Original Article

Prognostic value of Serum Uric Acid in predicting Hospital mortality and morbidity in Patient with acute Coronary syndrome

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Abstract

Background: Uric acid is an independent risk factor for cardiovascular disease. At present, Coronary artery disease (CAD) in one of the leading cause of death in the worldwide also in Bangladesh. Although studies were conducted abroad regarding association of serum uric acid with in hospital out comes in patient with acute coronary syndrome. No data is yet available to show the association in our country.

Objectives: The objective of the study was to assess the association of serum uric acid level on admission with in hospital outcomes of the patient, with acute coronary syndrome.

Materials and Methods: This study was carried out in the department of cardiology, Dhaka National Medical Institute Hospital, Dhaka from October, 2014 to September 2015. In this case series study, 102 diagnosed Patients of acute coronary syndrome free from gout, renal disease, hepatic disorder and other malignant conditions were enrolled by non random sampling. Serum uric acid of all subject was measured within 24 hours of presentation. During hospital stay the outcome (good and bad) were observed in all subjects.

Result: Patients with higher serum uric acid (SUA>6.5mg%, Group-ll) were compared with patients with lower serum uric acid (SUA<6.5mg%, Group-l). In Group I (n=60), good recovery, morbidity and mortality were found in 43 (65.2%), 21 (31.8%), 2 (3.0%) Patients and in Group II (n=42), good recovery, morbidity, mortality were 13 (31%), 23 (54.8%) and 6 (14.3%) patients respectively. In group II Patients having high Serum uric acid concentration had low good recovery but high morbidity and mortality compared to group I Patients. In group I (n=60), good outcome and bad outcome was found in 43 (65.2%), and 23(34.8%) patients and in group II (n=42), those were in 13 (31%) and 29 (69%) patents. Logistic regression analysis of serum uric acid concentration of study subjects were done considering uric acid as independent variable but outcome as dependent variable. It was shown that the odds ratio of mortality was 5.38 (95% CI p<0.007), odds ratio of morbidity was 4.10 (95% CI p<0.001) and odds ratio of bad outcome was 4.67 (95% CI p<0.001). This finding indicates a patient having high uric acid had 5.38 times increased bad outcome that patients having low serum uric acid concentration.

Conclusion: On admission serum uric acid estimation is a good predictor of in hospital bad outcome in patients with acute coronary syndrome. As it is a cheap and noninvasive procedure, it can be routinely practiced in cardiac emergency department for risk stratification of patients.

Key words: Coronary artery disease, Serum uric acid, Acute Coronary Syndrome, Mortality, Morbidity.

Introduction:

Coronary artery disease (CAD) is the most prevalent manifestation of cardiovascular disease and is associated with high mortality and morbidity.[1] Among the CADs, acute coronary syndrome (encompassing ST-segment elevation myocardial infarction, non-ST segment elevation myocardial infarction and unstable angina) is the leading cause of death in developed countries and second leading cause of death in developing countries and by the year 2020, CAD will hold the first place in the WHO's list of leading cause of disability.[2]

Uric Acid is the final oxidation product of purine catabolism in

human and higher primates. In last metabolic step, the conversion of hypoxanthine to uric acid is regulated by the enzyme xanthine oxidoreductase (XO). During this process reactive oxygen species (ROS) are produced. XO (xanthine oxidoreductase) activity is up-regulated in many cardiovascular disease, such as ischaemia to myocardium, left ventricular remodeling following acute coronary syndrome and heart failure.[3] Uric acid play a pivotal role in the progression of atherosclerosis. Moreover, increased uric acid levels may be associated with increased platelet adhesiveness, and this effect could potentiate thrombus formation.[4]

The Pathophysiological link between elevated serum uric acid (SUA) and atherosclerosis are endothelial dysfunction and inflammation. ROS (reactive oxygen species) production by XO (xathine oxidoreductase) can induce endothelial dysfunction by reducing bioavailability of nitric oxide. Endothelial dependent vasodilatation is impaired in hyperuricemia patients without any overt or other cardiovascular disease.[5] There is study that patients who have high uric acid level, they have more chance of short term adverse events.[6] Serum uric acid levels are strong independent predictor of cardiovascular mortality in middle aged men without clinical cardiovascular disease.[7] Higher serum uric acid on admission was independently associated with higher in hospital mortality.[8] In hospital mortality rate is significantly higher in patients with elevated uric acid than those with low uric acid. Major adverse cardiac events (MACE) are also higher in raised uric acid.[9] Hyperuricemia patients with acute Coronary Syndrome have a higher rate of left ventricular systolic, diastolic dysfunction and MACE.

