# SERUM URIC ACID ITS CORRELATION WITH OUTCOMES OF MYOCARDIAL INFARCTION

*Sahul Hameed Peer Mohamed[1], Gopal Bagialakshmi[2], Nagarajan Ragavan[3], Chandrasekaran Praveen Kumar[4], Santhana Krishnan Ramesh Kumar[5]*

*[1]Assistant Professor, Department of General Medicine, Madurai Medical College, Madurai.*
*[2]Professor, Department of General Medicine, Madurai Medical College, Madurai.*
*[3]Assistant Professor, Department of General Medicine, Madurai Medical College, Madurai.*
*[4]Junior Resident, Department of General Medicine, Madurai Medical College, Madurai.*
*[5]Scientist D. (Medical), National Institute for Research in Tuberculosis (ICMR).*

**ABSTRACT**

**BACKGROUND**

The role of serum uric acid in cardiovascular and renal diseases has been intensively investigated. High serum uric acid has been indicated as a risk factor for CAD and as an independent prognostic factor of poorer outcomes in patients with verified CAD.

**MATERIALS AND METHODS**

Study was done in one hundred patients with myocardial infarction admitted at Government Rajaji Hospital, Madurai. Detailed history and clinical examination done. Uric acid was estimated. The relationship of uric acid with severity of myocardial infarction, treatment response, ejection fraction, arrhythmia and hypotension were studied.

**RESULTS**

A total of 100 patients was recruited to the study. The mean age and mean uric acid level of the study sample was 56 years and 5.9 mg/dL, respectively. There were 65 (65%) males and 35 (35%) females. Males had higher uric acid level than females ($p<0.05$). Those who had SUA >7 mg/dL (n=17) had low ejection fraction, which was statistically significant p value, 0.03. Among the 15 patients belonging to KILLIP IV, 12 had SUA values more than 7 mg/dL ($p<0.05$).

**CONCLUSION**

Measuring serum uric acid level at admission for acute myocardial infarction patients we can stratify them and can treat effectively.

**KEYWORDS**

Serum Uric Acid, Myocardial Infarction.

**HOW TO CITE THIS ARTICLE:** Mohamed SHP, Bagialakshmi G, Ragavan N, et al. Serum uric acid its correlation with outcomes of myocardial infarction. J. Evid. Based Med. Healthc. 2017; 4(8), 427-431. DOI: 10.18410/jebmh/2017/82

## BACKGROUND

In humans, uric acid is the end product of purine catabolism. Its serum levels, governed by the production (liver) and elimination (mainly the kidney) rates are influenced by genetically determined factors, racial and demographic characteristics (e.g., sex, gonadal function in women, obesity), diet (e.g., purine-rich foods, fructose, alcohol), habits, morbidity (e.g., heart or renal failure, malignancies), and medications (e.g., diuretics, cytotoxic agents). The role of serum uric acid in cardiovascular and renal diseases has been studied[1-5] and elevated serum uric acid is highly predictive of mortality in patients with heart failure or coronary artery disease and of cardiovascular events in patients.[1]

On the molecular and cellular level, uric acid exerts a number of effects of potential interest. It is one of the most important antioxidants in plasma, but at high concentrations it may promote oxidative stress. It may induce endothelial dysfunction and vascular smooth muscle cell proliferation in vitro, platelet aggregation, and microinflammation. Uric acid being a potent antioxidant, its level rises shortly after vessel occlusion as it is locally produced by degradation of adenosine, which is a vasodilator. But, when this reaches a higher level, it becomes insoluble and pro-oxidant, aggravating free radical mediated tissue damage and injury.[6-9]

Clinical and epidemiological studies have linked increased serum uric acid to occurrence and outcomes of diabetes mellitus, metabolic syndrome and chronic renal failure.[10-13] It has also been suggested as a risk factor for occurrence and a predictor of poorer outcomes in acute stroke and a risk factor for occurrence/outcomes in various aspects of cardiovascular morbidity. Acute myocardial infarction is the most dramatic manifestation of the coronary

