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A Study of Serum Uric acid levels as a Prognostic Marker in Acute Myocardial Infarction

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Abstract
The aim was to evaluate any significant correlation between elevated serum uric acid levels and prognosis of patients with acute myocardial infarction primarily short term mortality.
Methods- *In this tertiary centre based prospective study 100 new cases of acute MI were divided into various subcategories using Killip classification .Serum uric acid levels were measured on day 0, 3 and 7.Serum uric acid and Killip class were compared on day 0,3 and 7 to assess the prognosis.*
Results: *Majority of the patients were in the age group of 51-60 years, who accounted for 37 cases i.e. 37% of total cases. In our study out of 100 patients 70 (70%) patients were males whereas 30 (30%) were female patients. Majority of patients (45%) had BMI in the range of 30-34.9 kg/cm^2 .49% patients were diabetics with 33 males and 16 females, and 41% were hypertensive with 27 males and 14 females. History of smoking was present in 59% patients . Previous history of stroke was observed in 6% patients with 4 males and 2 females. Mean uric acid level in patients on day 0 belonging to Killip class I was 4.4 mg/dl compared to 7.01 in Killip class II ,8.29 in Killip class III and 9.87 in Killip class IV. Mean serum uric acid levels on day 7 in patients with Killip class I is 4.67 and those with Killip class II is 6.62 mg/dl.Of the 100 patients, six expired during hospital stay and all 6 belonged to higher Killip class with serum uric acid levels in the highest quartile.*
Conclusion- *Hyperuricemia is an indicator of poor prognosis in acute MI. Serum uric acid can be used as a marker of short term mortality in acute myocardial infarction.*
Keywords- *Acute MI,Killip class, Serum uric acid,hyperuricemia, short term mortality,CVD.*

INTRODUCTION

Cardiovascular diseases (CVD) have been the leading cause of morbidity and mortality in India. Recent trends indicate that this group of diseases has escalated to younger age groups also. In India, cardiovascular diseases are significantly increasing in males and females in both urban and rural population[1]. As indicated by the data[5], the prevalence is now increased in rural areas also other than the clichéd urban areas indicating that as the disease matures and gets a stronger grip in the country, it will percolate to all categories of the population affecting the whole society. There is an increasing trend for reversal in the socioeconomic gradient for CVD, with the poor and disadvantaged having equal and sometimes higher burden of CVD and its risk factors[19].This could be due to the change in lifestyle, the pattern of dietary habits, lack of health care facilities etc. in the lower strata. In 1990, there were an estimated 1.17 million deaths from

CVD in India[3]. In addition to the high rate of CVD mortality in the Indian subcontinent, CVD manifests almost 10 yr earlier on average in this region as compared to the rest of the world[4] .

Uric acid is the final breakdown product of purine degradation in humans. Urates, the ionised form of uric acid, predominate in plasma extracellular fluid and synovial fluid, with 98% existing as monosodium urate at pH 7.4. In addition to the risk for gout and nephrolithiasis, there is increasing evidence that hyperuricemia, directly or indirectly may also be involved in the pathogenesis of CVD[5].

URIC ACID AND OXIDATIVE STRESS[20]-SUA in the early stages of atherosclerotic process is known to act as an antioxidant ,but unfortunately, later in the atherosclerotic process with elevated serum uric acid levels , the previously antioxidant becomes pro-oxidant[6] .

URIC ACID AND INFLAMMATION- Xanthine oxidase, the rate limiting enzyme for synthesis of uric acid, has been found localised in endothelial cells and smooth muscle cells of arteries. The resultant uric acid results in free radial injury to the vessel wall and contributes to development of degenerative vascular disease as well as worsening of acute thrombosis [7].

The aim of this study is to perform detailed clinical workup and record conventional risk factors of CVD among the 100 cases of acute MI. To estimate serum uric acid levels on day 0, and 7 and correlate these values with Killip class of patients to determine significant correlation between serum uric acid and prognosis.

MATERIALS AND METHODS

Study was prospective type conducted in MGM Medical College, Indore between March 2015 to August 2015. The study protocol was approved by M.G.M medical college ethics committee and written informed consent was obtained from all subjects prior to participation.

A total of 100 patients of acute MI admitted to the ICCU, Department of Medicine were included in the study after applying the below mentioned criteria.

INCLUSION CRITERIA-

1) Age>/=18 yrs
2) All new cases of acute MI patients having -acute chest pain within 12 hrs of presentation with ECG and TropI suggestive of STEMI or NSTEMI.

EXCLUSION CRITERIA-

1. Patients with atypical chest pain.
2. Patients with unstable angina.
3. Patients with psychosomatic illness, panic disorder, hysterical patients.
4. Patients with chronic kidney disease, gout or haematological malignancy.
5. Patients on drugs such as high dose salicylates, ethambutol, pyrazinamide, chlorthiazide etc.

METHODOLOGY OF DATA COLLECTION

1. Information was collected and workup of the cases was done as per standard proforma.
2. Relevant clinical workup including detailed history, general and physical examination, serial ECGs and relevant laboratory investigations were carried out in these patients.
3. Appropriate treatment was administered including thrombolysis, anticoagulation etc. as per standard ICCU treatment protocol, modified based on condition of patient.

