A Study of the Serum Uric Acid Level as Prognostic Indicator in Acute Myocardial Infarction

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Abstract
Background: Coronary artery disease (CAD) is the leading cause of mortality and morbidity in present days. Recent epidemiological and clinical evidences suggest that serum uric acid can be one of the useful markers in assessing the risk of mortality in acute myocardial infarction.

Objective: To find out the association in serum uric acid level and Killip classes and ejection fraction.

Methodology: It was an observational prospective study. 100 patients of acute myocardial infarction were enrolled and physical examination with special reference to Killip classification, ECG, 2D- Echocardiogram, Serum uric acid and all routine investigations were carried out on 0, 3rd and 7th day. Serum uric acid and Killip class and ejection fractions on day 0, day 3 and day 7 were compared.

Results: In this present study majority of the patients were in the age group of >50 years (68%). There was statistically significant increase in uric acid levels with increasing Killip class on day 0, day 3 and day 7. Mean serum uric acid level was 4.4 mg/dl in Killip class I, 7.01 mg/dl in class II, 8.29 mg/dl in class III, and 9.87 mg/dl in class IV on day 0; 4.46 mg/dl in Killip class I, 7.09 mg/dl in class II, 8.53 mg/dl in class III, and 9.43 mg/dl in class IV on day 3; 4.72 mg/dl in Killip class I, 6.62 mg/dl in class II, and 9.43 mg/dl in class IV on day 7. There was statistically significant negative correlation (p-value 0.0009, 0.001, 0.0326 at day 0, 3 & 7) between serum uric acid levels and ejection fraction at all the three occasions i.e. day 0, day 3 and day 7.

Conclusion: The present study concludes that serum uric acid level have significant association with Killip class, left ventricular failure and mortality i.e. higher the serum uric acid, higher the Killip class, more severe left ventricular dysfunction and higher the mortality.

Introduction
Coronary artery disease (CAD) is the leading cause of mortality and morbidity in present days. The global status on Non communicable disease report (2011) has reported that there were more than 2.5 million deaths from cardiovascular disease in India in 2008, two third due to coronary artery disease.1 According to World Bank estimates, cardiovascular disease had a 31% share in the total burden of disease in 2001.2 In 2003, the prevalence was estimated to be 3-4% in rural areas and 8-10% in urban areas according to population based cross sectional surveys.3-4 In United States approximately 525,000 experience a new acute myocardial infarction (AMI) and 190,000 experience recurrent AMI each year. More than half of AMI related deaths occurs before the individual reaches to hospital.5 In hospital mortality is approximately 6%. 1year mortality rate after AMI is about 15%. Persistent ischemia, depressed LV ejection fractions (40%), rales above the lung base, congestion on chest radiograph, symptomatic ventricular arrhythmias are some of the important factors, which decides prognosis after AMI.5

There are some markers indicating unfavourable prognosis in acute myocardial infarction. Uric acid is one of the markers that is being evaluated for research. The role of uric acid as a risk factor is controversial; because it is hypothesized that the antioxidant properties of uric acid might be protective against aging, oxidative stress and oxidative cell injury.6 However, recent epidemiological and clinical evidences suggest that hyperuricemia might be a risk factor for cardiovascular disease, where enhanced oxidative stress plays an important pathophysiological role. Some experts, such as the Framingham Heart study group, have argued that uric acid is not a risk factors for cardiovascular disease and that clinicians should not rely only on it.6 Nor have serum uric acid levels been considered a cardiovascular risk factor by major professional societies.7-8 Conversely, serum uric acid is one of the significant and useful marker in assessing the risk of mortality in acute myocardial infarction.9

Uric acid may impair kidney function by causing glomerular damage and pre-glomerular arteriosclerosis, ultimately results in arterial hypertension, which is highly predictive of mortality in patients with coronary artery disease or heart failure.10 It is matter of controversy as to whether serum uric acid is an independent cardiovascular risk factor or rather it only represents reinforcement of typical risk factors.11-13

The Killip classification is a system used to stratify the severity of left ventricular dysfunction and determine clinical status of post MI patients.14 There are studies that indicate high uric acid is a negative prognostic factor in patients with mild to severe heart failure.15 Moreover, serum uric acid...
reduction has been considered as a potential and novel approach to lower the burden of coronary artery disease. Recent studies has also indicated that concomitantly employing allopurinol (an uric acid lowering agent) with anti-hypertensive and lipid lowering drugs might act synergistically with these therapies to lower cardiovascular risk.

In view of above discrepancies between various studies and possibilities of newer treatment modalities and paucity of data in Indian population, we aimed to further study the relationship between serum uric acid and its use as a prognostic marker in patients with acute myocardial infarction.

Objectives

To find out the association between serum uric acid level and severity of left ventricular failure assessed clinically by Killip classification and to know the correlation between serum uric acid level and ejection fraction assessed objectively by 2D echocardiography.

