

Research Article

A study on prognostic significance of serum uric acid in acute myocardial infarction in a tertiary care institute

Kaushik Biswas¹, Subrata Halder^{2*}, Ramita Sarkar², Koushik Roy⁴

¹Consultant Endocrinologist, Department of Endocrinology, The Mission Hospital, Durgapur, West Bengal, India

²Assistant Professor, Department of Medicine, IPGME&R, Kolkata, West Bengal, India

³Senior Resident, Department of Medicine, Mathabhanga S.D Hospital, Cooch Behar, West Bengal, India

⁴Department of Medicine, Mathabhanga S.D Hospital, Cooch Behar, West Bengal, India

Received: 11 August 2016

Accepted: 07 September 2016

*Correspondence:

Dr. Subrata Halder,

E-mail: docsubrata09@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: This study was done to find out any relationship between serum uric acid and AMI severity and its short-term outcome. To see the correlation between serum uric acid level with Killip Class and mortality outcome following AMI.

Methods: 100 patients of AMI were included in this study based on the inclusion and exclusion criteria. Detailed history, physical examination and relevant systemic examination including detailed examination of CVS system were done as per a structured proforma and necessary laboratory investigations were done.

Results: 100 cases of myocardial infarction were studied, out of which 90 patients had STEMI and 10 patients had NSTEMI. There is significant difference of D0 uric acid level was observed for previous history of AMI. There is significant difference in mean uric acid level between dyslipidemic and non-dyslipidemic population. There is significant difference in mean uric acid level on D0 between diabetic and non-diabetic population. Serum uric acid level is low among patients with lower Killip class and high among higher Killip class. Lower the uric acid level, higher the percentage of survival and higher the uric acid level, higher the percentage of mortality.

Conclusions: Patients of Killip class III and IV had higher levels of uric acid as compared to patients of class I and II. Combination of Killip class and serum uric acid level after acute myocardial infarction is a good predictor of severity of heart failure after AMI.

Keywords: AMI, Killip class, Uric acid, STEMI, NSTEMI, Dyslipidemia, Diabetes

INTRODUCTION

Acute myocardial infarction has already established itself as a major threat to health both in developed and developing countries.¹ With the emergence of this epidemic, there is increased need of effective health care strategy as well as research in this field.

Assessment of severity of heart failure following acute myocardial infarction has been evaluated and categorized by several invasive and non-invasive techniques ranging from measurement of pulmonary capillary wedge pressure to estimation of several cardiac enzymes, most

of which are not feasible and not cost effective in our country.

Following myocardial infarction (MI) some proteins and enzymes labeled as cardiac markers (e.g. Creatinine Phosphokinase, Troponin T & I) are released in to the blood in large quantities from necrotic heart muscle. These markers and myoglobin have specific temporal profile in relation to AMI; however, they do not correlate with myocardial function. Previous studies have reported that a high concentration of uric acid (UA) is a strong marker of an unfavorable prognosis of moderate to severe heart failure and cardiovascular disease.^{2,3} Serum Uric

Acid has been indicated as a risk factor for CAD and as an independent prognostic factor of poorer outcomes in patients with documented CAD.⁴ With ischemia, ATP is degraded to adenine and xanthine, and there is also increased generation of xanthine oxidase.

The increased availability of substrate (xanthine) and enzyme (xanthine oxidase) results in increased uric acid generation as well as oxidant formation. The finding that ischemia results in an increase in uric acid levels may account for why uric acid is increased in congestive heart failure.³ There is evidence that high uric acid is a negative prognostic factor in patients with heart failure, although the development of hyperuricaemia is almost always associated with worsening of renal function in these patients.^{2,5}

Therefore, it is difficult to dissect the roles played by reduced renal function and high uric acid in affecting prognosis of these patients. Some studies 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.⁶ Few recent epidemiological studies have shown that higher serum uric acid determined on admission is associated with either higher in-hospital mortality and thirty-day mortality or poorer long-term survival after AMI.⁷

According to a recent study done in Japan (Japanese Acute Coronary Syndrome Study, there was a close correlation between serum uric acid concentration and Killip classification in patients of acute myocardial infarction. Patients who developed short-term adverse events had high uric acid concentrations.^{7,8} Serum uric acid levels, Killip class, age, and peak creatine phosphokinase level were significant predictors of long-term mortality.⁷ Thus, along with its new recognition as an active molecule likely to be involved directly in the pathogenesis of coronary artery disease, serum uric acid is also increasingly being identified as a prognostic marker of heart failure.