Materials and Methodology:

This study was carried out in the department of Cardiology, Dhaka National Medical Institute Hospital, Dhaka from October 2014 to September 2015. In this case series study, 102 diagnosed patients of acute Coronary Syndrome free from gout, rental disease, hepatic disorder and other malignant conditions were enrolled. Among 102 Patients, 80 patients were male and 22 patients were female. All subjects were categorized into group-1 (SUA less than 6.5 mg/dl) & group II (SUA more than 6.5 mg/dl). All enrolled subjects were explained about the nature and purpose of the study and their informed consent were taken. Then 4 ml blood was taken within 24 hours of presentation from all study subjects. Blood was collected into plastic micro centrifuged tube. Then they were stored at 20 degree centigrade until analysis. All patients were managed according to standard management protocol during their hospital stay. During hospital stay their outcome (good or bad) were recorded. Bad outcome included mortality & morbidity. Morbidity included cardiac arrhythmia, heart block, cardiogenic shock and acute left ventricular failure. Finally their outcome, good or bad (mortality and morbidity) were evaluated on the perspective of their base line serum uric acid level. Analysis was done by SPSS (Statistical Package for social science) by applying appropriate formula.

Result and observation

In this case series study, 102 diagnosed patients of acute Coronary Syndrome were enrolled. Among 102 patients, 80 patients were male and 22 patients were female with the mean age of 54.62 ± 12.14 years in group-I (range 32-80) and 60.29 ± 12.13 years in group-ll (range 35-85).

Table I shows distribution of SUA in both group. The mean uric acid was found 5.43 ± 0.72 mg/dl in group I and 8.22 ± 1 mg/dl in group II. The mean uric acid difference was statistically significant ($P<0.05$) between two groups in unpaired t-test.

Table II shows mean$\pm$SD of ejection fraction of patients of group I and group II were 55.94 ± 6.60 and $50.87\pm10.27\%$ respectively and difference between them was statistically significant ($P<0.05$).

Table III shows good outcome, mortality and morbidity in both groups. Good outcome was found 43(65.2%) in group I and 13(31.0%) in group II. Mortality was 2(3.0%) in group I and 6(14.3%) in group II. Morbidity was found 21(31.8%) and 23(54.8%) in group I and group II respectively. Bad outcome, mortality and morbidity were statistically significant ($P<03.05$). This table depicts patients with raised SUA had increased mortality and morbidity than lower SUA group. On the other hand lower SUA group had better outcome than raised SUA group.

Table IV shows outcome in both groups. Good outcome was high in group-I and bad outcome was high in group-II. Good outcome was found 43(65.2%) in group I and 13(31.0%) in group II. Bad outcome (mortality + morbidity) was 23(34.8%) and 29(69.0%) in group in Chi-square test.

Table-I

Distribution of the study patients according to uric acid level (mg/dl)(n=102)

	Group (n=60) Mean±SD	Group II (n=42) Mean±SD	P value
Uric acid level (mg/dl)	5.43±0.72	8.22±1.0	0.001$
Range (min-max)	(3.6-6.4)	(6.7-10.5)	

Table-II

Distribution of the study patients according to LVEF

Echocardiographic findings (LVEF%)	Group I (n=60) Mean±SD	Group II (n=42) Mean±SD	P value
	55.94±6.60	50.87±10.27	0.007[s]

%**Table-III**

Distribution of the study patients according to outcome (n=102)

Outcome	Group I (n=60)		Group II (n=42)		P value
	n	%	n	%	
Good	43	65.2	13	31.0	0.001[s]
Mortality	2	3.0	6	14.3	0.020[s]
Morbidity	21	31.8	23	54.8	0.001[s]
Cardiogenic Shock	2	3.0	6	14.3	0.037[s]
Acute LVF	8	12.1	12	28.6	0.004[s]
Arrhythmia	5	7.6	3	7.1	0.545[ns]
Heart Block	6	9.1	2	4.8	0.626[ns]

s= significant, ns=not significant
P value reached from chi square test.

Table-IV

Distribution of the study patients according to outcome (n=102)

Outcome	Group I (n=60)		Group II (n=42)		P Total (n=102)	P value
	n	%	n	%		0.001[s]
Good	43	65.2	13	31.0	56	
Bad	23	34.8	29	69.0	52	

s= significant,
P value reached from chi square test.

Table-V

Logistic regression considering uric acid level as independent variables and out come as dependent variable (n=102)

	Adjusted	95% CI		P value
		Lower	Upper	
	OR			
Mortality	5.38	1.918	60.244	0.007[s]
Morbidity	4.10	1.720	9.750	0.001[s]
Bad outcome	4.67	2.019	10.820	0.001[s]
Constant	0.28	-	-	0.001[s]

s=significant. P value derived from pearson chi-square test.

