

# Serum Uric Acid in Acute Myocardial Infarction

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## Abstract

**Background:** There is evidence that high uric acid is a negative prognostic factor in patients with mild to severe heart failure. A study showed a close correlation between serum uric acid concentration and Killip classification in patients of acute myocardial infarction.

**Material and Methods:** We studied 100 patients with acute myocardial infarction and 50 controls. Serum uric acid level was measured on day 0, 3 & 7 of MI.

**Results:** There was a statistically significant higher level of serum uric acid concentration in patients of MI on day of admission as compared to controls. Patients with history of MI in the past had higher serum uric acid levels. On all the days serum uric acid levels were higher in patients who were in higher Killip class. All the five patients who died after 3 days of hospital stay had serum uric acid level more than 7.0 gm/dL and all of them were Killip class IV.

**Conclusions:** Serum uric acid levels are higher in patients of acute myocardial infarction correlated with Killip class. Combination of Killip class and serum uric acid level after acute myocardial infarction is a good predictor of mortality after AMI. ©

## INTRODUCTION

Following myocardial infarction (MI) some proteins and enzymes labeled as cardiac markers (CPK, MB/Troponin T & I) are released in to the blood in large quantity from necrotic heart muscle. These markers viz. CPK-MB, Troponin-T, Troponin-I and myoglobin, have specific temporal profile in relation to MI; 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 a negative prognostic marker for mortality in subjects with pre-existing 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.<sup>1</sup>

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.<sup>2</sup> Xanthine oxidase activity<sup>3</sup> and uric acid synthesis<sup>4</sup> are increased in vivo under ischaemic conditions, and therefore elevated serum uric acid may act as a marker of underlying tissue ischaemia. Although the mechanisms by which uric acid may play a pathogenetic role in cardiovascular disease is unclear, hyperuricaemia is associated with deleterious effects on endothelial

dysfunction, oxidative metabolism, platelet adhesiveness, haemorheology, and aggregation.

There is evidence that high uric acid is a negative prognostic factor in patients with mild to severe heart failure,<sup>5</sup> although the development of hyperuricaemia is almost always associated with worsening of renal failure in these patients.<sup>6</sup> 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.<sup>7,8</sup>

According to a recent study done in Japan (Japanese Acute Coronary Syndrome Study,<sup>9</sup> 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. Serum uric acid levels, Killip class, age, and peak creatine phosphokinase level were significant predictors of long-term mortality. Patients with angiographically confirmed coronary artery disease with serum uric acid levels in the upper quartile were five times more likely to die than those in the lowest quartile. One mg/dL increase in serum acid levels was associated with a 26% increase in mortality.<sup>10</sup>

We carried out this study to note levels of serum uric acid in acute myocardial infarction, to correlate serum uric acid levels with Killip class and to note any relationship

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between serum uric acid level and mortality following acute myocardial infarction.

## MATERIAL AND METHODS

We studied patients more than 18 years of age who were diagnosed as ST segment elevation acute myocardial infarction (STEMI) or non-ST segment elevation acute myocardial infarction (NSTEMI) on the basis of clinical history, examination, ECG changes, biochemical markers, and admitted in a tertiary care hospital.

Any patient with a condition known to elevate uric acid level e.g. chronic kidney disease, gout, hematological malignancy, hypothyroidism etc. were excluded. Also patients on drugs which increase serum uric acid e.g. salicylates (>2 gm/d), diuretics, ethambutol, pyrazinamide etc. and also chronic alcoholics were excluded.

One hundred patients of acute myocardial infarction who fulfilled inclusion/exclusion criteria were enrolled for the study. A detailed history and physical examination with special reference to Killip class was carried out. All patients underwent routine investigations including Hb, CBC, renal function tests, liver function tests, ECG, chest x-ray. Patients were treated as decided by attending physician. Patients were followed up till hospital stay i.e. 7 days. Serum uric acid level was measured on day 0, 3 & 7 of MI.

Fifty age and sex matched healthy controls were also be evaluated for baseline serum uric acid level.

The study was approved by the Ethics Committee of the hospital. A detailed statistical analysis was carried out. Basal serum uric acid levels were compared with controls with unpaired 't' test. The levels of serum uric acid on day 0, 3, 7 were compared by paired 't' test. Uric acid levels and Killip class was compared with coefficient of correlation.

## RESULTS

We studied 100 patients with acute STEMI AND 50 age and sex matched healthy controls. The comparison of two groups and the profile of patients their comparative uric acid levels are given in Table 1 and 2. There was a statistically significant higher level of serum uric acid concentration in patients of MI on day of admission as compared to controls ( $P < 0.05$ ). There was no significant difference in serum uric acid levels as regards sex, hypertension and diabetes mellitus in patients with MI; however those with history of MI in the past had higher serum uric acid levels. Also, patients with history of IHD were in higher Killip class (Table 3).

Serum uric acid levels were comparable on Day 0, 3 and 7 in MI group,  $5.23 \pm 1.95$ ,  $5.20 \pm 2.15$  and  $5.28 \pm 2.52$  respectively ( $P = NS$ ).