We carried out this study to note levels of serum uric acid in the context of acute myocardial infarction, to correlate serum uric acid levels with Killip class and to note any relationship between serum uric acid level and mortality following acute myocardial infarction.

METHODS

100 patients of acute myocardial infarction admitted in Cardiology Department who fulfilling inclusion and exclusion criteria are included to my study. This study was undertaken over a period of one year. Valid consent was taken from all the patients who were included this study. Proper history from all patients was taken and relevant examinations of all systems especially cardiovascular system were done. According the patients profile relevant investigations (Like uric acid, blood

sugar, HBA1C, lipid profile, serum creatinine, ECG, echocardiography etc.) were done. All data were then analyzed statistically.

Inclusion criteria

Patients of more than 18 years of age who were diagnosed as cases of acute myocardial infarction on the basis of history, examination, electrocardiographic changes, biochemical markers.

Exclusion criteria of sample

Patients with

- Chronic Kidney disease
- Gout
- Hematological malignancy
- Hypothyroidism
- History of medications which increase the serum level of uric acid [e.g. salicylates (>2gm/ day) diuretics, ethambutol, pyrazinamide etc.
- Chronic alcoholism

RESULTS

In our study total N=100 cases of myocardial infarction were studied, out of which, 5 patients (5%) were <40 years, 58 patients (58%) were within 41-60 years and 37 patients (37%) were >60 years of age and 69 (69%) cases were male and 31 cases (31%) were female.

Table 1: Serum uric acid on day 0, 3 and 7.

Uric acid	Mean	Standard deviation
Day 0	5.25	1.41
Day 3	5.02	1.65
Day 7	4.51	1.65

100 cases of myocardial infarction were studied, out of which 90 patients (90%) had STEMI and 10 patients (10%) had NSTEMI. 100 cases of myocardial infarction were studied, out of which 90 patients (90%) had no family history of CHD and 10 patients (10%) had positive family history of CHD. All cases of myocardial infarction were studied, out of which 73 patients (73%) had no history of previous myocardial infarction (MI) and 27 patients had positive previous history of myocardial infarction.

100 cases of myocardial infarction were studied, out of which 65 patients (65%) were hypertensive and 35 patients (35%) were non hypertensive and 35 patients (35%) were diabetic and 65 patients (65%) were non diabetic. In present study 100 cases of myocardial infarction were studied, out of which 51 patients has increased Triglyceride (Tg) level; 41 patients had increased Total cholesterol (TC) level; 52 patients had increased LDL level and 52 patients had decreased HDL.

We measured serum uric acid on Day 0, Day 3 and Day 7. The mean and standard deviation is shown in the table 1. There is Significant difference (P=0.01) of D0 uric

acid level was observed for previous history of Myocardial Infarction (Mean 5.82 vs 5.04).

Table 2: Killip class and uric acid on day 0, 3 and 7.

Killip Class and Uric Acid (UA) on Day 0 (D0)						
		UA D0 (mg/dl)				Total
		≤4	4.1-5.5	5.6-7	>7	
Killip Class :D0	I	27	15	3	1	46
	II	7	9	5	0	21
	III	1	1	8	6	16
	IV	0	1	6	10	17
Total		35	26	22	17	100
Killip Class and Uric Acid (UA) on Day 3						
		UA (mg/dl)				Total
		≤4	4.1-5.5	5.6-7	>7	
Killip Class D3	I	40	17	3	0	60
	II	2	4	1	1	8
	III	0	1	2	1	4
	IV	0	1	4	19	24
Total		42	23	10	21	96
Killip Class and Uric Acid (UA) on Day 7						
		UA (mg/dl)				Total
		≤4	4.1-5.5	5.6-7	>7	
Killip Class :D7	I	66	0	0	0	66
	II	0	1	2	0	3
	III	0	0	3	2	5
	IV	0	0	1	13	14
Total		66	1	6	15	88

There is significant difference (P=0.028) in mean Uric acid level between dyslipidemic and non-dyslipidemic population (Mean 5.49 vs 4.8). There is significant difference (P=0.00) in mean Uric acid level on D0

between diabetic and non-diabetic population (Mean 6.57 vs 4.54) There is no significant difference (P=0.53) of mean serum Uric acid level on D0 between the hypertensive and non-hypertensive population (Mean 5.18 vs 5.37).

Table 3: Distribution of study population according to D0 uric acid level and living status (alive/dead) on D7.