Methodology

It was an observational prospective study done at Dr. Baba Saheb Ambedkar Medical College and Hospital, Rohini, New Delhi from September 2016 to August 2017. A total of 100 patients presented to Department of Medicine, meeting inclusion and exclusion criteria were taken. Patients older than 18 years, with suggestive features of acute myocardial infarction, ST elevation and Non ST elevation myocardial infarction (STEMI & NSTEMI) on ECG, and with rise in serum cardiac enzymes concentration, were included in the study. Patients with cardiogenic shock, pacemaker, valvular heart diseases, chronic use of alcohol, other clinical conditions affecting serum uric acid level (impaired renal functions, hypothyroidism, gout, haematological malignancy, chronic inflammatory disease) and patients on drugs affecting serum uric acid level (Salicylates, diuretics, ethambutol, pyrazinamide, corticosteroids, cytotoxic drugs, telmisartan and hydrochlorothiazide) were excluded from the study. Information was collected through a pre tested and structured performa for each patient, after taking informed consent. In all the selected patients detailed history and physical examination with special reference to Killip classification of heart failure was carried out. All patients were subjected to 12 lead ECG, 2D-Echocardiogram (Philips ultrasound system HD11XE) and cardiac enzymes beside all routine investigations (e.g. complete blood count with ESR, RBS, Blood urea, serum creatinine, serum TSH, USG whole abdomen for kidney size and Serum uric acid was measured (by fully automatic biochemistry analyser P800 modular) on 0, 3rd and 7th day. Serum uric acid and Killip class on day 0, day 3 and day 7 were compared to assess the prognosis. Patients were followed up till 7th day and then 30th day of acute myocardial infarction. All the information collected was kept confidential. Approval from Institutional Ethical and Scientific Committee was taken.

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Quantitative variables were compared using Unpaired t-test between the two groups and ANOVA among more than two groups. Qualitative variables were compared using Chi-Square test /Fisher’s exact test. Univariate and multivariate logistic regression was used to assess the risk factors of mortality. A p value of <0.05 was considered statistically significant.
Table 4: Correlation between serum uric acid levels and ejection fractions (left ventricular failure)

<table>
<thead>
<tr>
<th>Time</th>
<th>Spearman’s coefficient of rank correlation (rho)</th>
<th>p value</th>
<th>95% confidence interval for rho</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>-0.329</td>
<td>0.0009</td>
<td>-0.495 to -0.140</td>
</tr>
<tr>
<td>Day 3</td>
<td>-0.326</td>
<td>0.001</td>
<td>-0.493 to -0.137</td>
</tr>
<tr>
<td>Day 7</td>
<td>-0.221</td>
<td>0.0326</td>
<td>-0.405 to -0.0189</td>
</tr>
</tbody>
</table>

Source: Original

Results

In this present study majority of the patients were in the age group of >50 years (68%). Mean age was 54.77 years, youngest being 28 years and oldest being 80 years old. Younger population (<40 years) constitutes 11% of patients. In this study out of 100 patients 31 (31%) were females and 69 (69%) were male patients (Table 1).

47 (47%) patients were diabetics, out of them 14 were females and 33 were males. There were 41 hypertensive patients out of which 14 were females and 27 were males. History of smoking was seen in 59 patients, including 4 females and 55 males. 20 males had history of alcohol consumption. Significant difference was observed between males and females in smoking and alcohol use (Table 2).

In this study on day 0, out of 100 patients, 57 patients belonged to Killip class I, 16 belonged to class II, 14 belonged to class III and 13 patients belonged to class IV. There was no mortality on day 0. In present study on day 3 out of 100 patients, 65 patients belonged to Killip class I, 22 belonged to class II, 6 belonged to class III and 7 patients belonged to Killip class IV. There was no mortality on day 3. On day 7 out of 100 patients, 89 patients belonged to class I, 5 patients belonged to class II, and no patients belonged to Killip class III and IV. 6 patients expired during follow up between day 3 to day 7 (Table 3).

Mean uric acid level in patients on day 0 belonging class I was 4.4 mg/dl compared to 7.01 mg/dl in Killip class II, 8.29 mg/dl in Killip class III, and 9.87 mg/dl in Killip class IV. Mean uric acid level of all the patients on day 0 was 6.07 mg/dl. There was statistically significant difference in uric acid levels with increasing Killip class on day 0. Mean uric acid levels in patients on day 3 belonging to Killip class I was 4.46 mg/dl compared to 7.09 mg/dl in Killip class II, 8.53 mg/dl in Killip class III, and 9.43 mg/dl in Killip class IV.

Mean serum uric acid level on day 3 was 5.63 mg/dl. There was statistically significant difference in uric acid levels with increasing levels on Killip class on day 3. Mean uric acid on day 7 in patients with Killip class I was 4.72 mg/dl. Mean uric acid in patients with Killip class II was 6.62 mg/dl. There was statistical significant difference in uric acid levels with increasing Killip class on day 7 (Table 3).

