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**Original Research Article**

# Serum uric acid levels in patients of acute myocardial infarction

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## ABSTRACT

**Background:** Following Myocardial Infarction some proteins and enzymes, CPK-MB/ Troponin-I, T, are released into the blood from the necrotic heart muscle. Serum Uric Acid (SUA) may be a risk factor and negative prognostic marker for cardiovascular diseases. Aim of the study was to study serum uric acid levels in patients of acute Myocardial infarction with congestive heart failure, its relation with stages of congestive heart failure as per Killip classification and the role of serum uric acid levels as a marker of mortality.
**Methods:** The case control study was conducted on 120 patients divided into two groups. Group A included 60 patients of acute Myocardial infarction. Group A was further divided into two categories. One includes 30 patients of with congestive heart failure and another includes 30 patients without congestive heart failure. Group B consists of 60 control patients. Serum uric acid levels were measured in Group A on 1st, 3rd and 7th day of hospital admission and in Group B on 1st day.
**Results:** The study showed females have higher degree of hyperuricemia than males. SUA was significantly higher in patients of acute myocardial infarction than control group patients. SUA were also higher in patients with history of IHD, in patients with BNP >100 and it correlates with Killip class and mortality rates. Patients of acute myocardial infarction with diabetes mellitus had higher degree of hyperuricemia than nondiabetic and control group. No significant difference in SUA levels were observed with regard to age, alcohol intake, lipid profile, ejection fraction and hypertension.
**Conclusions:** In acute myocardial infarction, patients with hyperuricemia had higher mortality and may be considered as poor prognostic biomarker.

**Keywords:** Acute myocardial infarction, Congestive heart failure, Killip class, Uric acid

## INTRODUCTION

Worldwide 30% of all deaths can be attributed to Cardiovascular disease, of which more than half are caused by coronary artery disease and this percentage is expected to grow in future due to lifestyle changes in the developing countries.[1]

Following Myocardial Infarction (MI) some proteins and enzymes labelled as cardiac marker (CPK-MB/ Troponin-I/T) are released into the blood in large quantity from the necrotic heart muscle. These markers have specific temporal profile in relation to myocardial infarction, however they do not correlate with myocardial function. Epidemiological studies have recently shown that uric acid may be a risk factor for Cardiovascular diseases and is a negative prognostic marker. There has been growing interest in the link between serum uric acid level and coronary artery disease. Adenosine synthesized 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 ischemic conditions, and therefore elevated serum uric acid may act as a marker of underlying tissue ischemia. Although the mechanisms by which uric acid may play a pathogenetic role in cardiovascular disease is unclear, hyperuricemia is associated with deleterious effects on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, and aggregation. There is evidence that high uric acid is a negative prognostic factor in patients with mild to severe congestive heart failure, although the development of hyperuricemia is almost always associated with worsening of renal failure in these patients.

Therefore, it is difficult to dissect the roles played by reduced renal function and high uric acid in affecting prognosis of these patients. 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.[2]

Acute Myocardial Infarction is diagnosed in patients having evidence of myocardial necrosis with rise of cardiac biomarker values (preferably cardiac troponin) or having symptoms of ischemia. It also includes the patients having recent significant ST-segment-T wave changes, recent left bundle branch block or appearance of pathological Q wave in ECG and patients showing imaging evidence of recent loss of viable myocardium or recent regional Wall Motion abnormalities or showing intracoronary thrombus on angiography.[3]

The aims and objectives of this study were to study serum uric acid levels in patients of acute Myocardial infarction with congestive heart failure, to study the relation between serum uric acid levels with stages of congestive heart failure as per Killip classification and to study the role of serum uric acid levels as a marker of mortality in Acute Myocardial infarction.

## METHODS

The study was done on 120 patients which were further divided into two groups. Group A included 60 patients of Acute Myocardial infarction. Group A was further divided into two categories. One included 30 patients of acute myocardial infarction with congestive heart failure and another 30 patients of acute myocardial infarction without congestive heart failure. Group B consisted of 60 control patients.

Serum uric acid levels were measured in patients of Acute Myocardial infarction on 1$^{st}$, 3$^{rd}$ and 7$^{th}$ day of hospital admission and in controls at the time of contact with doctor.

This was a case-control study conducted at OPD/IPD/EMERGENCY of SGRD Hospital, Vallah, Sri Amritsar over a period of 1.8 years from Jan 2018 to Aug 2019. Written consent for the trial was obtained from all patients for participating in the study.

