ROLE OF URIC ACID AS A PROGNOSTIC FACTOR IN ACUTE MYOCARDIAL INFACRTION

Md Zahangir Alam Chowdhury[1] Mirza Golam Sarwar[2] Md Abdul Jalil[3]

Summary

Uric acid has been proven to be a negative prognostic indicator in patients with acute myocardial infarction and heart failure. So the aim of the present study is to evaluate the uric acid as a predictor of outcome after acute myocardial infarction. A total of 120 patients presenting with acute myocardial infarction were included in the study where case were the AMI with heart failure and arrhythmia and control were the only Ami patients. Patients were evaluated in relation with clinical features, risk factors, complications, heart failure with Killip Class and serum uric acid level. Sociodemographic profiles of the study populations were matched in case and control group. Regarding different biochemical variables of case and control where serum uric acid was found significantly higher among the case group than the control ($p<0.05$). Among different risk factors of MI where hypertension, smocking, DM and sedentary lifestyle were found common in both case and control group showing the different signs of the case and control where all were more or less common among both groups. Serum uric acid level and arrhythmia class among the case group. Regarding prognostic evaluation of uric acid after MI where complete recovery, arrhythmia, recurrent MI, hospital stay and death was significantly found associated with risk stratification. 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.

1. Assistant Professor of Physical Medicine & Rehabilitation
Chattagram Maa-O-Shishu Hospital Medical College, Chittagong.
2. Medical Officer of Medicine
Shahid Ziaur Rahman Medical College, Bogra.
3. Senior Consultant of Cardiology
Chittagong General Hospital, Chittagong.

***Correspondence:** Dr. Md. Zahangir Alam Chowdhury
Email : drzahangiralam@gmail.com
Cell: 01845 697110

Key words

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Introduction

In humans, Uric Acid (UA) is the end product of purine catabolism [1]. Its serum levels (SUA) governed by the production (Liver) and elimination (Mainly the kidney) rates, are influenced by genetically determined factors (eg. Activity of synthesizing enzymes or renal transporter systems) racial and demographic characteristics (eg. Sex, gonadal function in women, obesity) diet (eg. Purine-rich foods, fructose, alcohol) habits (eg. SUA is lower in smokers and increases after quitting) morbidity (eg. Renal failure, malignancies) and medications (eg. Diuretics, cytotoxic agents) [1-4]. The role of serum uric acid in cardiovascular and renal diseases has been intensively investigated, although not without controversy [5]. On the molecular and cellular level, uric acid exerts a number of effects of potential interest. It is one of the most important antioxidants in plasma, but at high concentrations it may promote oxidative stress, it may induce endothelial dysfunction and vascular smooth muscle cell proliferation in vitro, platelet aggregation and micro-inflammation, increased uric acid causes tubulointerstitial inflammation, morphological and functional changes in the glomeruli and renal arteriole and increased salt sensitivity [3,5]. There is now sufficient evidence to consider increased serum uric acid as an etiological factor in “hyperuricemic hypertension” or “salt-sensitive kidney dependent hypertension” [3,5].

Acute Myocardial Infarction (AMI) is the most dramatic manifestation of the Coronary Artery Disease (CAD). High serum uric acid has been indicated as a risk factor for CAD [6]. Less is known

about serum uric acid as a potential prognostic/risk factor for outcomes in patients affected specifically by AMI. A recent retrospective analysis from Japan (The Japanese Acute Coronary Syndrome Study) showed there is a close correlation between serum uric acid concentration and Killip classification (Suggestive of the severity of heart failure) in patients of acute myocardial infarction [7]. Patients who developed short-term adverse events had high uric acid concentrations. In that study, Serum uric acid levels, Killip classification, 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 [8].

