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Prognostic significance of serum uric acid in patients with acute coronary syndrome undergoing coronary angiography

Cardiology

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ABSTRACT

Background: Role of serum uric acid level as a prognostic marker in patients with acute coronary syndrome (ACS) is debatable. Aims and objectives: To evaluate the association of serum uric acid level on outcome in patients with acute coronary syndrome undergoing coronary angiography.

Material and methods: 142 patients with acute coronary syndrome were enrolled. Upon overnight fasting serum uric acid level was measured. One year follow-up was done and outcomes were evaluated in terms of major adverse cardiovascular events (MACE).

Results: The mean uric acid level was 7.11 mg/dl. In univariate analysis, serum uric acid level was found to be associated with adverse cardiovascular events HR1.283 (95% CI 1.169-1.408; P value 0.007) along with diabetes mellitus, complexity of coronary lesions and left ventricular dysfunction. However, multivariate cox regression analysis showed that uric acid is not independent predictor of adverse cardiovascular events HR1.055 (95% CI 0.953-1.169; P value 0.597).

Conclusion: Elevated serum uric acid level is not an independent predictor of adverse outcome in patients with acute coronary syndrome.

KEYWORDS

Acute Coronary Syndrome, Uric Acid, Prognostic Value

INTRODUCTION:

Increased serum uric acid level is found to be associated with endothelial dysfunction, free radicals generation and thrombus formation, all promoting atherosclerosis.[1] However, prognostic role of uric acid in acute coronary syndromes (ACS) patients is uncertain.

The present study is carried out to investigate the association between serum uric acid levels and outcome across the whole spectrum of patients with ACS undergoing coronary angiography.

Methods:

Study Design:

One hundred forty two patients who presented, in the department of Cardiology, NEIGRIHMS, with acute coronary syndrome {defined by typical chest pain, electrocardiographic changes, elevated serum biomarkers (creatine kinase, creatine kinase MB and/or troponin I) and echocardiographic evidence of regional wall motion abnormality} were enrolled for the study. Patients with renal disease, leukemia, lymphoma, hemolytic anemia, alcoholics and those receiving chemotherapy and radiation therapy were excluded from the study. One year clinical follow-up was done and outcomes were evaluated in terms major adverse cardiovascular events (MACE). Participation of all subjects was voluntary and written, informed consent was obtained from each subject. This study has been approved by institutional ethical committee.

Baseline measurements and Definitions:

After history and physical examination, all routine investigations along with serum cardiac markers, lipid profile, C-reactive protein were done. Blood for serum uric acid were collected, after overnight fasting, in plane vial and estimation was done by Uricase method using Beckman Coulter model number AU 2700 random access automated analyser. Left ventricular ejection fraction was measured using modified Simpson's method. Diabetes mellitus was diagnosed in patients with a history of oral antidiabetic or insulin medication or fasting blood glucose >126 mg/dl at study entrance. Hypertension was diagnosed by the Joint National Committee VII criteria on hypertension or currently taking antihypertensive treatment; dyslipidemia was diagnosed in patients with a history of lipid lowering medication or a total cholesterol level >200 mg/dl, LDL >130 mg/dl, HDL<40 mg/dl, triglyceride >150 mg/dl. Coronary artery disease was confirmed by the presence of coronary stenosis ≥70% luminal obstruction in ≥1 of coronary arteries. Infarct related artery was graded according to TIMI classification.

MACE was defined by recurrent angina, re-infarction, stent thrombosis (acute/subacute/late), urgent revascularization, heart failure and cardiovascular mortality. Re-infarction was defined as new ST-T changes and serum creatine kinase MB level five times the upper limit of normal. Stent thrombosis was defined as an abrupt onset of cardiac symptoms, elevation of biomarker levels or electrocardiographic evidence of myocardial injury or angiographic evidence of a flow limiting thrombus near the previously placed stent. Cardiovascular mortality was defined as unexplained sudden death, death due to acute myocardial infarction, heart failure and/or arrhythmia.

Statistical analysis:

Continuous variables were expressed as mean±standard deviation and percentages were used for categorical variables. Chi-square test was used to compare categorical variables and Z test was used to compare differences between the high and low uric acid group. Survival cumulative was assessed by Kaplan-Meier method. A multiple linear regression model was used to identify the independent correlates of uric acid level. A p-value of <0.05 was regarded as a statistically significant.

RESULTS:

Baseline characteristics of all patients are shown in table 1. The mean uric acid level was 7.11± mg/dl.40.1% of patients were diabetic and dyslipidemia was present in 34.5% of patients. 37.3% of patients had triple vessel disease whereas 27.5% of them had moderate LV dysfunction (Table 1).