***Inclusion criteria (Group A)***

- Patients having acute myocardial infarction (STEMI or NSTEMI, with or without congestive heart failure) diagnosed on the basis of history, clinical examination, ECG changes and reports of biochemical markers (Troponin-I, CPKMB and BNP).

***Exclusion criteria***

- All patients with CKD, Gout, hematological malignancy, hypothyroidism.

All patients on drugs like Salicylates, Ethambutol, Amiloride, Bumetanide, Chlorthalidone, Cisplatin, Cyclophosphamide, Cyclosporine, Ethacrynic acid, Thiazidediuretic, Furosemide, Indapamide, Isotretinoin, ketoconazole, levodopa, metolazone, Pentamidine, Phencyclidine, Pyrazinamide, Theophylline, Vincristine.

Patients who fulfilled the inclusion criteria were included in the study. All patients and their relatives were informed about the study in their vernacular language and written consent was taken. Detailed history of each patient was taken. Complete clinical examination was done and all the routine investigations like Complete Blood Count, Renal function tests, Cardiac biomarkers, Thyroid profile, Serum uric acid levels (on 1$^{st}$, 3$^{rd}$ and 7$^{th}$ day in Group A and on 1$^{st}$ day in Group B), Fasting Lipid profile, fasting blood sugar, Electrocardiogram, 2D-Echocardiogram were done.

The data collected was compiled and analyzed statistically. Statistical analysis was done using percentages, mean values, standard deviation, Pearson Chi-square test. The level of significance used was 0.05 level for the corresponding degree of freedom to draw the inference. A p-value <0.05 was considered statistically significant and a p >0.05 was considered as not statistically significant.

## RESULTS

In this study, Observations were made on 120 patients (60 controls and 60 cases) whose age ranged between 30 90 years with an average of and 60 years with SD of 11.22 yrs. among cases (Group A) and 55.16 years and a S.D. of 19.88 years among controls (Group B) (Table 1).

No significant correlation was found between the age and serum uric acid level in patients with acute MI and healthy controls (p value >0.05) i.e. in this study age-related changes in SUA were not seen (Table 2).

In this study sex distribution of case group (Group A) was 32 female (53.33%) and 28 males (46.67%). Control group (Group B) was comprised of 36 female (60%) and 24 males (40%) (Figure 1).

**Table 1: Frequency distribution according to age.**

| Age group | Control | | Case | |
|---|---|---|---|---|
| | No. | % | No. | % |
| 30-40 | 6 | 10.00 | 2 | 3.33 |
| 41-60 | 32 | 53.00 | 33 | 55.00 |
| 61-80 | 17 | 28.33 | 23 | 38.33 |
| >80 | 5 | 8.33 | 2 | 3.33 |
| Total | 60 | 100.00 | 60 | 100.00 |
| Mean age | 55.16±19.88 | | 60.00±11.22 | |
| p-value | 0.104 | | | |

**Table 2: Correlation of serum uric acid with age.**

| Age group | Serum uric acid | | | | p-value |
|---|---|---|---|---|---|
| | Control | | Case | | |
| | Mean | Sd | Mean | Sd | |
| 30-40 | 5.70 | 1.17 | 7.90 | 0.70 | 0.063 |
| 41-60 | 5.88 | 2.12 | 6.67 | 1.99 | 0.157 |
| 61-80 | 5.97 | 2.00 | 6.28 | 2.25 | 6.662 |
| >80 | 5.11 | 1.66 | 5.91 | 6.15 | 0.772 |

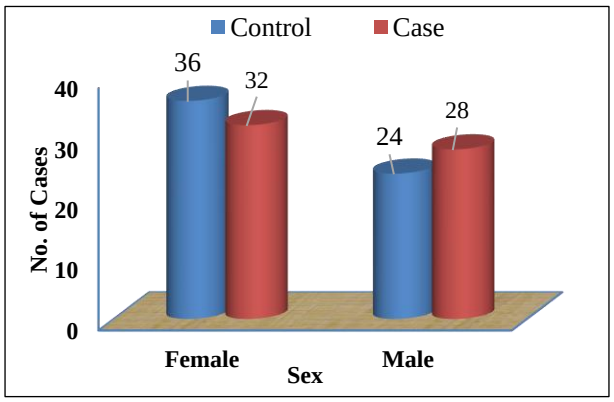


**Figure 1: Frequency distribution according to sex.**

**Table 3: Correlation of serum uric acid level of DM and NDM patients on day of admission.**

| Diabetes mellitus | Serum uric acid | | | | p-value |
|---|---|---|---|---|---|
| | Control | | Case | | |
| | Mean | Sd | Mean | Sd | |
| Yes | 4.59 | 2.67 | 6.76 | 2.01 | 0.014 |
| No | 5.62 | 1.74 | 6.98 | 1.15 | 0.104 |

In this study, there is significant difference in SUA with regard to diabetes mellitus in patients with acute MI and controls (p value = 0.014). The level of SUA in diabetic patients with acute MI (Group A) is 6.76±2.01 and the level of uric acid in controls (Group B) is 4.59±2.67 i.e. serum uric acid was higher in patients of acute MI with history of diabetes mellitus (Table 3).

