



Serum Uric Acid Levels As an Independent Short Term Prognostic Marker in Acute Myocardial Infarction

Authors

Dr Padmakumar Rajasekhara Pillai¹, Dr Suresh Muthezhathu Kesavadas²

¹Assistant Professor, Government Medical College, Thiruvanthapuram

²Professor, Government Medical College, Thiruvanthapuram

Background of study

Studies have shown that elevated serum uric acid level is highly predictive of mortality and morbidity in patients with coronary heart disease. Uric acid is an indicator for increased oxidative stress. Xanthine oxidase, a critical enzyme in degradation of purines to uric acid has shown to be an important source of superoxide free radical. Activity of xanthine oxidase increases during ischemia, clinically hyperuricemia occurs in hypoxic states. The goal of the study was to assess the prognostic value of serum uric acid in the outcome of acute myocardial infarct, both mortality and morbidity. Xanthine oxidase activity and uric acid synthesis are increased in vivo under ischemia and hence elevated uric acid may act as a marker for ischemia.

Introduction

The association of serum uric acid with cardiovascular disease has been appreciated for nearly half a century.¹ Several prospective studies have shown an association between baseline hyperuricemia and incident coronary heart disease. The LIFE study⁴-showed that Losartan, Atorvastatin, Fenofibrate risk reduction the rapies, are due to serum uric acid reduction. The LIFE⁴

study observed that 29% of the reduction in composite end point of death in myocardial infarction, is seen with the use of losartan and this was attributable to a decrease in the serum uric acid; Implying a link of serum uric acid with both stroke and coronary heart disease.

A 12 year longitudinal study in Sweden by Bengtsson² et al showed that uric acid had positive correlation with 12 year mortality in univariate analysis². The association between serum uric acid concentration and mortality was independent of age, body mass index, systolic blood pressure, adipose tissue distribution, smoking habit, serum cholesterol concentration and serum triglyceride concentration. NHANES³ found a significantly stronger association between time varying serum uric acid and cardiovascular outcome in women than in men. Using data from the NHANES 1³ study increment in uric acid by 60 mmol/l was associated with a 48% increase in risk for incident ischemic heart disease among women. In men uric acid levels gradually increased with age. Gerber et al⁹ also documented increased incidence of cardiovascular mortality among hyperuricemic subjects. Maden et al showed uric acid level predicted mortality in angiographic significant individuals. Study in Tel Aviv Souraski medical

centre by Wasserman et al⁸ showed initial serum uric acid an independent predictor of mortality. Monica Augsburg cohort data from 1044 men showed a strong positive correlation of serum uric acid with all-cause mortality. Michael et al showed a strong positive correlation of uric acid and myocardial infarction in 4385 participants of age >55 years. Korean study by Hong Lim et al on 716 patient who underwent coronary angiography showed a strong association with an increased risk of coronary artery disease and serum uric acid in women, than in man. Bano et al⁶ studied level of uric acid in heart failure according to NYHA functional class; found a strong positive correlation of uric acid and severity of heart failure (class IV-43%, class III 37%, class II- 20%, class I -13% class 0- 7%). Japanese study by Kojima et al⁷ showed serum uric acid level correlate with Killip classification, and high uric acid was associated with poor prognosis in a study of 1024 patients hospitalised within 48 hrs of chest pain. Serum uric acid reflects increased xanthine oxidase activity related to oxidative stress. Serum uric acid level is a suitable marker for predicting adverse event after acute myocardial infarction

Aim

- To estimate serum uric level in patients with myocardial infarction within 48 hrs of chest pain.
- To observe for correlation between serum uric level and immediate post MI complications.
- To observe correlation between Serum uric acid level and severity of cardiac failure using Killips class.
- To observe correlation between Serum uric acid level with in hospital mortality and hospital stay.

Materials and Methods

Patients admitted with Acute ST elevation Myocardial Infarction (STEMI) in Medicine

Department for a period of three months were taken for study

Inclusion Criteria

- ❖ Patient above age of 20 and less than 75
- ❖ Admitted Within 6hr of chest pain
- ❖ Thrombolysed

Exclusion Criteria

Patient with diabetes mellitus, hypertension, metabolic syndrome, renal failure, hepatic disease, chronic alcoholics, smokers, patients on diuretics, chemotherapy, gout, malignancy were excluded.