*Financial or Other, Competing Interest: None.*
*Submission 01-12-2016, Peer Review 15-12-2016,*
*Acceptance 13-01-2017, Published 25-01-2017.*
*Corresponding Author:*
*Dr. Sahul Hameed Peer Mohamed,*
*Habiba Speciality Hospital,*
*Vivekanandar Main Road,*
*Thasildar Nagar, Madurai-625020.*
*E-mail: peermdsh@gmail.com*
*DOI: 10.18410/jebmh/2017/82*

artery disease. Adenosine synthesised locally by vascular smooth muscle in cardiac tissue is rapidly degraded by the endothelium to uric acid, which undergoes rapid efflux to the vascular lumen due to low intracellular pH and negative membrane potential. Xanthine oxidase activity and uric acid synthesis are increased in vivo under ischaemic conditions. Therefore, elevated serum uric acid may act as a marker of underlying tissue ischaemia. Although, the mechanisms by which uric acid may play a pathogenic role in cardiovascular disease is unclear, hyperuricaemia is associated with deleterious effects on endothelial function, oxidative metabolism, platelet adhesiveness and aggregation. Therefore, it is evident that high uric acid is a negative prognostic factor in patients with mild-to-severe heart failure.

Some evidence 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. High serum uric acid has been indicated as a risk factor for CAD and as an independent prognostic factor of poorer outcomes in patients with verified CAD.

Retrospective analysis from Japan[14] observed a univariate association between higher serum uric acid on admission (within 48 hours since the symptom onset) and higher thirty-day mortality in MI patients. Thus, high serum uric acid at time of admission is a negative prognostic marker and helps in risk stratification of patients, high short-term mortality and poor long-term mortality and those patients also have increased risk of complications following PCI.

We proposed to assess the level of serum uric acid in patients with acute myocardial infarction and to assess whether there was any correlation between serum uric acid level with outcomes of MI such as heart failure, short-term mortality, arrhythmias and ejection fraction.

## MATERIALS AND METHODS

The study objective was to assess the level of serum uric acid in patients with acute myocardial infarction and to assess any correlation between serum uric acid level with outcomes of MI such as heart failure, short-term mortality, arrhythmias and ejection fraction. We hypothesised that elevated serum uric acid at the time of admission in MI patients is a negative prognostic marker with poor outcomes and MACE.

Study Design- Prospective, descriptive analytical study.

Study Setting- The study was conducted at Government Rajaji Hospital from January 2015 to August 2015.

### Study Population

Included, patients admitted at Government Rajaji Hospital, Madurai, with history and features of myocardial infarction.

### Inclusion Criteria

Patients with age more than 18 years from both sex, ST elevation in ECG or non-ST elevation MI with history, examination, ECG changes and elevated CK-MB.

### Exclusion Criteria

Patients with previous MI, chronic kidney disease, patients with history or clinical features of gout, patients with haematological malignancy, patients with drug history of taking thiazides or ATT and patients with history of CVA.

Sample Size- About 100 patients in the said period was recruited.

### Study Protocol

A previously designed proforma was used to collect the demographic and clinical details of the patients. A thorough clinical examination was done. An ECG in all six leads was recorded in each case as soon as possible (within 15 minutes of admission). Serial ECGs were obtained daily during the period of stay at hospital. Serum uric acid level at time of admission and echocardiogram in subsequent days was taken. Non-haemolysed serum was analysed for uric acid level.

### Ethical Consideration

The study was approved by Government Rajaji Hospital Ethics Committee. Informed consent was obtained before enrolling subjects to the study.

## RESULTS

A total of 100 patients were recruited to the study. The values of serum uric acid among the various categories are presented in Table 1. The mean age and mean uric acid level of the study sample was 56 years and 5.9 mg/dL, respectively. Level of uric acid increases with increase in age. There were 65 (65%) males and 35 (35%) females. Among males, the mean uric acid level was 5.8 mg/dL and among the females the mean uric acid level 5.2 mg/dL. Among males, 67% of people fall in the range of 5.9±0.6. and 20% of males had values above 7 mg/dL and 57% of females had normal range of 5.9±0.6. and 14% of females had above 7 mg/dL. Males had higher uric acid level than females ($p<0.05$).