Though many cardiac biomarkers are now being assayed for AMI, There is a need to find a simple, less expensive but accurate prognostic marker in developing countries like ours 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. Uric Acid may be a causative marker of mortality in patients who have AMI. In this regard, improvement of coronary reperfusion alone may be less effective in improving heart failure and decreasing mortality rate in patients who have AMI. Adjunctive therapy to decrease serum Uric Acid level in addition to coronary reperfusion may have a favorable effect on mortality in patients who have AMI.

Materials and methods

Present study was conducted in the Department of Cardiology, in a tertiary care hospital during a period of e duration of the study was 6 (Six) months. Sampling technique was purposive where case was sixty in number and control was sixty in number. Inclusion criteria were i) Age>18 yrs, ii) Both male and female iii) Patients to have verified as Acute Myocardial Infarction who have been admitted and laboratory evaluated within 48 hours from the symptom onset. And exclusion criteria :-

i) Conditions known to elevate uric acid level
ii) Patients presented after 48 hours from the onset of symptoms
iii) Patients who were dead on admission
iv) Patient refused to undergo our study.

A questionnaire and an informed written consent form (English & Bengali) was prepared. The cases were selected on the basis of inclusion & exclusion criteria, questionnaire were be filled with informed written consent. Relevant investigations were done.

Acute Myocardial Infarction was defined as the detection of a rise and/or fall of cardiac biomarker values, with at least one of the values being elevated (ie, > 99th percentile upper reference limit, URL).The preferred cardiac biomarker of necrosis is the highly sensitive and specific cardiac troponin. In addition, at least one of the five following diagnostic criteria should be meet:

i) Symptoms of ischemia
ii) New (or presumably new) Significant ST/T wave changes or Left Bundle-Branch Block (LBBB)
iii) Development of pathological Q waves on ECG
iv) Imaging evidence of new loss of viable myocardium or regional wall motion abnormality
v) Identification of intracoronary thrombus by angiography.

All data was recorded systematically in preformed data collection form (Questionnaire) and quantitative data were expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. During analysis Chi-square test was done for the comparison of qualitative variables and student 't' test was used for the comparison of continuous variables. Multivariable linear regression was used to assess the significance of covariate-adjusted relations between the continuous variables. Multivariate logistic regression was performed to measure the odds ratio among qualitative variables. Regression models were crude, age and sex adjusted and fully adjusted. Statistical analysis was performed by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-20) (SPSS Inc, Chicago, IL, USA). A p value of 0.05 (Two-tailed) or a 95% Confidence Interval (CI) not including the null point was regarded as statistically significant. Different statistical methods were applied for data analysis. Qualitative variables were analyzed by frequency, percentage and chi squared test and quantitative variables were analyzed by mean, standard

deviation, 't' test and ANOVA etc. Basic principles of research ethics according to 52nd WMA declaration of Helsinki 2000 & CIOMS guide lines will be maintained during the research processes. An informed written consent will be taken from the participants after full explanation regarding the study. An ethical clearance certificate will be taken from concern authorities of the institute.

Results

Table I : Characteristics of cases and control

Variables		Case (%) (N=60)	Control (%) (N=60)	P value
Sex Distribution	Female	23 (38.3)	24 (40.0)	0.01
	Male	37 (61.7)	36 (60.0)	
Mean Age	Total	39.9 ± 9.8	41.10 ± 11.1	
	Male	38.6 ± 5.7	39.0 ± 7.7	0.01
	Female	44.4 ± 6.9	45.0 ± 5.8	
Marital Status	Married	54 (90.0)	55 (91.6)	0.03
	Others	6 (10.0)	5 (9.4)	
Occupation	Housewife	20(33.3)	21(35.5)	
	Business	23(38.3)	19(31.6)	0.87
	Service	5(8.3)	9(15.0)	
	Others	12(20.0)	11(18.3)	
Socio-Economic Status	Upper	9 (6.6)	8 (13.6)	0.012
	Middle	10 (16.4)	12 (20.0)	
	Lower	41 (77.0)	40 (68.4)	

Case: Patients with AMI with MACE (Major Adverse Cardiac Events) (In Hospital) Control: patients with AMI without complications.

