



S. URIC ACID IN PATIENTS OF ACUTE MI: HOW SIGNIFICANT?

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ABSTRACT

Introduction: MI (Myocardial Infarction) remains an important health problem, Various studies have recently found that uric acid may be a risk factor for cardiovascular diseases and a negative prognostic marker for mortality in subjects with pre-existing congestive 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. Many studies including the National Health and Nutrition Examination Survey (NHANES) study concluded that uric acid is an independent risk factor for development of cardiovascular and cerebrovascular diseases.

Objective: To observe uric acid levels in patients with acute myocardial infarction
Methodology: It was a hospital based observational study performed from December 2015 to September 2017 in which 75 patients were enrolled. Patients more than 18 years of age diagnosed to have acute MI who presented to hospital within 24 hours of onset of symptoms were included in the study, while patients with condition known to elevate UA (Uric Acid) levels or patients receiving drugs affecting serum UA levels & Chronic alcoholics patients were excluded. Statistical analysis was done by a software.

Results: Patients of higher age with AMI had higher uric acid level as well as those who had previous history of MI had higher uric acid levels. Patients with AMI who died during hospitalization had higher uric acid levels compare to alive patients.

Conclusion: SUA (Serum Uric Acid) can be used as a marker for increased risk of acute MI. Furthermore, SUA can also be used for risk stratification after acute MI.

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INTRODUCTION

Myocardial infarction (MI) remains an important health problem responsible for considerable morbidity and mortality all over the world. Many risk factors have already been identified but it has also been felt that there might be many unidentified as yet.

The role of serum uric acid (SUA) in the development of cardiovascular disease has been debated for over 50 years.¹ Elevated serum uric acid has been reported to be highly predictive of mortality in patients with heart failure or coronary artery disease.² It has been suggested that hyperuricemia is associated with increase in level of circulating endothelin and the vessel wall; particularly endothelium is a major site for production of uric acid in cardiovascular system. Also, atherosclerotic plaque contains more uric acid than control arteries; thus, it is supposed that UA (Uric Acid) may have a role in atherosclerotic process directly or indirectly. Hyperuricemia has also been suggested to promote thrombus formation through purine metabolism³.

The relation between UA and cardiac disease is observed not only with frank hyperuricemia (defined as more than 6mg/dl in women & more than 7 mg/dl in men) but also with uric acid levels considered to be normal but at high range⁴.

However, studies have shown conflicting results. Many studies including the National Health and Nutrition Examination Survey (NHANES) study⁵ concluded that uric acid is an independent risk factor for development of cardiovascular and cerebrovascular diseases. In contrast the Framingham Heart study⁶ concluded that an association between hyperuricemia and cardiovascular diseases merely reflects the link between serum uric acid and other risk factors, including hypertension, renal disease, elevated lipoprotein levels and the use of diuretics.

Hence, we performed this study to determine whether raised serum UA levels were an independent risk factor for acute MI and to determine its prognostic importance with it if any.

METHODOLOGY

It was a hospital based observational study which was performed from December 2015 to September 2017. The study was approved by the Institutional Ethics committee. Patients more than 18 years of age diagnosed to have acute MI and who

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presented to hospital within 24 hours of onset of symptoms were included in the study. Patients with a condition known to elevate UA levels e.g. chronic kidney disease, gout, haematological malignancy, hypothyroidism, who were chronic alcoholics and patients receiving drugs affecting serum UA levels (diuretics, ethambutol, pyrizinamide, salicylates, losartan, allopurinol, probenecid, atorvastatin, fenofibrate) were excluded.

Acute MI was defined as, 'increased myocardial enzyme concentrations with typical chest pain persisting for more than 30 minutes, or electrocardiographic changes (including ischaemic ST-segment depression, ST-segment elevation or pathologic Q waves). Increased enzyme concentrations were defined as peak creatine phosphokinase level more than two times upper limit of normal⁷. Serum UA was measured with the Uricase Method^{8,9,10}. Uricase converts UA to allantoin and hydrogen peroxide. Hydrogen peroxide further reacts with a phenolic compound and 4 aminoantipyrine by the catalytic action of peroxidase to form a coloured dye complex. Intensity of the colour formed is directly proportional to the amount of UA in the sample.

All the included patients were subjected to routine investigations. Apart from this, serum uric acid levels were also measured on the day of admission and then on days 3 and 7. Data regarding duration of hospital stay and outcome was also collected. The data so collected was analysed with paired T test for any significant difference between serum uric acid levels on days 0, 3 and 7 as well as for possible correlation of serum uric acid level with heart failure and final outcome. Statistical analysis was performed with the help of SPSS 13.0 software on a personal computer.

RESULTS

Total 75 patients were included in the study. 18% patients were in the age group 30-45years, 43% patients were in the age group 45-60 yrs and 39% patients were in age group 60-75yrs. There were 44 male patients and 31 female patients in the study. Of the total 75 cases, 58 cases had ST-elevation myocardial infarction (STEMI) whereas 17 cases had non-ST elevation myocardial infarction (NSTEMI). Out of 58 cases of STEMI 34 cases were of anterior wall MI (AWMI) and 24 cases were of inferior wall MI (IWMI).