Study Design

Patients admitted with Acute ST elevation Myocardial Infarction in medicine department. Demographic data was recorded. Histories to exclude factors that cause uric elevation were taken. BMI calculated. Clinical examination for evidence of cardiac failure or acute MR and AR was done at the time of admission. Serum Uric acid levels at the time of admission was estimated using dry chemistry method; echocardiography was done on all subjects to look for systolic and diastolic dysfunction and other mechanical complications. Any incidence of arrhythmias was noted. Duration of ICU stay and in hospital mortality was recorded. Statistical analysis is done using SPSS version 21. Biochemical and physical variables were expressed as MEAN \pm SD. Students t- test and chi square test were used to compare categorical variables. A p value of <0.01 is considered significant.

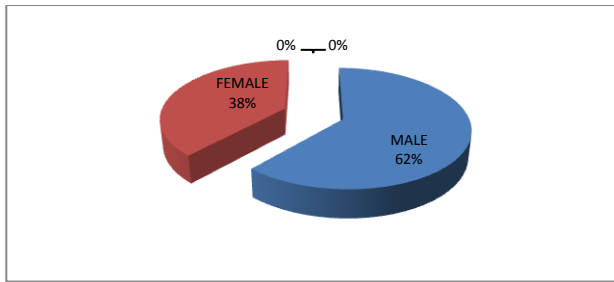
Results

Out of 240 acute myocardial infarction cases, 148 were males and 92 were females. Male predominance was noted.

Table 1: Sex wise distribution of study group

SEX	Number of cases	Percent
MALE	148	62
FEMALE	92	38

Fig 1: Sex wise distribution of study group

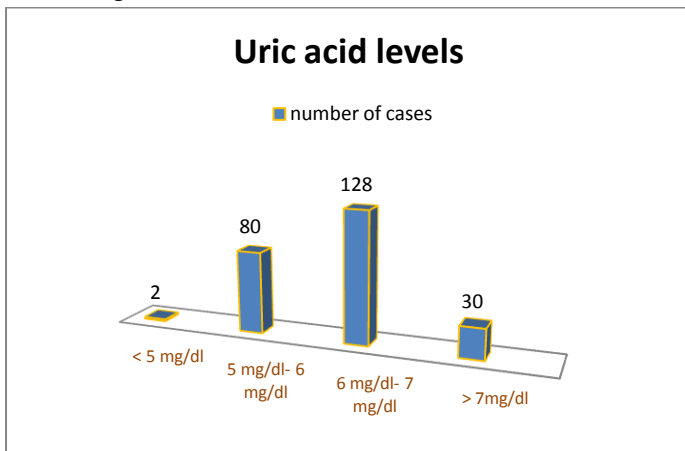


Serum uric acid level of 6mg/dl to 7mg/dl was noted in 53% of patients. Mean \pm SD of Serum uric acid level was calculated as 6.4 ± 0.8 mg/dl.

Table 2: Percentage of distribution of sample according to uric acid levels

Uric acid	No of cases	Percent
<5	2	0.8
5-6	80	33.6
6-7	128	53.3
>7	30	12.5
Mean \pm SD	6.4 ± 0.8	

Fig 2 Percentage of distribution of sample according to uric acid levels

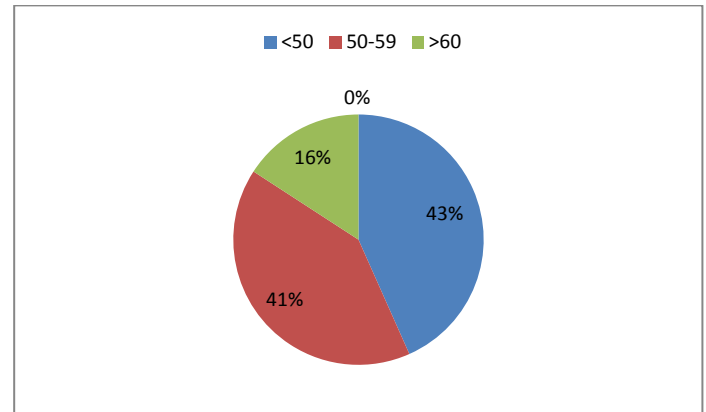


Mean \pm SD of ejection fraction was found as 50.6 ± 7.2 %. 43% of patients had ejection fraction <50.

