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Original Research Article

Study of serum uric acid levels in acute ST elevation myocardial infarction patients and its correlation with Killip's classification of heart failure

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Abstract

Background: Acute myocardial infarction (AMI) continues to be a significant health problem in industrialized countries & increasingly significant problem in developing Countries. ST elevation MI constitutes approximately 40% of all AMI. Serum uric acid produced from xanthine & hypoxanthine (purines) by xanthine oxidase. Serum uric acid (UA) levels reflect circulating xanthine oxidase activity and oxidative stress production. Hyperuricemia is associated with deleterious effects on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, haemorrheology and aggregation. Hence this study is conducted to estimate serum uric acid levels in acute ST elevation myocardial infarction patients and its correlation with Killip's classification of heart failure.

Methods: 100 Patients with Acute ST elevation myocardial infraction admitted between October 2011 to April 2013 were studied. Serum uric acid level was measured on day 0, day 3 & day 7 of MI. A detailed history and physical examination with reference to Killip's classification was carried out and correlated with serum uric acid levels. Statistical analysis: Data presented with mean±SD. Uric acid levels and Killip's class compared with spearman correlation coefficient.

Results: The mean age of the patients was 58.43±13.77. The male to female ratio was 65:35 showing a male predominance. Mean uric acid levels on day 0 is 5.179±1.910, on day 3 is 5.0325±1.755, on day 7 is 4.953± 1.446. Uric acid levels was compared with Killip class on day 0 and it is found to be significant($r = 0.7374$ and $p < 0.0001$) and results remain significant on day 3($r = 0.5898$ $p<0.0001$).In case of patients who expired ($n = 20$) the mean serum uric acid level was 6.845±2.715 and in other 80 patients was 4.783±1.386($t=4.828$, $p<0.0001$).Out of 20 patients who expired, 16 patients were having elevated serum uric acid levels(>7mg/dl). 19 patients were in Killip's class IV at the time of death. On all the days serum uric acid levels were higher in patients who were in higher Killip class.

Conclusion: Patients with elevated serum uric acid levels belonged to higher Killip's classification and were associated with higher mortality.

Keywords: Serum uric acid, ST elevation, Killip class, Acute Myocardial infarction, Heart failure

1. Introduction

Coronary heart disease (CHD) is the leading cause of death in India and the leading cause of death worldwide. Previously thought to affect primarily high-income countries, Coronary heart disease now leads to more death and disability in low and middle-income countries, such as India, with rates that are increasing disproportionately compared to high-income countries [1].

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 [2]. 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 ischaemia [3]. Although the mechanisms by which uric acid may play a pathogenic role in cardiovascular disease is unclear, hyperuricemia is associated with deleterious effects

on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, haemorrheology, and aggregation. There is evidence that high uric acid is a negative prognostic factor in patients with mild to severe heart failure [3,4]. A study showed a close correlation between serum uric acid concentration and Killip's classification in patients of acute myocardial infarction[5].

Hence this study is conducted to estimate serum uric acid levels in Acute ST elevation myocardial infarction patients and its correlation with Killip's classification of heart failure.

2. Materials and Methods

Hundred and thirty six patients with Acute ST elevation myocardial infraction admitted in Shri B.M. Patil Medical College Hospital and research centre, Vijayapur, Karnataka were studied. Study was done for a period of 18 months. Any patient with a condition known to elevate uric acid level e.g. chronic kidney disease, gout, hematological malignancy, hypothyroidism, patients on drugs which increase serum uric acid e.g. salicylates (>2 gm/d), Ethambutol, Pyrazinamide and Chronic alcoholics were excluded .

Out of 136 patients 36 were excluded because 30 were chronic alcoholics and 6 had chronic kidney disease. A detailed history and physical examination with special reference to Killip class was carried out. All patients underwent routine investigations including CBC, ECG and Renal function tests. Serum uric acid levels were measured on day 0, 3 & 7 of AMI. Patients were followed for consecutive 7 days from the date of admission. Total numbers of mortality due to heart failure are classified according to Killip classification and are correlated with serum uric acid levels.

2.1 Statistical analysis

Data presented with mean ± SD.

Uric acid levels and Killip's class compared with spearman correlation coefficient.

The levels of serum uric acid on day 0,3rd day 7th day following acute myocardial Infarction compared by Wilcox on Matched Pairs Signed ranks test because of strong association.