This study depicts on day 1, SUA levels was significantly higher in patients who were in higher killip class (p value=0.042).On day 3,SUA levels was significantly higher in patients who were in higher killip class (p value=0.031) and similar trend was also observed on day 7 (Figure 2).

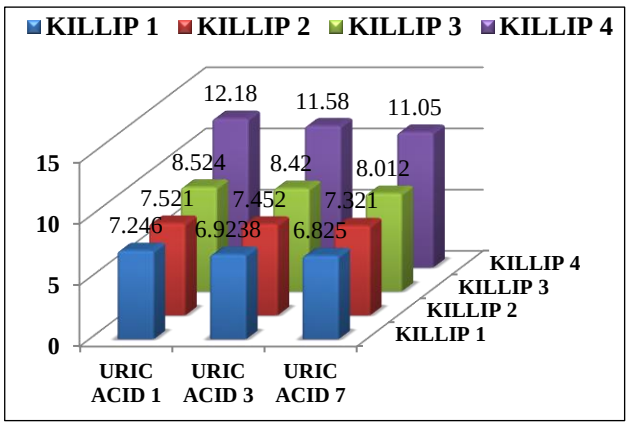


**Figure 2: Comparison of mean SUA with KILLIP class on day 1,3,7.**

**Table 4: Relation of serum uric acid with BNP among cases (Group A) on day 1,3 and 7.**

| BNP | No. of cases | Serum uric acid | | | | | |
|---|---|---|---|---|---|---|---|
| | | Day 1 | | Day 3 | | Day 7 | |
| | | Mean | Sd | Mean | Sd | Mean | Sd |
| <100 | 17 | 6.96 | 2.34 | 6.65 | 1.56 | 8.07 | 2.32 |
| >100 | 43 | 8.14 | 1.89 | 8.56 | 1.83 | 8.96 | 1.85 |
| p-value | | 0.002 | | 0.001 | | 0.023 | |

p-value 0.002 0.001 0.023

Mean SUA for patients having BNP >100 on Day 1 is 8.14±1.89, on Day 3 is 8.56±1.83, on Day 7 is 8.96±1.85. SUA was significantly higher in patients with BNP >100 on Day 1,3 and 7. (p value on Day 1=0.002, p value on Day 3=0.001, p value on Day 7=0.023) (Table 4).

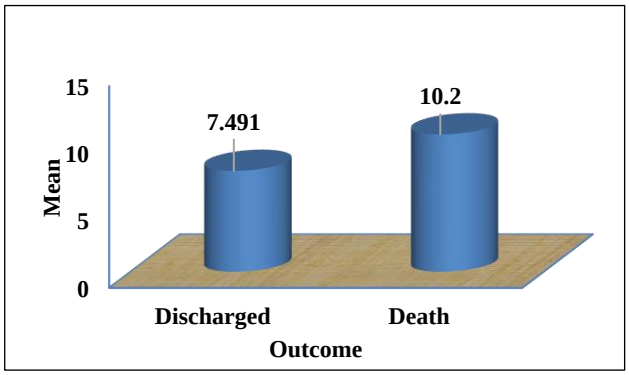


**Figure 3: Relation of serum uric acid with mortality.**

Mean SUA for discharged patients of Group A was 7.49±1.9171 and it was 10.200±1.1314 for patients who died in hospital. Serum uric acid levels were significantly higher in patients who died as compared to those who were discharged (Figure 3).

BNP for discharged patients of Group A was 598.145 and it was 1823.500 for patients who died in hospital. BNP was significantly higher in patients who died as compared to those who were discharged (p value= 0.001) (Table 5).