		Alive/dead on d7		Total
		Alive	Dead	
UA D0 (mg/dl)	Less than or equal to 4mg/dl	30 (85.71%)	5 (14.2%)	35
	4-5.5	26 (100%)	0 (0%)	26
	5.6-7.0	20 (90%)	2 (9%)	22
	>7.0	12 (70.5%)	5 (29.4%)	17
Total		88	12	100

There is significant difference (P=0.00) of mean serum Uric acid level on D0 between the population of increased and normal serum creatinine (6.9909 vs 4.7606). There is significant difference (P=0.004) of

mean serum Uric acid level on D0 between the population of increased and normal serum Triglyceride (5.6418 vs 4.8449). There is significant difference (P=0.02) of mean serum Uric acid level on D0 between

the population of increased and normal serum Total cholesterol (Mean 5.6629 vs 4.9653).

There is no significant ($P=0.16$) difference of mean serum Uric acid level on D0 between the population with decreased and normal serum HDL cholesterol (Mean 5.4400 vs 5.0469). There is significant ($P=0.01$) difference of mean serum Uric acid level on D0 between the population of increased and normal serum LDL (Mean 5.5596 vs 4.8744).

Killip class and Uric Acid (UA) on Day 0 (Table 2): Most of the patient who belong to Killip Class I was in the lower quartiles of uric acid level. 58.69% of that class have serum uric acid ≤ 4 mg/. On the contrary, 58.82% of patients who belong to Killip Class IV have serum uric acid >7 mg/dl. So we can say that serum uric acid level is low among patients with lower Killip class and high among higher Killip class. Thus, serum uric acid level can predict the severity of heart failure and the prognosis in essence. The p value is significant (<0.05)

Killip class and Uric Acid (UA) on Day 3 (Table 2): Most of the patient who belong to Killip Class I were in the lower quartiles of uric acid level. 66.66% of that class have serum uric acid ≤ 4 mg/. On the contrary, 79.16% of patients who belong to Killip Class IV have serum uric acid >7 mg/dl. So we can say that serum uric acid level is low among patients with lower Killip class and high among higher Killip class. Thus, serum uric acid level can predict the severity of heart failure and the prognosis in essence. The p value is significant (<0.05).

Killip class and Uric Acid (UA) on Day 7 (TABLE 2): Most of the patient who belong to Killip Class I were in the lower quartiles of uric acid level. 100% of that class have serum uric acid ≤ 4 mg/. On the contrary, 92.85% of patients who belong to Killip Class IV have serum uric acid >7 mg/dl.

So we can say that serum uric acid level is low among patients with lower Killip class and high among higher Killip class. Thus, serum uric acid level can predict the severity of heart failure and the prognosis in essence. The p value is significant (<0.05). Distribution of study population according to D0 uric acid level and living status (alive/dead) on D7 (Table 3): High level of D0 uric acid was significantly associated with mortality on 7 day follow up. Lower the uric acid level, higher the percentage of survival and higher the uric acid level, higher the percentage of mortality.

DISCUSSION

Present study was conducted in 100 patients of acute myocardial infarction, who presented to hospital within 24 hrs of onset of symptoms. Out of 100 patients, 90 had ST-elevation myocardial infarction (STEMI), while 10 patients had non-ST elevation myocardial infarction (NSTEMI).

In present study the mean age of presentation was (60.66 ± 10.63) years which corroborates with worldwide data (58.1 ± 12.2) but does not with the Indian perspective where mean age of AMI is (53 ± 11.4).⁹ The percentage of cases <40 years of age in the worldwide basis is 6% (9). This value, almost similarly has been represented in our study. However the number of cases presenting below the age of 40 years are quite higher in South Asia (8.9%) and in India (11.7%).⁹

Study finding is also quite similar with the study result of Danga et al who showed that AMI occurrence was mostly prevalent among older age group and the mean age of the old age AMI was 62 years.¹⁰ The mean age of male and female patients were (59.59 ± 9.74), (63.03 ± 12.22) respectively. The mean age of female in our study, corroborates with worldwide data but both the mean age of male or female do not corroborate with data on Indian perspective where mean age for both male and female are quite lower than our findings.⁹

In present study, we found 47% patient as active smoker and all of them were male. Our study result was consistent with that of Esteghamati et al.¹¹ However other study results had shown more frequency of smoking as a risk factor for CHD or AMI.⁹ It has also been noted that it is difficult to identify any condition that is as prevalent, lethal and yet so prone to neglect as tobacco addiction.