Among the 100 subjects, 57 people were hypertensive and remaining 43% did not have hypertension and among these 57% of hypertensive 71% (n=41) falls within the normal range and 12% (n=7) had uric acid level above 7 mg/dL. Among non-hypertensives, 53% (n=23) fall in normal range and 23% of them had uric acid level >7 mg/dL.

Those had SUA <5 mg/dL (n=19) had higher ejection fraction (61-70%) after myocardial infarction. Those who had SUA >7 mg/dL (n=17) had low ejection fraction and the patients who had higher values above 7 mg/dL had very low ejection fraction <40%, which was statistically significant p value, 0.03 (Table 2).

In the study of 100 patients, 52 of them had type 2 diabetes, out of the 52 patients, 12 patients had values more than >7 mg/dL and 9 patients had values less than 5 mg/dL and in 48 patients 5 patients had values more than 7 mg/dL and 10 patients had values less than 5 mg/dL. Among 100 patients, 83 of them had STEMI and 17 had N-STEMI. Among the 83 patients, 16 had values more than 7 mg/dL and 14 had values less than 5 mg/dL.

Among 100 patients, only 7 patients had arrhythmia (3 had ventricular tachycardia and 4 had VPC). All the 3 patients who had VT had values more than 7 mg/dL and they expired during hospital stay. Among the 100 patients, 18 people went for hypotension. Out of the 18, fifteen patients had values >7 mg/dL and one patient had resistant hypotension who expired during the hospital stay.

All 100 patients who were enrolled for study were classified by Killips. The classification at day of admission was as follows-

In Killips I 36 patients, in Killips II 33 patients, in Killips III 6 patients and in Killips IV 15 patients.

Among the 15 patients belonging to Killip IV, 12 had values more than 7 mg/dL ($p<0.05$) when compared with others in Killips I to III (Table 3). Most of the patients belonged to Killips I and II.

On day 5, Killips classification was done again for the same patients, 70 of them falls in stage I, 10 of them in II, 6 patients in III, 10 patients in IV. Four patients with Killip IV and uric acid level >7 mg/dL on the day of admission expired during hospital stay due to arrhythmia and hypotension. It was found that those had high serum uric acid had poor prognosis ($p<0.05$) and this might affect their long-term morbidity and outcome.

| Age in Years | SUA <5 | SUA 5-7 | SUA >7 |
|---|---|---|---|
| <40 (6) | 1 | 4 | 1 |
| 41-50 (19) | 6 | 12 | 1 |
| 51-60 (36) | 5 | 27 | 4 |
| 61-70 (4) | 6 | 21 | 8 |
| >70 | 1 | 0 | 3 |
| **Total** | **19** | **64** | **17** |
| Sex | | | |
| Male (65) | 9 | 44 | 13 |
| Female (35) | 10 | 20 | 5 |
| **Total** | **19** | **64** | **17** |
| Hypertension | | | |
| Yes (57) | 9 | 41 | 7 |
| No (43) | 10 | 23 | 10 |
| **Total** | **19** | **64** | **17** |
| Diabetes | | | |
| Yes (52) | 9 | 31 | 12 |
| No (48) | 10 | 33 | 5 |
| **Total** | **19** | **64** | **17** |
| Type of MI | | | |
| STEMI (83) | 14 | 53 | 16 |
| N-STEMI (17) | 5 | 11 | 1 |
| **Total** | **19** | **64** | **17** |
| Arrhythmia | | | |
| Yes (7) | 0 | 4 | 3 |
| No (93) | 19 | 60 | 14 |
| **Total** | **19** | **64** | **17** |

***Table 1. Different Levels of Serum Uric Acid Among the MI Patients, Age, Sex, Hypertension, Diabetes Wise and Presence of Arrhythmia***

| Ejection Fraction | Uric Acid <5 | Uric Acid >7 |
|---|---|---|
| <50 | 0 | 13 |
| >50 | 19 | 4 |

***Table 2. Comparison of Uric Acid Level with the Ejection Fraction by Echocardiogram***

| Killip D0 | <5 | 5-7 | >7 | Total |
|---|---|---|---|---|
| I | 19 | 27 | 0 | 36 |
| II | 0 | 32 | 1 | 33 |
| III | 0 | 2 | 4 | 6 |
| IV | 0 | 3 | 12 | 15 |
| **Total** | **19** | **64** | **17** | **100** |

***Table 3. Comparison of Uric Acid Level with the Killips score***

Among the 15 patients belonging to Killip IV, 12 had SUA values more than 7 mg/dL and this comparison to patients in Killips I to III was statistically significant, $p<0.05$.

