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Research Article

Serum Uric Acid as a prognostic biomarker and its correlation with Killip Class in Acute Myocardial Infarction

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Abstract

Introduction: Uric acid has been proven to be a negative prognostic indicator in patients with acute myocardial infarction and heart failure. There is a need to find a simple, less expensive but accurate marker that could be use in rural areas where fibrinolytic treatment is the first choice of acute reperfusion therapy.
Materials and Methods: 80 patients presenting with acute myocardial infarction were included in the study and serum uric acid levels and Killip Class was assessed on Day 0,3 and 7.
Results: Serum uric acid levels were raised in patients who presented with higher Killip Class on admission and all the 6 patients who succumbed belonged to either Killip Class 3 or 4 at presentation with a serum uric acid level of more than or equal to 7mg/dL.
Conclusion: Serum uric levels are raised during an episode of myocardial infarction and more so when the patient is in heart failure. There is a positive correlation between rising serum uric acid levels with higher Killip Class at the time of admission. Thus uric acid can be used as a prognostic indicator in patients presenting with myocardial infarction more so if they are in heart failure.
Keywords: Heart Failure, Killip Class, Myocardial Infarction, Uric Acid

1. Introduction

Uric acid has several effects of potential interest in cardiovascular diseases (CVD). Though it acts as a potent antioxidant, is also promotes oxidative stress. Its action on vascular smooth muscle and mononuclear cells explains its role in pathophysiology of CVD. Increased serum uric acid (SUA) levels is linked to various CVD risk factors like hypertension, dyslipidemia, diabetes, metabolic syndrome thus making it difficult to assess if it was the cause or effect of such conditions.[1,2] Acute myocardial infarction (AMI) is the most dramatic manifestation of coronary artery disease (CAD). Though high SUA has been indicated as a risk factor for CAD, it is also an independent prognostic factor for occurrence of AMI, fatal MI, sudden cardiac death. A recent retrospective analysis from Japan showed a univariate associate between higher SUA on admission & higher 30 day mortality in AMI patients.[3] Killip Classification is a simple clinical tool constructed by Killip & Kimbal, to clinically stratify patients in heart failure. They were classified into four classes based on clinical examination. Patients with higher Killip Class on admission for AMI showed more severe angiographic CAD.[4] Though many cardiac biomarkers are now being assayed, occasionally there is a need to find a simple & accurate prognostic marker in developing countries where fibrinolytic therapy is still the first choice of reperfusion therapy either due to non-availability of percutaneous coronary intervention or due to financial constraints.

2. Materials & Methods

A total of 80 patients more than 18 years of age who presented with AMI (ST elevation & non ST elevation) were included in this study which was conducted from June 2010 to June 2012 at a our tertiary care hospital. The diagnosis of AMI was done based on clinical history, examination, ECG changes & rise in biochemical markers. Any patients with conditions known to elevate uric acid levels like chronic kidney disease, gout, haematological malignancies hypothyroidism etc. were excluded from the study. Also patients on hyperuricemic drugs like salicylates (more than 2g/d), diuretics, ethambutol, pyrazinamide & chronic alcoholics were excluded. A detailed history & physical examination with special reference to Killip Class was also carried out. Serum uric acid was estimated on admission (Day 0), Day 3 & Day 7.Killip Class was also assessed & recorded on these 3 days. The institutional ethics committee approval was also obtained. A detailed statistical analysis was carried out. Levels of SUA on Day 0 & Day 7were compared using the paired "t" test. SUA & Killip Class was compared with coefficient of correlation.

3. Results

Our study included 80 patients who presented with AMI (STEMI and NSTEMI) out of which 55 were males & 25 were females. Majority of the patients (22 males & 12 females) were more than 60 years of age (Table 1).

Table 1: Age & Gender Distribution

Age (yrs)	Male	Female
Less than 40	5	-
41-50	12	2
51-60	16	11
More than 60	22	12
Total	55	25

P= 0.136 (Not Significant)

There were totally 42 hypertensives, 27 diabetics, 31 smokers & 5 patients had a past history of IHD. Out of 80, 66 of them presented with STEMI whereas 14 of them presented with NSTEMI. 27 patients had left ventricular dysfunction on admission as assessed by echocardiography (Table 2).

Table 2: Baseline Characteristics, (n=80)

Characteristics	Number of patients
Hypertension	42
Diabetes	27
Past h/o IHD	5
Smoking	31
Killip Class: 1 2 3 4	D0 D3 D7 25 42 61 35 25 13 13 05 - 05 07 03
CKMB	<100 >100 71 29
STEMI	66
NSTEMI	14
LV Dysfunction	27
Uric Acid (mean +SD)D0	6.18 ± 1.3
Uric Acid (mean +SD)D7	5.52 ± 1.4

Basic demographic data was analysed and there was no significance in SUA levels with respect to age, gender, hypertension, diabetes or past history of IHD. SUA were comparable on Day 0 & Day 7 in all the patients and on both the days SUA was higher in patients who were in higher Killip Class (P<0.05). Three patients who died between Day 0 & Day 3 belonged to Killip Class 3 and 4 and presented with SUA levels more than 7mg/dL. Three patients succumbed between Day 3 & Day 7 who belonged to Class 1 and 2 also had persistingly high uric acid levels. All the six patients who expired had moderate to severe left ventricular systolic dysfunction with high serum uric acid levels (more than 7mg/dL). Out of the study group, there were 22 patients who had a creatinine level of more than 1.2mg/dl on admission with no past history of renal disease. (Table 3 & 4)