Table I showing that there were significant differences between the case patients and control subjects with regard to gender, age, marreital status and socieconomic condition.

Table II : Comparison of biochemical changes between Control and AMI patients

Variables	Control (%) n = 60	Case (%) n = 60	p-value
Fasting Glucose (mg /dl)	114±16.90	120±22.30	0.008
Creatinine (mg /dl)	1.11±0.22	1.12±0.30	0.25
Total cholesterol (mg/ dl)	204±10.7	201±21.8	0.19
Triglyceride (mg/dl)	169.0±34.96	178.65±120.8	0.002
HDL-cholesterol (mg /dl)	37.58±8.86	34.95±10.12	0.163
LDL- cholesterol (mg/dl)	130.0±34.96	134.0±34.96	0.002
Uric acid (mg/dl)	4.94±1.10	6.56±1.56	0.014

Table II showing the analysis of different biochemical variables of case and control where serum uric acid was found significantly higher among the case group than the control ($p<0.05$)

Table III : Serum uric acid level and arrhythmia class among the case group

Type	4.0 (mg/dl)	4.1-5.5 (mg/dl)	5.6-7.0 (mg/dl)	>7.0 (mg/dl)	Total
AF	12	4	3	4	23
VT	4	3	3	1	11
VF	3	2	1	1	7
AVB	2	1	1	0	6
None	4	2	5	4	15
Total	25	12	13	10	60

p=0.001(Calculated by Chi square test where Chi square value is 19.680).

AF: Atrial Fibrillation VT: Ventricular Tachycardia VF: Ventricular Fibrillation AVB: Atrioventricular Block.

Table III showing the distribution of heart different types of arrhythmia with levels of uric acid among the case where more patients had AF with change of uric acid level.

Table IV : Multivariate Analysis of uric acid as a prognostic factor outcome after AMI in case and control

Variables	Adjusted Odds Ratio (95% CI)	p - value
Complete recovery	4.87 (2.102 – 9.220)	0.022
Arrhythmia	6.002 (1.386 – 17.359)	0.010
Recurrent MI	2.392 (.491 – 4.457)	0.003
Long term hospital stay	3.452 (1.285 – 20.134)	0.011

Table IV showing prognostic evaluation of uric acid after MI where complete recovery, arrhythmia, recurrent MI, long term hospital stay was significantly found associated with risk stratification.

Discussion

Present study was done in the Department of Cardiology in a tertiary care hospital where 60 patients of AMI with heart failure and arrhythmia were selected as case and 60 patients with acute myocardial infarction were taken as control. Serum uric acid level were measured in both groups and compared for outcome.

In the present study more patients were male than female which signify male gender is a risk factor of AMI. In different study done in outside also showed higher male to female distribution.

Regarding occupation most of the female were found as housewives and others had diverse occupation. As sample were collected by purposive sampling these may not represent the actual population scenario of Bangladesh.

In our study there significant difference in uric acid levels between case and control patients, It was also found in a study done earlier [9]. 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. This is different than other studies which showed that hypertensive patients had more hyperuricaemia [9]. A total of 27 patients in case and control patients were known diabetic in our study. Non-diabetic and diabetic patients had comparable serum levels. This finding is consistent with study by Tuomilheto et al in which there was no significant association between serum uric acid level and diabetic status [10]. However, this finding is in contrast to other study by Safi et al which showed that hyperuricemia is significantly associated with type 2 diabetes mellitus [11]. There was significant difference between serum uric acid concentration at the time of admission and h/o ischemic heart disease. 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 as seen in study by Kojima et al [9].

Conclusion

Thus in conclusion we can say that serum uric acid levels are higher in patients of acute myocardial infarction with complication as compared to AMI without complication. 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.

Disclosure

All the authors declared no competing interest.

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