menopause, excessive alcohol intake and diuretic use. Uric acid level reflects xanthine oxidase pathway activity, which has the potential to contribute into the progression of left ventricular dysfunction by interfering with myocardial energetics and myofilament calcium sensitivity as shown in a study done by Aringer Met al.⁴

Elevated serum uric acid is highly predictive of mortality in patients with heart failure or coronary artery disease. as shown in a study done by Castelli P et al.⁶. Evidences suggest that high uric acid is a negative prognostic factor in patients with mild to severe heart failure as demonstrated in a study done by Ochiai ME et al.⁷. 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 as shown in a study done by Hare JM et al.⁸. Our study is in accordance with the study done by Nadkar et al.⁹, 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. Sukhanova S et al.⁵ concluded that there was a meaningful relation between hyperuricemia and MI wherein serum uric acid behaved as an independent variable and had no relationship with other risk factors. Jacobs D et al.¹² in his study found that hyperuricemia correlated strongly as an associated risk factor in MI. He stated that serum uric acid is a variable, subject to modification by a large array of complex and often associated factors and suggested that possible risk factors such as hyperuricemias be assessed and treated as a routine, so as to possibly reduce the incidence of MI. In a similar study done by Fang J et al.¹, hyperuricemias is associated with MI and they suggested hyperuricemia levels are independently and significantly associated with risk of cardiac mortality. Seo Young Kim et al.¹¹⁻¹², in 2009, conducted a meta-analysis to determine the association between hyperuricemias and the risk of Cerebro vascular accidents.

CONCLUSION

Serum uric acid was significantly high in patients with myocardial infarction. Serum uric acid had highly significant positive correlation with CK-MB levels in patients with myocardial infarction. The above results of our study showed that hyperuricemia is associated with myocardial infarction by promoting vascular dysfunction and coronary thrombosis. Serum uric acid levels are higher in patients of acute myocardial infarction as compared to normal healthy persons. Serum uric levels increase in patients with higher Killip class. Combination of Killip class and serum uric acid level after acute myocardial infarction is a good predictor of mortality after acute myocardial infarction.

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