Table 3: Killip Class versus Uric Acid levels on Day 0

Killip Class	Uric Acid(mg/dL)			Total
	< 5	5-6.9	>7	
1	-	25	-	25
2	-	27	10	37
3 (*1)	-	3	8	11
4 (*2)	-	1	6	7
Total	0	56	24	80

*1= number of mortality cases, P< 0.001

Table 4: Killip Class versus Uric Acid levels on Day 7

Killip Class	Uric Acid(mg/dL)			Total
	< 5	5-6.9	>7	
1 (*1)	48	12	-	60
2 (*2)	4	10	-	14
3	-	-	-	-
4	-	-	-	-
Total	52	22	0	74

*1=mortality cases, P< 0.001

3. Discussion

SUA levels have been known to go up in cardiac failure & Kojima *et al*[5,6] in 2005 showed that SUA correlates with Killip Class. We thus used this study as reference to assess this tool of combining Killip Class with SUA levels as a good predictor or mortality in patients with AMI. Out of the 66 patients who presented with STEMI, 62 patients were thrombolysed and 4 were not due to either contraindications or delayed presentation. The demographic characteristics and presentation along with mean SUA on Day 0 & Day 7 are shown in Table 1.

Chiarra Lazzeri *et al*[7] in 2012 also showed similar results in their study of 856 patients with STEMI where SUA was in the third centile in patients belonging to Killip Class 3 and 4 and that SUA was an independent factor to predict mortality in the cardiac care unit. In our study, most of our patients were beyond 60 years but there was no correlation of SUA with age, gender and SUA (P=NS). However in the study done by Dae Woo Hyun *et al*[8] 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 postmenopausal. As in our study, Sokhanvar and Maleki[9] in 2007 in Iran also studied 256 patients who presented with AMI had a significant correlation between hyperuricemia, hypertension and men but not so in the case with other risk factors like diabetes,

dyslipidemia or smoking. However another study done in north eastern India by Mriganka Baruah *et al*[10] in 2012 showed that all their patients who presented with AMI had high SUA and CRP (C-reactive protein) levels along with significantly low HDL (high density lipoprotein) values (P< 0.05). Killip Class at presentation during an episode of AMI is known to be associated with higher 30 day mortality. In our study, 35 patients out of 80 presented in Killip Class 2. When assessed on Day 0, most of the patients had SUA between 5-6.9 mg/dL and belonged to Killip Class 1 and 2. There were 3 mortality cases between Day 0 and Day 3 and all of them fell either in Class 3 or 4 and had a presenting SUA more than 7mg/dL. When assessed on Day 7, none of the patients were in Class 3 or 4 & there were 3 additional mortality cases between Day 3 and Day 7 who had SUA less than 7mg/dL. All the 6 mortalities were the patients who presented in either Class 3 or 4 and who had SUA more than 7mg/dL on admission.

There was significant correlation between higher Killip Class and SUA in all patients assessed on Day 0 and Day 7 as seen in tables 3 and 4 (P<0.001). Younes Nozari and Babak Garaiely[11] in 2010 published a study done in 188 patients presenting with AMI where they found significant correlation between heart failure and SUA. Patients who belonged to Killip Class 4 had the highest SUA levels and the explanation given was due to tissue hypoperfusion in higher Killip Classes. They finally concluded that SUA could be used as a predictor for the possibility of occurrence of severe heart failure in patients with AMI. Ayman El-Manyar *et al*[4] in 2010 studied 6689 patients presenting with non ST elevation acute coronary syndrome and showed that patients presenting in Killip Class 2, 3 and 4 had higher risk profiles and rates of major adverse cardiac events across acute coronary syndrome; however in this study the progression between the Killip Class during the hospital course was not documented.

Andrea Papp *et al*[12] in 2011 presented a poster based on their study on 19,158 patients presenting with AMI out of which 3.9% had cardiogenic shock (Killip Class 4) and this group had the highest in-hospital mortality. Sinisa Car and Vladimir Trkulja[3] studied 621 MI patients whose SUA values were analysed. Their study also demonstrated that an "on-admission" high SUA was associated with higher in-hospital mortality, 30 day mortality and poorer long term survival after AMI. They also found an independent cross sectional association between higher creatinine and SUA levels. They finally suggested that risk stratification systems for AMI patients like GRACE would probably benefit from inclusion of SUA in addition to serum creatinine.

Thus based on pooled estimates and individual studies, high SUA on admission (range of hyperuricemia or high normal values) predicts higher short term and medium/long term mortality and incidence of MACE in AMI patients[1].

4. Conclusion

Till date several studies have evaluated the predictive value of on-admission SUA and its outcomes in AMI; it has been shown to have an adverse short and long term outcome in patients. From our study, we conclude that SUA levels are correlated with Killip Class and patients with higher Killip Class have higher SUA levels and that SUA and Killip Class are influenced by previous myocardial infarction. There are many developed countries that are using pharmacoinvasive approach for their AMI system of care (fibrinolytic treatment in pre-hospital setting with an invasive procedure backup) but in slow developing countries like India, SUA is an economical biomarker that is readily, quickly and reliably obtainable and thus along with Killip's Classification, should be incorporated for risk stratification in patients with AMI.

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