Tables 4, 5 and 6 show the levels of uric acid in relation to Killip class on Day 0, 3 and 7 of admission. On all the days serum uric acid levels were higher in patients who were in higher Killip class ( $P < 0.05$ ). All the five patients who died after 3 days of hospital stay had serum uric acid level more

than 7.0 gm/dL and all of them were Killip class IV.

Table 1 : Comparison of patients and controls

	Patients (N=100)	Controls (N=50)	P
AGE	58.29±11.31	56.84±8.98	NS
Sex M:F	64:36	28:22	NS
Sr. Uric acid D0	5.23±1.95	3.78±0.74	0.03

Table 2 : Patient profile and serum uric acid levels on D0

Parameter			P
Sex	Males - 64	Females - 36	
Sr. Uric acid D0	5.25±1.18	5.19±2.19	NS
Hypertension	Yes - 59	No - 41	
Sr. Uric acid D0	5.38±2.05	5.01±1.78	NS
Diabetes mellitus	Yes - 33	No - 67	
Sr. Uric acid D0	5.50±2.14	5.09±1.85	NS
Previous IHD	Yes - 21	No - 79	
Sr. Uric acid D0	7.07 ±2.024	4.74±1.613	0.001

Table 3 : Killip class on day 0 and previous myocardial infarction

	Killip class	I	II	III	IV
Previous IHD	No (79)	43	22	9	5
	Yes (21)	2	2	10	7
Total	100	45	24	19	12

$P < 0.05$

Table 4 : Serum uric acid level and killip class on Day 0

Killip class	≤ 4.0	4.1-5.5	5.6-7.0	>7.0	Total
I	26	16	2	1	45
II	7	10	7	0	24
III	2	2	9	6	19
IV	0	1	3	8	12
Total	35	29	21	15	100

$P < 0.05$

Table 5 : Serum uric acid level and killip class on day 3

Killip class	≤4.0	4.1-5.5	5.6-7.0	>7.0	Total
I	1	36	20	3	59
II	2	3	5	2	11
III	3	2	2	3	8
IV	4	0	1	3	21
Total	41	28	11	19	99

$P < 0.05$

## DISCUSSION

Previous studies have shown that serum uric acid increases in cardiac failure.<sup>5</sup> In a study done in Japan in 2005 by Kojima et al,<sup>8</sup> it was shown that serum uric acid levels correlate with Killip classification. Combination of Killip class and serum uric acid level after acute myocardial infarction is a good predictor of mortality in patients who have acute myocardial infarction. Using this study as referral study, we

Table 6 : Serum uric acid level and killip class on day 7

Killip class	≤ 4.0	4.1-5.5	5.6-7.0	>7.0	Total
I	43	23	3	1	70
II	0	0	2	0	2
III	0	0	3	2	5
IV	0	1	0	16	17
Total	43	24	8	19	94

P<0.05

tried to find correlation between serum uric acid and Killip class and their prognostic value in our patients.

Present study was conducted in 100 patients of acute myocardial infarction, who presented to hospital within 24 hrs of onset of symptoms. Fifty age and sex matching healthy controls were also evaluated for comparison of uric acid levels.

Out of 100 patients, 65 had ST-elevation myocardial infarction (STEMI), while 35 patients were of non-ST elevation myocardial infarction (NSTEMI). Sixty one patients were thrombolysed while four were not thrombolysed due to delayed presentation. Uric acid was treated as a continuous variable and as a categorical variable, and variables were divided into quartiles according to serum uric acid concentrations same as in referral study by Kojima et al.<sup>9</sup>

Our patients and controls were age and sex matched as shown in Table 1. The patients had higher serum uric acid level probably because of acute myocardial infarction. Similar finding was seen in a referral study<sup>9</sup> with 1124 patients who presented with acute myocardial infarction within 48 hrs of onset of symptoms

In our study there was no difference in uric acid levels between male and female patients (Table 2); however in referral study males had higher uric acid levels as compared to females.<sup>9</sup> There was no significant correlation ( $p=0.396$ ) between serum uric acid level and patients who were known or found to be hypertensive on admission (Table 2). This is different than other studies which showed that hypertensive patients had more hyperuricaemia.<sup>9,11</sup> Thirty three percent patients were known diabetic in our study. Non-diabetic and diabetic patients had comparable serum uric acid levels on Day 0 (Table 2). This finding is consistent with study by Tuomilheto et al<sup>12</sup> 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<sup>13</sup> which showed that hyperuricaemia is significantly associated with type 2 diabetes mellitus. Twenty one percent patients had history of ischemic heart disease. There was significant difference between serum uric acid concentration at the time of admission and h/o ischemic heart disease (Table 2). Serum uric acid levels were higher in patients with past history of IHD as seen in previous study. Also, Patients who were known case of IHD were in higher Killip class (Table 3) as seen in study by Kojima et al.<sup>9</sup>

Killip classification is indicator of severity of heart failure. There was a correlation between serum uric acid level and Killip class on day of admission (Table 4) as in earlier study.<sup>9</sup> Previous studies have shown that serum uric acid level increases in cardiac failure.<sup>14,15</sup> In our study serum uric acid levels correlate with severity of cardiac failure (Tables 4, 5 and 6). There was statistically significant correlation found between serum uric acid level and Killip class ( $p=0.028$ ) on day 3 and. patients of Killip class III and IV had higher levels of uric acid as compared to patients of class I and II. This finding is consistent with referral study.<sup>9</sup> There is statistically significant association ( $p<0.05$ ) between serum creatinine on day of admission and Killip class, in our study. Kojima et al<sup>9</sup> have shown that there is graded relation between serum uric acid concentration and creatinine concentration in patients of acute myocardial infarction.