## DISCUSSION

Studies conducted by Sunao Kojima et al[14] concluded that hyperuricaemia after acute myocardial infarction is associated with the development of heart failure. Serum UA level is a suitable marker for predicting AMI related future adverse events and the combination of Killip's class and serum UA level after AMI is a good predictor of mortality in patients who have AMI.

Nadkar et al[15] did a study in India and the results were that the higher level of serum uric acid concentration in patients was associated with poor Killip classification and poor short-term mortality. When we tried to find correlation between serum uric acid and Killip class and their prognostic value in our study, there was difference in uric acid levels between male and female patients. However, in Nadkar et el study, males and females had similar uric acid levels. But, other studies like Kojima et al had reported males having higher uric acid levels than females.

Fifty two percent patients were known diabetic in our study. Non-diabetic and diabetic patients had comparable serum uric acid levels on day 0. This finding is consistent with study by Tuomilheto et al[11] in which there was no significant association between serum uric acid level and diabetic status. However, this finding is in contrast to other study by Safi et al,[12] which showed that hyperuricaemia is significantly associated with type 2 diabetes mellitus.

Similar studies conducted in Croatia by Vladimir Trkulj et al[16] and Ersan Tatli et al[17] concluded that high serum uric acid at admission independently predicts worse short-term and medium/long-term outcomes after AMI, poor outcomes in MACE and associated with higher in-hospital mortality and thirty-day mortality and poor long-term survival after AMI.

These patients were followed up for period of 5 days and monitored for adverse cardiac events. Among the 100 patients, only 7 patients had arrhythmia. 3 had ventricular tachycardia and 4 had VPC. All the 3 patients who had VT had values more than 7 mg/dL and they expired during hospital stay. Those had VPC had values within 5-7 mg/dL, but higher than the confidence interval.

Studies by Hongyu Zhang et al and Leonardo Tamariz et al[18] concluded that there is an association between increased levels of serum UA and AF in women. Hence, serum UA maybe a new risk factor for AF. Yuansheng Liu et al has shown that SUA levels are associated with an increased risk for future AF in both sexes.[19] Filippo Valbusa et al[20] concluded that elevated SUA levels are strongly associated with an increased incidence of AF in patients with type 2 diabetes mellitus even after adjustment for multiple clinical risk factors for AF.

When compared with day of admission, 4 of them belonging to Killip IV and uric acid level >7 mg/dL expired during hospital stay due to arrhythmia and hypotension. These observations showed that those who had higher uric acid at time of admission had poor Killips score and they stayed at poor stage even after treatment. In contrast, those who had lower uric acid improved well with treatment with improvement in Killips score. All the 4 patients who expired during the study in spite of effective treatment belonged to Killips IV and had uric acid >7 mg/dL. This finding was similar to results of Nadkar et al.

As Yildiz, Alia et al[21] has established that serum uric acid level is significantly associated with coronary blood flow and that elevated uric acid might be an independent predictor for the presence of slow coronary flow, we may justify the outcome of the myocardial infarction influenced by the elevated uric acid.

**Limitation**

One limitation of the study was that subgroup analysis could not be done as this was based on small population. Also, the period of follow up was short and we could not look for other outcomes. Also, elevated uric acid associated with poor outcomes after PCI was not analysed in this study.

## CONCLUSION

Serum uric acid has its effect on short and long-term morbidity and mortality in MI patients. It affects treatment outcome of the patient as well, thus by measuring serum uric acid level at admission for acute myocardial infarction patients, we can stratify them and can treat effectively.

## ACKNOWLEDGEMENT

We would like to acknowledge Dean, Madurai Medical College for his administrative support; HOD, Department of Medicine, Madurai Medical College; HOD, Department of Cardiology, Madurai Medical College; HOD, Department of Biochemistry, Madurai Medical College for their supports. We would also like to acknowledge the subjects who took part in the study.