3. Results

The mean age of the patients included in the study is 58.43 ± 13.77, ranging from 35 years to 88 years. In this study there was no significant difference in uric acid levels between male and female patients (p=0.6463 - NS). Out of 100 patients, antero septal wall MI was seen in 44 patients, extensive anterior wall MI was seen in 22 patients, inferior wall MI in 30 patients, anterolateral wall MI in 4 patients. 2D Echocardiogram showed mild LV dysfunction in 24 patients, moderate LV dysfunction in 43 patients, severe in 23 patients and normal LV function in 10 patients. Out of 100 patients, 18 patients were hypertensive and 14 patients had diabetes, mean uric acid levels on day 0 in hypertensive patients was 5.505 ± 1.624 and in non hypertensive patient was 5.107 ± 1.969(Table 2). There was no significant difference in uric acid levels between hypertensive and non hypertensive patients (P = 0.2463 - NS). Mean uric acid levels on day 0 in diabetic patients were 4.55 ± 1.029 and in Non diabetic patient were 5.28 ± 2.003(Table 2). There was no significant difference in uric acid levels between diabetic and Non diabetic patients (P = 0.2411- NS).

Mean uric acid levels on day 0 is 5.179 ± 1.910, on day 3 is 5.0325 ± 1.755, on day 7 is 4.953 ± 1.446.There is a significant reduction of uric acid levels on Day 7 on comparing with day 0 (P = 0.0274) and day 3 (P = 0.0424).

Killip classification used as an indicator of severity of heart failure. On day of admission out of 100 patients, 16 patients had serum uric acid >7mg/dl in which 13 patients in Killip class IV and 3 patients in Killip class III (Table-3) (p<0.0001-highly significant). 100% of patients who had serum uric acid >7mg/dl were in higher Killip class (class III&IV). On day 3, out of 84 patients 12 patients had serum uric acid >7mg/dl in which 5 patients in Killip class IV and 5 patients in Killip class III (Table 4) (P<0.0001-highly significant). 83% of patients who had serum uric acid >7mg/dl were in higher Killip class. On day 7 out of 81 patients 4 patients had serum uric acid >7mg/dl in which 1 patient in Killip class IV and 1 patient in Killip class III (Table 5) (p<0.3921-not significant). 50 percent of patients who had serum uric acid >7mg/dl were in higher Killip class. Thus patients of Killip class III&IV had higher levels of uric acid as compared to patients of Killip class I & II.

Out of 100 patients, 20 expired during 7 day follow up. The mean uric acid level in expired patients is 6.845 ± 2.715 and in other patients is 4.783 ± 1.386, which was a statistically significant difference (t = 4.82, p < 0.0001 -highly significant). Out of the 20 patients who died, 16 had serum uric acid level more than 7.0 mg/dl and 4 patients had serum uric acid less than 7mg/dl (Table 6). Of these 20 patients, 2 was in Killip class I, 6 in class III and 12 in class IV at the time of admission. Thus 90 % of patients were in higher class i.e. class III and IV at time of admission.

Out of 20 patients, 14 died on day of admission in which 10 patients were in Killip class IV, 3 patients in Killip class III and 1 patient in Killip class I (Table 7). 5 patients died on day 3 follow up of these 1 patient was in Killip class I, 2 patients in

Killip class III initially, later shifted to Killip class IV on day 3, who died later. 1 patient died on day 7 follow up who was initially in Killip class III at the time of admission, Killip class II on day 3,shifted to Killip class IV, who died later(p=0.0003-highly significant).

Thus, 19 patients who expired were in Killip class IV and 16 patients had serum uric acid levels >7mg/dl at the time of death i.e. 80% patients had higher serum uric acid levels. Therefore it shows that mortality significantly correlated with serum uric acid concentration and Killip class.

Table 1: Comparison of Serum uric acid in acute MI with gender

Sex	Male(65)	Female(35)	P value
Serum uric acid on Day 0	5.244 ± 1.986	5.057 ± 1.781	0.6463 (not significant)

Table 2: Comparison of serum uric acid in acute MI with risk factors

Variables	Yes	No	Statistical Analysis
Hypertension Serum uric acid on Day 0	18 5.505 ± 1.624	82 5.107 ± 1.969	P = 0.2463 (not significant)
Diabetes Mellitus Serum uric acid on Day 0	14 4.55 ± 1.029	86 5.28 ± 2.003	P = 0.2411 (not significant)

Table 3: Comparison of serum uric acid level in acute MI and Killip class on Day 0

Killip class	Uric acid (<7mg/dl)	Uric Acid (>7mg/dl)	Total
I	52	00	52
II	13	00	13
III	16	03	19
IV	02	13	16
Total	84	16	100
Mortality	04	10	14

Table 4: Comparison of serum uric acid level in acute MI and Killip Class on day 3

Killip class	Uric acid (<7mg/dl)	uric acid (>7mg/dl)	Total
I	49	00	49
II	22	02	24
III	03	05	08
IV	00	05	05
Total	74	12	86
Mortality	00	05	05