We observed that the serum uric acid levels on days 0,3 and 7 were similar and there was no statistically significant difference between the mean serum uric acid levels on days 0, 3 and 7. (Table 1 and 2).

Table 1 Serum uric acid concentration on days 0, 3 and 7:

	Number	Range	MEAN+ SD
UA-DAY 0	75	3.2 - 9.6	5.24 ± 1.53
UA-DAY 3	74	3.0 - 9.0	5.30 ± 1.68
UA -DAY 7	69	3.3 - 9.2	5.05 ± 1.5987

Table 2 Comparison of serum uric acid on day 0,3and 7 with paired T test

	N	P-VALUE
PAIR 1 UA D0 & UA D3	75	0.820
PAIR2 UA D0 & UA D7	74	0.466
PAIR3 UA D3 & UA D7	69	0.363

There was no correlation between serum uric acid level and gender of the patients. However, age of patients on the day of

admission was found to have positive correlation higher age group patients. (p value <0.05).

Table 3 Correlation of serum uric acid levels after acute myocardial infarction with pre existing ischaemic heart disease

History of previous MI	No.	MEAN±SD.	P value
Present	14	5.6 ± 1.68	<0.05
Not present	61	5.14 ± 1.51	

There was a statistically significant correlation between serum uric acid level after acute myocardial infarction and previous history of myocardial infarction. Patients who had myocardial infarction in past had higher serum uric acid level at the time of presentation as compared to patients who didn't have any previous history of myocardial infarction. (Table 3)

Table 4 Relation between serum uric acid and MI outcome.

Outcome	Discharge (n=69)	Death (n=6)	p value
Mean SUA ± SD (in mg/dl)	4.67 ± 1.95	7.1 ± 1.45	0.000
Range (in mg/dl)	3.2-7.8	5.8-9.6	

The mean SUA for discharged patients was 4.67 ± 1.95 /dl and it was 7.1 ± 1.45 mg/dl for the patients who died in the hospital. SUA levels were significantly higher in the patients who succumbed as compared to those who were discharged from the hospital (p = 0.000).

DISCUSSION

Acute MI is a major cause of mortality and morbidity in developed as well as developing countries. The well recognized risk factors like age, male sex, smoking, diabetes, hypertension, metabolic syndrome explain only a part of the cases. Many studies have found conflicting role of uric acid in patients with cardiovascular disease. This study was conducted to study the role of serum uric acid in acute MI and its relation with outcome.

In our study the serum uric acid (SUA) levels showed statistically significant increase with increasing age (p = 0.002). A study done by M Kuzuya *et al*¹¹ also reported that serum UA levels increase with age. The mean SUA levels were same among males and females and there was no statistically significant difference. (5.41 ± 1.77 v/s 5.21 ± 1.59; p = 0.305). M. Y. Nadkar *et al*¹² also reported that SUA levels in patients of MI had no relation with gender. However, in Japanese Acute Coronary Syndrome Study conducted by Kojima S *et al*¹³, males had higher SUA levels as compared to females. Another study by Christoph Bickel *et al*¹⁴ also observed higher SUA among males compared to females which they attributed to lower SUA in younger females. Framingham heart study⁶ also showed higher SUA levels in males. The discrepancy observed can be explained by difference in mean ages of the participants in different studies.

In our study, there were 17 cases with previous history of IHD. It was observed that mean SUA level in cases with previous IHD was significantly higher as compared to those without previous IHD. (p < 0.05). Similar results were observed in the

Japanese Acute Coronary Syndrome Study conducted by Kojima S *et al*¹³ and M. Y. Nadkar *et al*¹².

In our study, the mean SUA for discharged patients was 4.80 ± 1.25 mg/dl while it was 7.94 ± 0.36 mg/dl for the patients who died in the hospital during 7 days of hospital stay. SUA levels were significantly higher in the patients who succumbed as compared to those who were discharged from the hospital ($p = 0.000$). Christoph Bickel *et al*¹⁴ studied 1017 patients with angiographically proven coronary artery disease. After a follow up of 2.2 years they found increased risk for death with increasing UA levels.

Siniša Car and Vladimir Trkulja *et al*¹⁵ also observed that higher SUA on admission was independently associated with higher in-hospital mortality and higher thirty-day mortality and poorer long-term survival after AMI. In another study by Bae MH *et al*¹⁶, during 6-month follow-up, UA was higher in patients with MACE (major adverse cardiac event) than in those without MACE. They reported that UA was an independent predictor of short-term prognosis and has incremental value to NT-ProBNP in patients with AMI. Lazzeri *et al*¹⁷ aimed at assessing the relation between uric acid, measured on Intensive Cardiac Care Unit (ICCU) admission, and mortality at short term follow-up, in 466 consecutive STEMI patients. In-hospital mortality was higher in patients with elevated UA. The data strongly suggested that in the acute phase of STEMI patients submitted to PCI, uric acid holds a prognostic role for in-hospital mortality.

CONCLUSION

Serum uric acid levels are increased in patients of MI from the first day and remains elevated for at least seven days. Higher levels are seen with increasing age and in patients with previous history of IHD. Many studies have reported that patients with higher levels on day of admission had worse outcome. Thus, there is an indication that serum uric acid level may be a risk factor for MI and its level on admission can be used as a marker for increased risk of acute MI.

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