INVESTIGATIONS

1. CBP including Hb%,TLC,DLC etc.
2. Baseline and subsequent serial ECGs.
3. 2D Echo Doppler
4. Random Blood Sugar/Urea/S.Creatinine
5. Serum uric acid on day 0,3 and 7.
6. Trop I on admission
7. Lipid profile

Statistical methods applied in this study are:

1. Cross tabs procedure (Contingency coefficient test)
2. ANOVA- Analysis of variance-two way.
3. Frequencies and percentages.
4. Descriptive statistics.

RESULTS

Table 1-Age distribution of 100 cases of acute MI

Age group	No. of cases	Percentage
<40	11	11.00
41- 50	18	18.00
51-60	37	37.00
61-70	23	23.00
71+ yrs	11	11.00
Total	100	100.00

Table 2 – Sex distribution of study population (n=100)

Sex	No. of cases	Percentage
Male	70	70%
Female	30	30%
Total	100	100%

Table 3 – BMI of study population

BMI	Frequency	Percentage
<18.5	0	0%
18.6-24.9	11	11%
25-29.9	42	42%
30-34.9	45	45%
>35	2	2%
Total	100	100%

Table 4 – Thrombolysis in study population

Thrombolysis	Male	%	Female	%	Total
No	16	22.86	8	26.67	24
Yes	54	77.14	22	73.33	76
Total	70	100.00	30	100.00	100

Table 5- Comparison of male and female with different risk factors

Factors	M	F	Total	%age	Chi-square	p-value
Diabetes	33	16	49	49	0.3190	0.5720
HTN	27	14	41	41	0.5630	0.4530
Stroke	4	2	6	6	0.0330	0.8550
Smoking	56	3	59	59	42.113	0.00001
Alcohol	20	0	20	20	10.6070	0.0010

Table 6- Comparison of day0, day 3 and day 7 with Killip class by Wilcox matched pairs test

Killip class	Day 0	Day 3	Day 7
Death	0	0	6
Class 1	57	65	89
Class 2	16	22	5
Class 3	14	6	0
Class 4	13	7	0
Total	100	100	100

Table 7- Comparison of Killip classes with serum Uric acid at day 0 by ANOVA (analysis of variance) test

KILLIP class	Mean	Std. Deviation
Class 1	4.40	0.78
Class 2	7.01	1.12
Class 3	8.29	0.50
Class 4	9.87	0.44
Total	6.07	2.22
F-value	236.2100	
p-value	0.00001*	
Pair-wise comparisons by Tukeys multiple posthoc procedure		
Class 1 vs Class 2	p=0.0001*	
Class 3 vs Class 3	p=0.0001*	
Class 1 vs Class 4	p=0.0001*	
Class 1 vs Class 3	p=0.0002*	
Class 1 vs Class 4	p=0.0001*	
Class 1 vs Class 4	p=0.0001*	

Table 8- Serum Uric acid distribution into quartiles on day 0 vs Killip class

URIC ACID LEVELS AND KILLIP CLASS ON DAY 0					
	<4.0 mg /dl	4.1-5.5mg/dl	5.6-7.0 mg/dl	>7 mg/dl	Total
Killip class-1	17	36	4	0	57
Killip class-2	0	1	5	10	16
Killip class-3	0	0	0	14	14
Killip class-4	0	0	0	13	13
	17	37	9	37	100

Table 9- Comparison of Killip classes with serum Uric acid at day 3 by ANOVA (analysis of variance) test

KILLIP class	Mean	Std. Deviation
Class 1	4.46	0.79
Class 2	7.09	0.89
Class 3	8.53	0.70
Class 4	9.43	0.80
Total	5.63	1.88
F-value	146.3145	
p-value	0.00001*	
Pair-wise comparisons by Tukeys multiple posthoc procedure		
Class 1 vs Class 2	p=0.0001*	
Class 1 vs Class 3	p=0.0001*	
Class 1 vs Class 4	p=0.0001*	
Class 2 vs Class 3	p=0.0002*	
Class 2 vs Class 4	p=0.0001*	
Class 3 vs Class 4	p=0.2000	

Table 10- Serum Uric acid distribution into quartiles on day 3 vs Killip class

URIC ACID LEVELS AND KILLIP CLASS ON DAY 3					
	<4.0 mg /dl	4.1-5.5mg/dl	5.6-7.0 mg/dl	>7 mg/dl	Total
Killip class-1	20	43	2	0	65
Killip class-2	0	2	7	13	22
Killip class-3	0	0	0	6	6
Killip class-4	0	0	0	7	7
	20	45	9	26	100

Table 11- Comparison of Killip classes with serum uric acid at day 7 by t test

Killip class	Mean	Standard deviation
Class 1	4.67	0.80
Class 2	6.62	1.01
Total	4.7	1.00
T-value	-4.7053	
p-value	0.00001*	