Table 3: Percentage of sample size according to ejection fraction

Ejection fraction	No of cases	Percentage
<50	104	43.3
50-59	98	40.8
>60	38	15.8
Mean \pm SD	50.6 ± 7.2	

Fig 3 Percentage of sample size according to ejection fraction



Majority of patients at the time of admission were on KILLIPS class I. (75%)

Table 4: Percentage of distribution of the sample according to Killips class

Killip class	Count	Percentage
I	180	75
II	32	13.3
III	16	6.7
IV	12	5

Fig 4 : Percentage of distribution of the sample according to Killips class

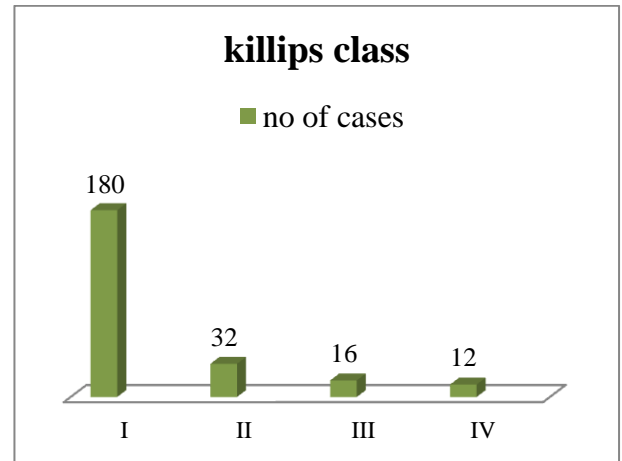


Table 5: Percentage distribution of sample according to outcome

Outcome	Count	Percent
Expired	20	8
Not expired	220	92

Fig 5: Percentage distribution of sample according to outcome

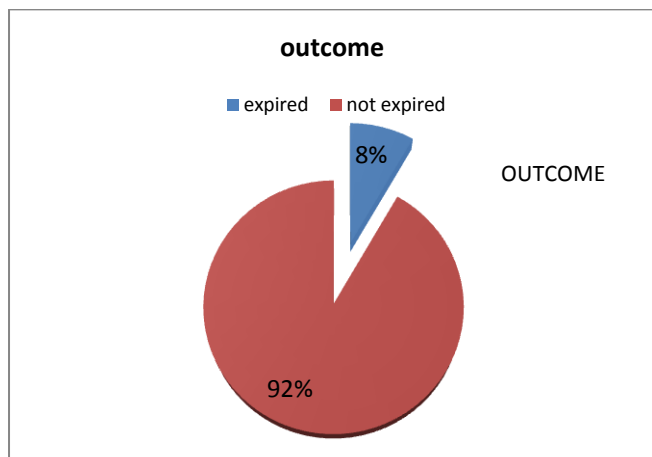


Table 6: Distribution of sample according to mechanical complication

Complication	detected	Not detected
MR	30	210
AR	12	228
TR	10	230
VSD	0	240
Pericardial effusion	13	227

Fig 6: Distribution of sample according to mechanical complication

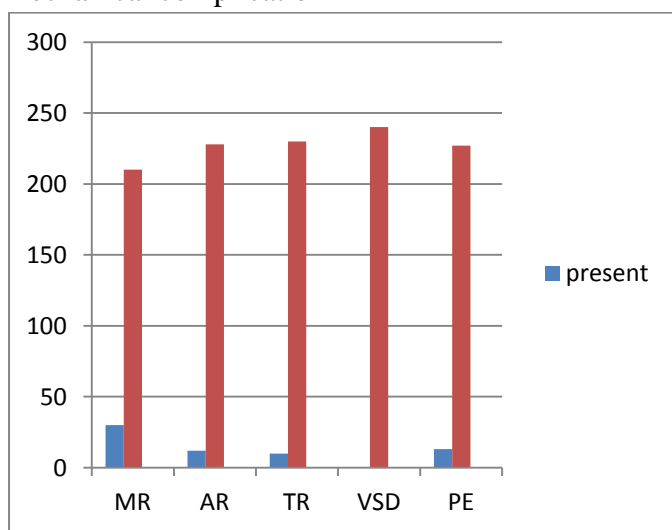


Table 7: Distribution of uric acid according to Killips class

Uric acid	Class I	Class II	Class III	Class IV
5-6	66	16	0	0
6-7	58	40	28	2
>7	0	0	10	20

$\chi^2=93.08$ p=0.001

All patients with Killips class- IV had uric acid level >7 mg/dl. Patients with ejection fraction <50 % had mean uric acid level 6.6±0.6 mg/dl.

Table 8: Comparison of uric acid based on ejection fraction levels.