Table 5: Comparison of serum uric acid level in acute MI and Killip class on day 7

Killip class	Uric acid (<7mg/dl)	Uric acid (>7mg/dl)	Total
I	65	01	66
II	12	01	13
III	00	01	01
IV	00	01	01
Total	77	04	81
Mortality	0	01	01

Table 6: Correlation between serum uric acid in acute MI and mortality

Variables	UA < 7 mg/dl	UA> 7 mg/dl	Total
Day 0	04	10	14
Day 3	00	05	05
Day 7	00	01	01
Total	04	16	20

Table 7: Correlation between mortality and Killip's classification in acute MI

Variables	Class I	Class II	Class III	Class IV	Total
Day 0	1	0	3	10	14
Day 3	0	0	0	5	5
Day 7	0	0	0	1	1
Total	**1**	**0**	**3**	**16**	**20**

4. Discussion

In the present study, we found a close relation between serum uric acid (UA) concentrations and Killip's classification suggestive of left ventricular failure. High UA concentrations on admission were strongly associated with adverse clinical outcome in patients who had Acute ST elevation Myocardial infarction. Killip classification used as an indicator of severity of heart failure. Previous studies have also shown that serum uric acid level increases in cardiac failure.[15,16] This observation is corroborated with our present study (Tables 3, 4 and 5). There was statistically significant correlation found between serum uric acid level and Killip class on day 0($p<0.0001$) and day 3($p<0.0001$) but not in day 7($p= 0.3921$). This finding is consistent with studies of Kojima *et al*[5]. Thus patients of Killip class III&IV had higher levels of uric acid as compared to patients of Killip class I & II.

Kojima *et al* conducted a study on 1124 patients showed males had higher uric acid levels as compared to females and hypertensive patients had higher uric acid levels than non hypertensive patients. In our study there was no significant difference in uric acid levels between male and female patients ($p = 0.6463$ - NS) Similarly no significant difference in uric acid levels between hypertensive and Non hypertensive patients ($P = 0.2463$ - NS) were found.

There was no significant difference in uric acid levels between diabetic and Non diabetic patients ($P = 0.2411$- NS) in our study which supports the finding of Tuomilheto *et al*[7]. However, these observations are in contrast to other study by Safi *et al*[58] which showed a significant association between hyperuricemia and type 2 diabetes mellitus.

Out of 100 patients, 20 expired during 7 day follow up period. Out of the 20 patients who had died, 16 had serum uric acid level more than 7.0 mg/dl. It reflects 80% of dead patients had higher serum uric acid levels during 7 day follow up. Serum uric acid significantly higher in patients who expired compared to other patients ($t = 4.82$, $p < 0.0001$). Further adding Killip's class to serum UA concentration improved its prognostic power.

Prompt restoration of myocardial blood flow is the therapeutic goal in AMI because early reperfusion decreases mortality rates. In patients who had AMI, were in a high Killip's class, and had high UA concentrations. A failing heart due to AMI may cause tissue hypo perfusion and hypoxia, which trigger xanthine oxidase activation and oxidative stress production. Xanthine oxidase and oxidative stress as reflected by UA may form a vicious cycle that promotes severe heart failure. Therefore, UA may not be only a bystander marker but also a causative marker of mortality in patients who have AMI. In this regard, improvement of coronary reperfusion alone may be less effective in ameliorating heart failure and decreasing mortality rate in patients who have AMI and high UA level and are in a high Killip's class [5].

Adjunctive therapy designed to decrease xanthine oxidase activity and inhibit oxidative stress production is expected to sever the vicious cycle. The Losartan Intervention for Endpoint reduction in hypertension (LIFE) study demonstrated that lowering serum UA concentrations by losartan was associated with a beneficial effect on cardiovascular outcome.[13] The UA-lowering effect of atorvastatin may have contributed to the decrease in cardiovascular mortality in the Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) study.[14]

However this study has few limitations, among patients cardiomyopathy and myocarditis were not ruled out as coronary angiography was not done and co existing infectious or inflammatory disease which increase acute phase reactant like uric acid were not completely excluded. Further studies are necessary with higher sample size.

Therefore, any drug interventions, such as therapy to decrease serum UA level in addition to coronary reperfusion, may have a favourable effect on mortality in patients who have AMI. In future correlation of uric acid with transmural or subendocardial infarction can be carried out.

5. Conclusion

Patients with elevated serum uric acid levels belonged to higher Killip's classification and had higher mortality. Hence we can use serum uric acid as an inexpensive cardiovascular risk marker and prognostic marker in acute myocardial infarction patients.

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