Table V shows adjusted odds of mortality (5.38),

morbidity (4.10) and bad outcome (4.67). A subject having higher uric acid level had 5.38 (95% CI 1.918% to 60.244% P<0.007) time increased mortality. A subject having higher uric acid level had 4.10 (95% CI 1.720% to 9.750% p<0.001) time increased morbidity. A subject having higher uric acid level had 4.67 (95% CI 2.019% to 10.820% P<0.001) time increased bad outcome.

Discussion:
Hyperuricemia was postulated to be a risk factor for coronary artery disease (CAD) more than 5 decades ago. In recent decades, serum uric acid has been recognized as a potential risk factor for CVD.[10] Others reported that it was only confounded by the relation of uric acid with conventional risk factors for Coronary artery disease.[11] Serum uric acid level had a significant statistical relation with cardiovascular disease or mortality due to cardiovascular disease.[12]

The result of present study revealed, mortality was 2 (3.0%) in group I and 6(14.3%) in group II. Mortality was statistically significant (P<0.05). On the other hand lower SUA group had better outcome than raised SUA group. Lazzeri et al. found that In-hospital mortality was higher in "high" SUA patients (9.0% vs. 2.5%), p<0.006.[13] Kojima S et al (2005) made a comparison of mortality between 4th quartile and 1st quartile of uric acid which was 11% vs. 2% and our study revealed it was 14.3% vs. 3% in group-II and group-I.[6] Bickel C et al made a comparison between highest quartile of uric acid. The mortality rate was increased from 3.4% to 17.1% (fivefold increase). These findings are consistent with our study.[14]

The present study revealed that morbidity was 21(31.8%) and 23(54.8%) in group I and group II respectively. Morbidity were statistically significant (P<0.05). Bae J H et al evaluated the effects of the serum uric acid levels on major adverse cardiovascular events (MACEs). MACE rate increased from 7.2% to 20.1% (Lowest quartile vs. highest quartile).[15] This is consistent with our study. Hyan DW et al[16] showed that for all patients highest uric acid quartile was associated with increased risk of MACE (p=0.000).[16] Basher Net al showed that mortality was 2.8% in lower uric acid group and 6.6% in higher uric acid group (p<0.01). MACE also increased from 5.7% to 11.1% from non-hyperucemia to hyperuricemia (p<0.01). These findings are consistent with our study.[17]

In our study incidence of acute LVF was 28.6% and 12.1% in case of raised SUA group and low SUA group respectively. Chen Li et al. demonstrated that left ventricular dysfunction was 36.4% vs. 15.1% (p<0.001)

in case of hyperuricemia and non-hyperuricemia. Our study revealed consistent findings.[18]

Our study revealed good outcome was high in group-I and bad outcome was high in group-II. Good outcome was found 43(65.2%) in group I and 13(31.0%) in group II. Bad outcome (mortality-Morbidity) was 23(34.8%) and 29(69.0%) in group I and group II respectively. The mean outcome was statistically significant (P<0.05) between two groups in Chi-square test.

In the present study we have found adjusted odds ratio for mortality was 5.38 (95% CI, 1.918-60.244, p<0.007) and morbidity was 4.10 (95% CI, 1.720-9.750, p>0.001). This indicates a patient having higher uric acid level had 5.38 times increased mortality and 4.10 times increased morbidity than patients with low uric acid level. Kaya MG et al (2012) revealed that high plasma UA levels were an independent predictor of major adverse cardiac events in the hospital (odds ration 2.03,95% confidence interval 1.25 to 3.75, p=0.006), MACEs were more frequent in hyperuricemia (16% vs 7%) and in hospital mortality rate was higher in patients with high UA levels (9% vs. 2%, p<0.001).[9] Valente S et al. had a study on STEMI patients presenting with a cardiogenic shock. On admission SUA>6.5md/dl was associated with higher odds of in hospital death. OR+ 6.7 (95% CI 1.4-31.8),[19] Kojima et al (2005) demonstrated that mortality was 3.7 times higher in highest quartile of uric acid and lowest quartile of uric acid (OR=3.7 95% CI, p<0.0004).[6] Lazzeri et al (2010) found that risk of mortality was 3.9 times more in patients with hyperuricemia than normal uric acid (OR, 3.9, 95% CI, P<0.01).[13] These findings are consistent with our study.

Conclusion:
On admission serum uric acid estimation is a good predictor of in hospital bad outcome in patients with acute Coronary Syndrome. As it is a cheap and noninvasive procedure, it can be routinely practiced in cardiac emergency department for risk stratification of patients. This can guide the physicians in monitoring Acute Coronary Syndrome patients.

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