Ejection fraction	uric acid (Mean±SD)	No of cases
<50	6.6±0.6	104
50-59	6.3±0.22	98
>60	6.3±0.5	38

P=0.039 ,f = 3.33

Table 9: Comparison of uric acid with outcome

Outcome	No of cases	Mean± SD	t
Expired	12	7.5± 0.6	4.77
Not expired	228	6.4± 0.6	
<7hospital stay	58	6.4±0.7	0.11
>7hospital stay	182	6.4±0.6	
ICU stay <24hr	174	6.3±0.5	4.66
ICU stay>24hr	66	6.8±0.7	

ICU stay, hospital stay and mortality here high for patients with elevated serum uric acid levels with a p value< 0.001.

Table 10: Comparison of uric acid with Mechanical Complication

Complication	No of cases	Mean± SD	t
MR	30	6.9±0.8	4.39
AR	13	7 ± 1	2.88
TR	10	7.1±0.8	3.99
PERICARDIAL EFFUSION	13	6.4±0.08	1.77

Mechanical complication were more in higher uric acid level, p <.001.relation of uric acid with pericardial effusion was statistically insignificant.

Discussion

Study was conducted in 240 thrombolysed patients with ST ELEVATION acute myocardial infarction, admitted within 48 hours of chest pain. Of these 148 were males(61.7%)and 92 were females(38.3%).Uric acid was treated as a continuous variable and categorical variable. 12.5% had a uric acid level greater than 7mg/dl.In our study 53.3%had a value between 6.1-7mg/dl. Mean uric acid level was 6.4±0.6mg/dl. There was no significant difference in uric acidin males and females, contradictory to finding of Larson et al¹⁰. Patients who expired had a significantly high uric acid 7.5±0.6mg/dl. Serum uric acid level correlated with severity of cardiac failure and Killips class similar to study by Kojima Set al⁷.All patients with Killips class-IV had uric acid level more than 7mg/dl, similar to study by Sinisa Car

et al¹¹. Serum uric acid level was inversely related to ejection fraction, mechanical complication and hospital stay. All patients who died had a uric acid level more than 6.9 mg/dl with a mean value 7.48mg/dl, serum uric acid make a significant contribution to serum anti-oxidant capacity leading to vascular injury. Treatment with allopurinol in cardiac failure might restore the endothelial function, due to anti- oxidant capacity. Study of direct effect of uric acid on vascular function was hampered by poor solubility. Newer direct study on action of uric acid on endothelial function, platelet aggregation, vessel wall elasticity and autonomic regulation of cardiovascular system required.

Ethical Issues

No ethical issues or financial grants involved in this study.

Bibliography

1. Gertler M M, Garn S.M et al. Serum uric acid in relation to age and physique in health and coronary heart disease. *Ann Intern Med.* 1951; 34;1421-31.
2. Bengtsson C, Lapidus L et al. Hyperuricemia and risk of cardiovascular disease and overall death 12 yr follow up of participant in the population study of women in Gothenburg Sweden. *Acta Med Scand.* 1988;224;549-55.
3. Bang J, Alderman et al. serum uric acid and cardiovascular mortality the NHANES 1 epidemiologic follow up study 1971-92. *JAMA* 2000;283; 2404-10.
4. Ha Ieggen et al. the impact of serum uric acid in cardiovascular mortality -Life study. *Kidney International.* 2004 65;1041-9.
5. Alderman M, Aiyer KJ et al. cardiovascular disease and effect of losartan. *Current Med Res Opin* 2004 ;20 ;369-79 .
6. Levya F , Patel et al. Serum uric acid as an index of impaired oxidative metabolism in

chronic cardiac failure. *Arch Med Sci.* 2008 4(3);219-225.

7. Kojima S Sakamoto et al. Prognostic usefulness of serum uric acid in myocardial infarction. *Am J Cardioi* 2005 ;96;489-90
8. Wasserman A, Shnell M et al. prognostic significance of serum uric acid in patients admitted to department of medicine. *Am J Med Sci.* 2010;Jan339(1) 15-21
9. Gerber Yariv, Tanne et al .serum uric acid and long term mortality from stroke and cardiovascular disease *European journ of cardiovascular prevention and rehabilitation* 2006 volume 13 issue 2 193-98.
10. Larson et al. serum uric acid and risk of cardiovascular disease and death, The Framingham heart study.
11. SinisaCar et al. Higher uric acid on admission associated with short term mortality after MI. *Current Med Jour* .2009,56,559-66.