## REFERENCES

[1] Alderman M, Aiyer KJ. Uric acid: role in cardiovascular disease and effects of losartan. Curr Med Res Opin 2004;20(3):369-379.

[2] Cicoira M, Zanolla L, Rossi A, et al. Elevated serum uric acid levels are associated with diastolic dysfunction in patients with dilated cardiomyopathy. Am Heart J 2002;143(6):1107-1111.

[3] Olexa P, Olexova M, Gonsorcik J, et al. Uric acid--a marker for systemic inflammatory response in patients with congestive heart failure? Wien Klin Wochenschr 2002;114(5-6):211-215.

[4] Bickel C, Rupprecht HJ, Blankenberg S, et al. Serum uric acid as an independent predictor of mortality in patients with angiographically proven coronary artery disease. Am J Cardiol 2002;89(1):12-17.

[5] Ochiai ME, Barretto AC, Oliveira MT, et al. Uric acid renal excretion and renal in sufficiency in decompensated severe heart failure. Eur J Heart Fail 2005;7(4):468-474.

[6] Kroll K, Bukowski TR, Schwartz LM, et al. Capillary endothelial transport of uric acid in guinea pig heart. Am J Physiol 1992;262(2 Pt 2):H420-431.

[7] Castelli P, Condemi AM, Brambillasca C, et al. Improvement of cardiac function by allopurinol in patients undergoing cardiac surgery. J Cardiovasc Pharmacol 1995;25(1):119-125.

[8] Kogure K, Ishizaki M, Nemoto M, et al. Evaluation of serum uric acid changes in different forms of hepatic vascular inflow occlusion in human liver surgeries. Life Sci 1999;64(5):305-313.

[9] Anker SD, Doehner W, Rauchhaus M, et al. Uric acid and survival in chronic heart failure: validation and application in metabolic, functional, and haemodynamic staging. Circulation 2003;107(15):1991-1997.

[10] Johnson RJ, Rodriguez-Iturbe B, Kang DH, et al. A unifying pathway for essential hypertension. Am J Hypertens 2005;18(3):431-440.

[11] Tuomilehto J, Zimmet P, Wolf E. Plasma Uric acid level and its association with diabetes mellitus and some biologic parameters in a biracial population of FIJI. Am J Epidemiol 1988;127(2):321-336.

[12] Safi AJ, Mahmood R, Khan MA, et al. Association of serum uric acid with type II diabetes mellitus. J Postgrad Med Inst 2004;18:59-63.

[13] Cirillo P, Sato W, Reungjui S, et al. Uric acid, the metabolic syndrome, and renal disease. JASN 2006;17(12 Suppl 3):S165-S168.

[14] Kojima S, Sakamoto T, Ishihara M, et al. Prognostic usefulness of serum uric acid after acute myocardial infarction (Japanese Acute Coronary Syndrome Study). Am J Cardiol 2005;96(4):489-495.

[15] Nadkar MY, Jain VI. Serum uric acid in acute myocardial infarction. J Assoc Physicians India 2008;56:759-762.

[16] Trkulja V, Car S. On-admission serum uric acid predicts outcomes after acute myocardial infarction: systematic review and meta-analysis of prognostic studies. Croat Med J 2012;53(2):162-172.

[17] Tatli E, Aktoz M, Buyuklu M, et al. The relationship between coronary artery disease and uric acid levels in young patients with acute myocardial infarction. Cardiology Journal 2008;15(1):21–25.

[18] Tamariz L, Agarwal S, Soliman EZ. Association of serum uric acid with incident artrial fibrillation (from the atherosclerosis risk in communities [ARIC] study) Am J Cardiol 2011;108(9):1272-1276.
[19] Liu Y. Hyperuricemia and risk of atrial fibrillation. Journal of Atrial Fibrillation 2014;6(5):967.
[20] Valbusa F, Bertolini L, Bonapace S, et al. Relation of elevated serum uric acid levels to incidence of atrial fibrillation in patients with type 2 diabetes mellitus. American Journal of Cardiology 2013;112(4):499-504.
[21] Yildiz A, Yilmaz R, Demirbag R, et al. Association of serum uric acid level and coronary blood flow. Coron Artery Dis 2007;18(8):607-613.