**Table 5: Relation of BNP levels with mortality in Group A patients.**

| Outcome | BNP | p-value |
|---|---|---|
| Discharged | 598.145 | 0.001 |
| Death | 1823.500 | |

## DISCUSSION

In this study the mean age of case group was (60±11.2 year) and 55.16±19.88 in control group (p value = 0.104). There is no significant difference with regard to age in patients with acute MI and healthy controls whereas study conducted by Sokhanvar and others in 2007 recorded relationship between MI and hyperuricemia in patients of advancing age.[4] Age-related changes in SUA remain unknown.[5]

In Group A there were 32 female (53.33%) and 28 males (46.67%). Group B was comprised of 36 female (60%) and 24 males (40%) (p value = 0.143). High serum uric acid had been found in patients of MI, out of these females have higher degree of hyperuricemia (7.71±1.82) than males (7.06±2.13) (p value <0.05). The results in this study were similar to study conducted by Freedman and others in 1995, Culleton in 1995 who observed such association with females.[6,7] These sex differences of serum uric acid levels in females might be reported due to the influence of sexual hormones, whereas study conducted by Liu and others in 2015, showed that gouty patients of both the sexes fall under increased risk of MI.[8,9]

In this study, 44 patients (73.33%) in cases and 7(11.67%) in controls had history of documented DM. There is significant difference in SUA with regard to diabetes mellitus in patients with acute MI and healthy controls (p value = 0.014). SUA levels are increased during the early stages of impaired glucose metabolism. Furthermore, in diabetic patients, hyperuricemia has been linked to both micro-and macrovascular complications. [10]

In this study among Group A, it was observed that on all the three days i.e. on day 1,3 and 7, Serum uric acid levels were significantly higher in patients who were in higher killip class. Serum Uric Acid (UA) levels reflect circulating xanthine oxidase activity and oxidative stress production. Hyperuricemia has been identified in patients who have congestive heart failure and is a marker of poor prognosis, results suggest that hyperuricemia after AMI is associated with the development of heart failure.[11]

Kojima S, Sakamoto T et al, in 2005, also observed that there was a close relation between serum uric acid concentration and Killip's classification. The combination of Killip's class of left heart failure and serum UA level after acute myocardial infarction is a good predictor of mortality in patients who have acute myocardial infarction.[11] Nakdar MY, jain Vi in 2008 also showed that Serum uric acid levels were higher in patients who were in higher Killip class.[2] Shetty and others in 2013 conclude that SUA levels are correlated with Killip Class and patients with higher Killip Class have higher SUA levels.[12] Agarwal and others in 2014 found that serum uric acid was significantly higher in case group as compared to control group and it was associated with higher Killip's class classification (III, IV) and higher mortality.[13] A recent study by Kumar and others in 2015 found a statistically significant higher level of SUA in patients of acute MI on day of admission as compared to controls (p<0.05). It concluded that higher SUA and higher killip class can be considered as indicator of bad prognosis in patients of MI.[14]

B-type Natriuretic Peptide (BNP), a protein synthesized and released into the circulation by the myocardium in proportion to mechanical strain, has emerged as a commonly used tool for acute heart failure diagnosis and risk stratification. In this study, mean SUA for patients having BNP >100 on Day 1 is 8.14±1.89, on Day 3 is 8.56±1.83, on Day 7 is 8.96±1.85. SUA was significantly higher in patients with BNP >100 on Day 1,3 and 7. (p value on Day 1=0.002, p value on Day 3=0.001, p value on Day 7=0.023). BNP for discharged patients was 598.145 and it was 1823.500 for patients who died in hospital. BNP was significantly higher in patients who died as compared to who were discharged (p value= 0.001).[15]

## CONCLUSION

Female have higher degree of hyperuricemia (7.71±1.82) than males (7.06±2.13) (p value <0.05).

SUA is significantly higher in diabetic patients with acute MI than controls (p value = 0.014).

SUA and BNP was significantly higher in patients who died as compared to who were discharged.

SUA was significantly higher in patients with BNP >100 on Day 1,3 and 7(p value <0.05).

There is no significant difference in SUA levels with regard to age, hypertension, intake of alcohol in patients with acute MI and controls.

SUA level was higher in patients with previous history of IHD but no significant difference had been observed (p value= 0.6555).

No significant correlation in SUA level was observed with regard to serum triglyceride and serum cholesterol level in patients with acute MI and controls (p value>0.05).

In this study Relation of serum uric acid with ejection fraction on day 1,3 and 7 was not significant (p value=0.767 on day 0) (p value=0.814 on day 3) (p value=0.606 on day 7).

This study depicts on day 1, 3 and 7, SUA levels was significantly higher in patients who were in higher killip class (p value<0.05).

Thus, it is concluded that in acute myocardial infarction, patients with hyperuricemia had higher mortality rate and hence serum uric acid may be considered as practical and useful biomarker for prognostication in patients with acute myocardial infarction.

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