There was statistically significant negative correlation (p-value 0.0009, 0.001, 0.0326 at day 0, 3 & 7) between S. Uric Acid levels and ejection fraction at all the three occasions i.e. day 0, day 3 and day 7. Higher level of s. uric acid would be associated with lower level of ejection fraction, indicating severity of left ventricular failure. Thus s. Uric acid level appeared to be a bad prognostic factor in cases of left ventricular failure in acute myocardial infarction (Table 4).

In univariate logistic regression, it was found that SUA on day 0, day 3, random blood sugar and Killip class day 3 are significant risk factors of mortality. With increase in serum uric acid by 1 unit on day 0 and day 3, risk of mortality increases with odds ratio of 11.162 and 31.703 respectively.

In multivariate logistic regression no factors was found significantly affecting mortality after adjusting for confounding factors.

Discussion

The role of uric acid as a risk factor for myocardial infarction is controversial. There are a lot of studies suggesting that hyperuricemia is a risk factor for cardiovascular disease. In few studies, association of SUA with cardiovascular disease was uncertain after multivariate adjustment as in the Framingham Heart Study (1985) and the ARIC (Atherosclerosis risk in community) study (1996), and therefore most medical societies have not considered serum uric acid level as a cardiovascular risk factor, but in few other studies the association remained certain and significant. Serum uric acid levels have been known to go up in cardiac failure in study conducted by Kojima et al in 2005 and M Y Nadkar et al in 2008 showed that Serum uric acid correlates with Killip class. We thus used these studies as reference to assess this tool of combining Killip class with Serum uric acid levels as a prognostic indicator in patients with acute myocardial infarction.

In this present study we have found a significant association between uric acid level and Killip class, as well as significant correlation between serum uric acid and severity of left ventricular failure on day of admission (day 0), day 3 and day 7 in patients of acute myocardial infarction admitted to this hospital.

Total 100 patients were enrolled in this present study, age of the patients varied from 28 years to 80 years. Mean age of patients was 54.77 ± 11.44 years. Females constitute 31 (31%), while males are 69 (69%). These findings are in concurrence with other previous studies. Previous studies have also shown that myocardial infarction is common in males compared to females.

In present study all the patients were classified in different Killip classes according to their clinical condition on day of admission (day 0), again on day 3 and on day 7. On day 0, more than half of the patients (57%) belonged to Killip class I, 16% belonged to Killip class II, 14% belonged to Killip class III and 13% belonged to Killip class IV. Similar finding were observed in the study conducted by M Y Nadkar et al and Gandaiah et al wherein on day of admission majority of patients belonged to Killip class I.

Mean uric acid levels were higher on day of admission in this study as compared to mean uric acid level on day 7. This findings correlates with Shetty et al and S Agarwal et al however it does not correlate with M Y Nadkar et al. It can be explained that in this study on day 7 all patients belonged to Killip class I or II, hence lower mean uric acid levels.

In this present study mean uric acid level in different Killip classes was calculated and compared. We found statistically significant (<0.0001) association of increase in Killip class with increasing mean uric acid level on day 0, day 3 and day 7. M Y Nadkar et al, Shetty et al, S Agarwal et al and Gandaiah et al also observed similar
findings of higher Killip class having higher serum uric acid level.

In this present study there is significant correlation between elevated serum uric acid level and ejection fraction measured by echocardiographic evaluation.

In this present study, mortality among different Killip classes was analysed and it was found that 6 had expired during 7 day follow up. These patients belonged to subset of Killip class IV on the day of admission. (Mean uric acid was >9 mg/dl). It was observed that mortality was higher in patients with higher Killip class and higher Killip class had higher mean uric acid level.

Hence it can be suggested that mean serum uric acid levels increases with increase in Killip class and mortality is high in patients with higher mean uric acid on admission.

Limitations of this study

Because of time limitation the number of patients (cases) studied in this analysis according to reference statistical formula are 100, but to formulate a definite analytical conclusion for better understanding of correlation of SUA and Killip classes and its prognostics usefulness, a greater cohort would be desirable to improve the power of the study.

We also relied on clinical data to rule out infection and other inflammatory diseases before sampling, but we cannot exclude that some patients had unrecognized conditions responsible for the elevated serum uric acid levels observed. We supposed to mean that these limitations might not have a significant influence on study data interpretation.

Conclusion

The present study concludes that serum uric acid level have significant association with Killip class, left ventricular failure and mortality i.e. higher the serum uric acid, higher the Killip class, more severe left ventricular dysfunction and higher the mortality. As serum uric acid is an economical bio marker that is readily, quickly and reliably obtainable, it can be one of the predictable prognostic indicators in acute myocardial infarction. Further studies on larger cohort are needed to establish these findings.

References