Table 12- Association between Killip classes at day 0 with status of mortality

Killip class day 0	Alive	Death	Total
Class 1	57	0	57
Class 2	16	0	16
Class 3	14	0	14
Class 4	7	6	13
Total	94	6	100
Chi-square=42.7173 p=0.00001*			

Table 14- Association between Killip classes at day 3 with status of mortality

Killip class day 3	Alive	Death	Total
Class 1	65	0	65
Class 2	22	0	22
Class 3	4	2	6
Class 4	3	4	7
Total	94	6	100
Chi-square=45.9643 p=0.00001*			

*p<0.05

Discussions

Kojima et al[8] in 2005 & M Y Nadkar et al[9] in 2008 showed that SUA correlates with Killip Class. We thus used these studies as reference to assess this tool of combining Killip Class with SUA levels as a prognostic indicator in patients with AMI. This study was done in 100 patients with AMI admitted to ICCU wards / Medicine Department of MGMMC & MYH, Indore. These patients were assessed for uric acid and Killip class on day 0, day 3, day 7 of admission.

Total 100 patients were enrolled in the study, age of the patients varied from 29 years to 75 years .Mean age of patients was 54.9±11.59 yrs. This correlated with other previous studies by S Agarwal et al[10], Gandaiah et al[11], M Y Nadkar et al[9]. In our study out of 100 patients enrolled 70% patients were male, 30% patients were female. Majority of the patients were male .This finding is in concurrence with other previous studies[15]. Previous studies have also shown that Myocardial infarction is common in males compared to females. It was found that there was no significant difference in uric acid levels with regards to sex of the patients (Chi-square=5.2631 P = 0.2612). However in the study done by Dae Woo Hyun et al in 2007 showed that SUA levels were better predictor of cardiovascular events in male patients with CAD than females. This was proposed to be due to the protective action of estrogen up to menopause following which uric acid levels rise in females also. This can probably explain the gender insignificance in our study as majority of the women who presented with AMI were postmenop-ausal. In our study we found statistically significant difference in uric acid levels between hypertensives and non hypertensives .This correlates with Kojima et al[8] Sokhanvar et al[12] study. This finding did not correlate with other studies like MY Nadkar et al, Shetty et al[13], S Agarwal et al[10] who found no statistical significance in uric acid levels between hypertensives and non hypertensives. In our study 49% patients were diabetics. It was found that hyperuricemia is significantly associated with diabetes mellitus. (t=4.1682, p=0.0001 on day 1; t=3.1784, p=0.0020 on day 3 and t=3.5805, p=0.0006 on day 7). This is in agreement with findings of Safi et al[14] which showed significant relationship between diabetes and serum uric acid level. This is contrary to studies done by Kojima et al [8], M Y Nadkar et al[9], Gandaiah et al[11] found no significant difference in uric acid levels. In our study 56 patients had history of smoking and 3 patients had history of tobacco chewing. We found statistically significant difference in uric acid levels

between smokers & nonsmokers (chi square 42.1130, p =0.00001*).In our study the mean uric acid on the day of admission in males was 6.13±2.3mg/dl and 5.94±1.96mg/dl (p=0.6943). There is no statistical difference between the mean uric acid levels of males and females. This finding correlates with Gandaiah et al[11] & Shetty et al[13].Mean uric acid levels were higher on day of admission in our study as compared to mean uric acid level on day7.This finding correlates with Shetty et al[13] and S Agarwal et al[10],however it does not correlate with M Y Nadkar et al[9].It can be explained that in our study on day 7 all patients belonged to Killip class 1 or 2,hence lower mean uric acid levels.In our study on day 0, 57% belonged to Killip class I, 16% belonged to Killip class II,14% belonged to Killip class III &13% belonged to Killip class IV. This finding correlates with findings in with M Y Nadkar et al[9] & Gandaiah et al[11], herein on day of admission majority of patients belonged to Killip class I.We found that on all days, with increasing Killip class there is increasing mean uric acid level. We found statistically significant difference (p<0.00001) on day0,3 and 7.Out of 100 patients included in the study 6 patients expired during 7 day follow up all of whom belonged to Killip class IV on admission. These patients expired between day 3 and 7, their mean uric acid was>9 mg/dl. Thus in our study mortality was high in patients with higher Killip class with higher Killip classes having higher mean uric acid levels. Therefore it shows that serum uric acid concentration is significantly correlated with Killip class and mortality. These findings correlate with previous studies i.e.M Y Nadkar et al[9], Gandaiah et al[11], Shetty et al[13]& S Agarwal et al[10].

CONCLUSION

From our study, we conclude that serum uric acid levels are correlated with Killip class and patients with higher Killip class have higher SUA levels in acute MI. Hyperuricemia is an indicator of poor prognosis in acute MI. Serum UA can be used as a marker of short term mortality in acute MI.SUA levels were elevated in systemic hypertension and DM patients with acute MI in our study. Serum uric acid is an economical biomarker that is readily, quickly and reliably obtainable and thus along with Killip's classification should be considered for risk stratification in patients with AMI. However, this study is limited by relatively small study population and needs to be supplanted by other similar studies.

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