Table 1: Baseline Characteristics of all patients

Variabes	All patients
Age, mean, years	57.13±7.674
Male, number, %	109 (76.8)
Risk factors, number, % HTN DM Dyslipidemia Smoking	66 (46.4) 57 (40.1) 49 (34.5) 57 (40.1)
Presentation, number, % STEMI NSTEMI UA	88 (62) 25 (17.6) 29 (20.4)

LV function, number, % Normal Mild dysfunction Moderate dysfunction	25 (17.6) 78 (54.9) 39 (27.5)
Coronary angiography, number, % SVD DVD TVD	52 (36.6) 37 (26.1) 53 (37.3)
MACE	30 (21.1)
Uric acid, mean, mg%	7.11

In univariate analysis, serum uric acid level was found to be associated with adverse cardiovascular events HR1.283 (95% CI 1.169-1.408; P value 0.007) along with diabetes mellitus, complexity of coronary lesions and left ventricular dysfunction (Table 2). However, multivariate cox regression analysis showed that uric acid is not independent predictor of adverse cardiovascular events HR1.055 (95% CI 0.953-1.169; P value 0.597) (Table 3).

Table 2: Univariate predictors of cardiovascular events

Variables	HR (95% CI)	P value
Age	1.021 (0.976-1.069)	0.367
Male	0.972 (0.417-2.265)	0.947
HTN	1.769 (0.845-3.705)	0.13
DM	2.734 (1.3-5.748)	0.008
Dyslipidemia	1.266 (0.610-2.629)	0.526
Smoking	1.572 (0.768-3.215)	0.216
NSTEMI	10.020 (4.263-23.547)	0
UA	2.359 (0.818-6.8)	0.112
LV dysfunction	0.266 (0.177-0.398)	0.001
DVD	0.068 (0.032-0.141)	0
TVD	0.198 (0.115-0.34)	0.003
Serum uric acid	1.283 (1.169-1.408)	0.007

Table 3: Multivariate predictors of cardiovascular events

Variables	HR (95% CI)	P value
HTN	1.037 (0.68-1.58)	0.93
DM	1.216 (0.782-1.89)	0.658
Dyslipidemia	1.242 (0.812-1.900)	0.61
Smoking	1.495 (1.00-2.24)	0.318
NSTEMI	0.446 (0.236-0.845)	0.206
UA	3.047 (1.79-5.186)	0.036
LV dysfunction	0.705 (0.438-1.137)	0.465
DVD	0.128 (0.056-0.294)	0.014
TVD	0.232 (0.127-0.425)	0.016
Serum uric acid	1.055 (0.953-1.169)	0.597

Survival analysis:

For survival analysis, patients were divided into four groups on the basis of serum uric acid level, group 1 (3.5 mg/dl to <6.05 mg/dl), group 2 (6.05 mg/dl to <6.7 mg/dl), group 3 (6.7 mg/dl to <8 mg/dl) and group 4 (8 mg/dl to <12.7 mg/dl)

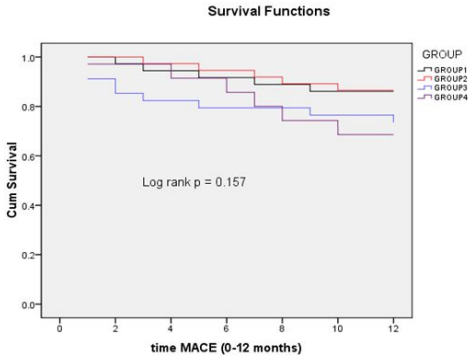

Fig 1: Kaplan-Meier survival curve. Quartiles of uric acid and survival of patients with acute coronay syndrome Cum survival=cumulative survival.

However, Kaplan-Meier survival curve showed no difference in cumulative survival between patients with different uric acid level groups. (log-rank test, p=0.157) (Figure 1).

Discussion:

There is difficulty in determining whether uric acid per se should be considered a cardiovascular risk. A number of epidemiological studies have suggested that uric acid is not independent of other established risk factors, especially hypertension, for the development of cardiovascular disease.[2] In the Framingham Study, serum uric acid levels were not independently associated with risk of coronary heart disease.[3] Furthermore, mechanism by which uric acid cause cardiovascular disease is not apparent. The present study also did not find independent association between serum uric acid level and cardiovascular outcome.

However, some previous studies have shown strong association between serum uric acid level and adverse outcomes in ischemic heart disease especially in patients with heart failure.[4]Ndrepepa G et al[5] reported increased 1 year mortality in ACS patients with raised serum uric acid undergoing percutaneous coronary intervension. Lazzeri and colleagues found serum uric acid to be a significant and independent predictor of mortality in patients with ST-elevation myocardial infarction.[6]

Limitations:

The present study was done enrolling a small number of patients with a short follow-up. Therefore, the result needs to be confirmed by a larger study with a longer follow-up.

Conclusion:

Elevated serum uric acid level is not an independent predictor of adverse outcome in patients with acute coronary syndrome..

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