In present study population, hypertension appeared to be the most prevalent risk factors second only to age. Sixty five percent (65%) of our patients were hypertensive. The finding is quite corroborative with Nadkar et al.¹² Many study had found hypertension as an important risk factor for AMI but the prevalence of hypertension among the patients of these study group were lower than us.¹³⁻¹⁵

In present study, we found 35 cases of diabetes. Present finding is quite corroborative with the results of study by Jafari et al and Khot et al and others.¹³⁻¹⁵ Inter heart study has shown that the prevalence of diabetes as a risk factor in AMI in South Asia is 20.2% and the combined data of this study expressed the prevalence of diabetes as 7.52% in the control group. We found dyslipidemia in 63 patients (63%) in our study population. Our finding corroborates with the study result of Sharma et al However Jafari et al found 18.2% cases of hyperlipidemia in their study.^{13,14}

In our study, the mean uric acid levels were (5.16 ± 1.34) and (5.45 ± 1.58) in male and female patients respectively ($p=0.35$). So, there is no significant difference in male and female patients. This finding does not correlate with the referral study in which males had higher uric acid levels as compared to females; however present finding is consistent with that of Nadkar et al.^{7,12} There was no significant correlation ($p=0.53$) between serum uric acid level and patients who were known or found to be hypertensive on admission. This is different than other studies which showed that hypertensive patients had

more hyperuricaemia.⁷ On the contrary, our finding was consistent with that of Nadkar et al.¹²

There was significant difference in mean serum uric acid levels between diabetic and non-diabetic patients [$p=0.00$]. This finding is consistent with study by Safi et al which showed that hyperuricaemia is significantly associated with type 2 diabetes mellitus.¹⁶ However, this finding is in contrast to other study by Nadkar et al where no significant association between serum uric acid and diabetes mellitus were found.¹²

There was significant difference between serum uric acid concentration at the time of admission and h/o ischemic heart disease ($p=0.01$). Serum uric acid levels were higher in patients with past history of IHD as seen in previous study. This finding is consistent with that of Nadkar et al.¹² In present study we have found significant difference in mean uric acid level between dyslipidemic and patients with normal lipid profile ($p=0.028$) which is consistent with the finding of Young-quan et al.¹⁷

In our study population, there was significant difference in mean uric acid level between the patients of increased triglyceride concentration and normal triglyceride concentration ($p=0.004$). Present results is corroborative with study result of Cohen et al who found that serum uric acid level was strongly associated with serum triglyceride.¹⁸ We have found significant difference of mean uric acid level on day 0 between the patients with increased cholesterol and patient with normal cholesterol level ($p=0.02$) which is corroborated by the study result of Yong-quan et al.¹⁷

Patients who were known case of IHD were in higher Killip class as seen in study by Kojima et al.¹¹ There was statistically significant association ($p<0.05$) between serum creatinine on day of admission and Killip class, in our study. Kojima et al have shown that there is graded relation between serum uric acid concentration and creatinine concentration in patients of acute myocardial infarction.⁷ There was statistically significant correlation found between serum uric acid level and Killip class ($p<0.05$) on day 0,3 and day 7.

Patients of Killip class III and IV had higher levels of uric acid as compared to patients of class I and II. From the correlation tabulations it is evident that most of the patient who belong to Killip Class I were in the lower quartile of uric acid level and most of the patients who belong to Killip class IV were in the highest quartile of uric acid level. So we can say that serum uric acid level is low among patients with lower Killip class and high among higher Killip class. Thus, serum uric acid level can predict the severity of heart failure and the prognosis in essence. This finding is consistent with referral study and that of Nadkar et al.^{7,12}

Out of 100 patients, twelve expired during 7 day follow up. Out of these twelve patients ten had serum uric acid

level in quartile 4 on day 0. Only two patients who was in Killip class I and had uric acid in 1st quartile; however their uric acid raised to quartile 4 with shift of Killip class to class IV on day 3.

On day 3 all ten patients were in Killip class IV and had uric acid level in 4th quartile. Thus, all twelve patients who expired were in Killip class IV and had uric acid level in 4th quartile. Therefore it shows that serum uric acid concentration is significantly correlated with Killip class. High level of Day 0 uric acid level was significantly associated with mortality on 7 day follow up. Lower the uric acid level, higher the percentage of survival and higher the uric acid level, higher the percentage of mortality.

CONCLUSION

There was significant difference in mean serum uric acid levels on Day 0, between diabetic and non-diabetic patients. There was significant difference between serum uric acid concentration at the time of admission and h/o ischemic heart disease. Serum uric acid levels and Killip class are influenced significantly by previous myocardial infarction. Patients who had history of previous IHD were on higher Killip class.