Out of 100 patients, six expired during 7 day follow up. All the patients who died had serum uric acid level more than 7.0 mg/dL. Of these six patients, one was in Killip class I, one in Killip class III and four were in Killip class IV at the time of admission. Thus, 83% of patients who died were in higher class i.e. class III and IV at time of admission. Two patients (one each) of Killip class I and III shifted to Killip class IV on day 3. One patient expired on day 3 was in Killip class IV on day 0. Rest five patients were in Killip class IV on day 3, who died later. Out of these six patients five had serum uric acid level in quartile 4 on day 0. Only one patient who was in Killip class I and had uric acid in 1st quartile; however his uric acid raised to quartile 4 with shift of Killip class to class IV on day 3. On day 3 all five patients were in Killip class IV and had uric acid level in 4th quartile. Thus, all six pts who expired were in Killip class IV and had uric acid level in 4<sup>th</sup> quartile. Therefore it shows that serum uric acid concentration is significantly correlated with Killip class. However, because of small number of patients statistical significance could not be proved.

Thus, from present study we conclude the following:

Serum uric acid levels are higher in patients of acute myocardial infarction as compared to normal healthy persons.

Serum uric levels are correlated with Killip class; patients in higher Killip class have higher serum uric acid levels.

Serum uric acid levels and Killip class are influenced significantly by previous myocardial infarction. Patients who had myocardial infarction in past have higher serum uric acid levels and are in higher Killip class.

Combination of Killip class and serum uric acid level after acute myocardial infarction is a good predictor of mortality after AMI.

## REFERENCES

1. Alderman M, Aiyer KJ. Uric acid: role in cardiovascular disease and effects of losartan. *Curr Med Res Opin* 2004;20:369-79.
2. Kroll K, Bukowski TR, Schwartz LM, Knoepfler D, Bassingthwaite JB. Capillary endothelial transport of uric acid in guinea pig heart. *Am J Physiol* 1992, 262:H420-31.

3. Castelli P, Condemni AM, Brambillasca C, et al. Improvement of cardiac function by allopurinol in patients undergoing cardiac surgery. *J Cardiovasc Pharmacol* 1995;25:119–25.
4. 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;64:305–13.
05. 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;22:1991–97.
6. Ochiai ME, Barretto AC, Oliveira MT, et al. Uric acid renal excretion and renal insufficiency in decompensated severe heart failure. *Eur J Heart Fail* 2005;7:468–74.
7. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med* 2005;21:1685–95.
8. Festa A, Haffner SM. Inflammation and cardiovascular disease in patients with diabetes: lessons from the Diabetes Control and Complications Trial. *Circulation* 2005;11: 2414–15.
9. 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: 489-95.
10. 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;89:12-7.
11. Johnson RJ, Rodriguez-Iturbe B, Kang DH, et al. A unifying pathway for essential hypertension. *Am J Hypertens* 2005;18:431-40.
12. Tuomilhto J, Zimmet P, Ewawolf. Plasma Uric acid level and its association with Diabetes Mellitus and some Biologic Parameters in a Biracial Population of FIJI *Am J Epidemiol* 1988;127:32136.
13. Safi AJ, Mahmood R, Khan MA, Haq A. Association of serum Uric Acid with type II diabetes mellitus. *J Postgrad Med Inst* 2004;18:59-63.
14. 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;143:1107-11.
15. 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;28:211–15.

### Announcement

VI Dr. KS Shadaksharappa National Symposium in Cardiology to be held on 8th November 2008 At API Bhavan, Miller Tank Bed Ara, Vasanthnagar, Bangalore.

The me- Cardiac Emergency  
Registration Fees Rs. 200/- only

For further details contact : Dr. P Chandrasekhara, Programme Director and Dr. GG Shetty, Convenor, Medical Education and Research Trust, API Bhavan, No. 16/F, Millers Tank Bed Area, Vasanthnagar, Bangalore - 560052. Ph. No. 080-22353525; Email : poocha\_sekhara@yahoo.co.in

### Announcement

64<sup>th</sup> Annual Conference of Association of Physicians of India – will be held from 29<sup>th</sup> January to 1<sup>st</sup> February, 2009, at India Expo Centre, Greater Noida, National Capital Region ( NCR ), it will be Hosted by API Ghaziabad Branch.

For registration & other details, please contact : Dr. NK Soni, Organising Secretary, Soni Cardiometabolic & Lifestyle Management Centre, KF – 90, Kavi Nagar, Ghaziabad – 201002. U.P.  
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