In present study we have found significant difference in mean uric acid level on day 0, between dyslipidemic and patients with normal lipid profile. There was significant difference in mean uric acid level on day 0 between patients of normal and increased creatinine level. Patients of Killip class III and IV had higher levels of uric acid as compared to patients of class I and II.

Out of 100 patients, twelve expired during the 7 day follow up. All the patients who died had serum uric acid level in the 4th quartile that is more than 7.0 mg/dL. Combination of Killip class and serum uric acid level after acute myocardial infarction is a good predictor of severity of heart failure after AMI.

ACKNOWLEDGEMENTS

Authors would deeply indebted to his esteemed teacher Dr. Sobhan Biswas, Professor, Department of Medicine, Medical College, Kolkata, Dr Santanu Guha, Professor, Department of Cardiology, Medical College, Kolkata and Dr. Utpal Chaudhuri for their active involvement at all times.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Yusuf S1, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable

- risk factors associated with myocardial infarction in 52 countries (the interheart study): Case-control study. *Lancet.* 2004;364(9438):937-52.
2. Anker SD, Doehner W, Rauchhaus M, Sharma R, Francis D, Knosalla C, et al. Uric acid and survival in chronic heart failure: validation and application in metabolic, functional, and hemodynamic staging. *Circulation.* 2003;107:1991-97.
 3. Leyva F, Anker S, Swan JW, Godsland IF, Wingrove CS, Chua TP, et al. Serum uric acid as an index of impaired oxidative metabolism in chronic heart failure. *Eur Heart J.* 1997;18:858-65.
 4. Allison TG. Coronary heart disease epidemiology. In: Murphy JG, Lloyd MA, editors. *Mayo clinic cardiology.* 3rd edition. Rochester (MN): Mayo Clinic Scientific Press. 2007;687-93.
 5. Ochiai ME, Barretto AC, Oliveira MT Jr, Munhoz RT, Morgado PC, Ramires JA. Uric acid renal excretion and renal insufficiency in decompensated severe heart failure. *Eur J Heart Fail.* 2005;7:468-74.
 6. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med.* 2005;21:1685-95.
 7. Kojima S, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Yamagishi M, et al. Prognostic usefulness of serum uric acid after acute myocardial infarction (Japanese Acute Coronary Syndrome Study). *Am J Cardiol.* 2005;96:489-95.
 8. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol.* 1967;20:457-64.
 9. Joshi P, Islam S, et al Risk Factors for Early Myocardial Infarction in South Asians Compared With Individuals in Other Countries. *JAMA.* 2007;297(3):286-94.
 10. Dang A, Dias A. Differences in risk factors and mortality in young and old AMI in Goa. *Journal of Clinical and Diagnostic Research.* 2008;2:715-9.
 11. Esteghamati A, Abbasi M, Nakhjavani M, Yousefzadeh A, Basa AP, Afshar H. Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. *Cardiovascular Diabetology.* 2006;5:15.
 12. Nadkar MY, Jain VI. Serum Uric Acid in Acute Myocardial Infarction. *JAPI.* 2008;56:759-62.
 13. Sharma LCJ, Kumar BMS. Clinical and angiographic profile of aircrew with coronary heart disease undergoing cardiac evaluation before being reflighted. *IJASM.* 2002;46(2):32-8.
 14. Jafary MH, Abdus Samad, Ishaq M, Awaid SA, Ahmad M, Vohra EA, et al. Profile of AMI in Pakistan. *Pak J Med Sci.* 2007;23(4):485-9.
 15. Khot UN, Monica B. Khot et al. Prevalence of Conventional Risk Factors in Patients With Coronary Heart Disease. *JAMA.* 2003;290(7):898-904.
 16. Safi AJ, Mahmood R, Khan MA. Association of serum Uric Acid with type II diabetes mellitus. *J Postgrad Med Inst.* 2004;18:59-63.
 17. Wu YQ, Li J, Xu YX, Wang YL, Luo YY, Hu DY, et al. Predictive value of serum uric acid on cardiovascular disease and all-cause mortality in urban Chinese patients. *Chinese Med J.* 2010;123(11):1387-91.
 18. Conen D, Wietlisbach V, Bovet P, Shamlaye C, Riesen W, Paccaud F, et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. *BMC Public Health.* 2004;4:9.

Cite this article as: Biswas K, Halder S, Sarkar R, Roy K. A study on prognostic significance of serum uric acid in acute myocardial infarction in a tertiary care institute. *Int J Res Med Sci* 2016;4:4557-62.