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Original Research Article

Association of serum uric acid level with angiographic severity of coronary artery disease: a study in a tertiary care hospital, Chittagong, Bangladesh

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ABSTRACT

Background: Coronary artery disease (CAD) is a major global health issue. Serum uric acid (SUA), a byproduct of purine metabolism, is linked to CAD development and progression. Elevated SUA levels are an independent risk factor for cardiovascular mortality and may indicate endothelial dysfunction. The aim of the study was to the observed associate serum uric acid level with the angiographic severity of CAD.
Methods: This observational study was conducted at Chittagong medical college hospital in Bangladesh from October 2020 to September 2021. It included 130 patients and used unpaired t-tests to analyze the association between serum uric acid level and angiographic severity of CAD patients. Ethical clearance was obtained from the institutional review board of Chittagong medical college and hospital.
Results: A study of 130 patients found a significant relationship between serum uric acid (SUA) levels and CAD (CAD), vessel involvement, and CAD severity (p=0.001). Patients with CAD had higher SUA levels (mean 5.26±1.32 mg/dL) compared to those without CAD (mean 4.22±1.03 mg/dL). A SUA level range of 3.94-6.58 mg/dL was associated with CAD presence. Gender also showed a highly significant association with SUA levels (p=0.001), while age, BMI, and smoking status did not show significant differences.
Conclusions: A strong positive association has been found between serum uric acid level and the severity of CAD. The findings of this study approve the effectiveness of hyperuricemia as an emerging risk factor for CAD.

Keywords: CAD, SUA, Gensini score, CAG

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of mortality worldwide, with projections showing an increase in cardiovascular mortality from 18.1 million in 2010 to 24.2 million by 2030.[1] CAD is the most common and overwhelming cardiac disease. Nonetheless, remarkable progress has occurred in their prevention, detection, and management over the last three decades. Serum uric acid (SUA), the end product of purine metabolism, has been associated with the development and progression of CAD through its role in mediating inflammation, inducing endothelial dysfunction,[2] and stimulating smooth muscle cell proliferation.[3] The abnormal iso-type of xanthine oxidase, which acts as an enzyme to produce reactive oxygen species, has been shown to have injurious effects in individuals with hyperuricemia.[4,5] However, SUA may also play a dual role as both pro- and anti-oxidants, with its differential role in individuals with other cardiovascular disease risk factors suggesting the presence of a molecular switch that controls its role.[6] There is a strong and significant

association between borderline SUA levels and the risk of both coronary heart disease and stroke.[7] Hyperuricemia, defined as elevated SUA levels, has been identified as an independent risk factor for higher cardiovascular mortality, with every 1 mg/dl increase in SUA from the normal range associated with a 48% higher risk of cardiovascular events.[8] Elevated SUA levels may also be a marker of endothelial dysfunction since the endothelium is a major site of uric acid production in the cardiovascular system. Uric acid concentrations have been shown to correlate inversely with flow-mediated brachial artery vasodilation, an in vivo measurement of vascular nitric oxide reactivity.[9] Additionally, hyperuricemia has been shown to increase platelet adhesiveness, and atherosclerotic plaque contains more uric acid than control arteries.[10] Recent studies have reported significant associations between SUA levels and CAD severity. A study found that SUA was significantly associated with the presence and severity of CAD and could be used for assessing CAD severity.[11] Another concluded that measuring SUA levels in patients presenting with acute coronary syndrome could help determine the patient's general probability of atherosclerotic disease and is both sensitive and efficient.[12] Moreover, assessing SUA levels in addition to traditional risk variables in routine clinical practice may offer important predictive advantages in terms of assessing overall cardiovascular risk and managing patients.[13,14] However, the study aimed to determine the association between SUA levels and the angiographic severity of CAD.

METHODS

This study was an observational, cross-sectional, descriptive study conducted in the department of cardiology at Chittagong medical college hospital in Chittagong, Bangladesh over one year from October 2020 to September 2021. The consecutive sampling technique was used, and the calculated sample size was 130. After selection, the aim, objectives, and design of the study were explained in detail to the subjects, and informed written consent was obtained from all study patients. The history was taken, and a clinical examination was performed following the standard procedure of clinical methods. Data on the demographic profile of the patient, including age, diabetes, hypertension, smoking, family history of CAD, and medication history (anti-hypertensive and anti-diabetic), were collected. Transthoracic echocardiography was performed using a GE Vivid S5 cardiac ultrasound machine with a 2.5-MHz phased-array transducer, and the left ventricular ejection fraction was measured using modified Simpson's rule. The investigation tools used were Shimadzu Bransist Alexa-c-12 (Ceiling mounted angiographic machine) made by Japan for coronary angiography, and GE Vivid S5 cardiac ultrasound machine made by India for measuring the left ventricular ejection fraction. The serum fasting uric acid was measured by an enzymatic colorimetric method using uricase. The collected data were analyzed using SPSS software, version-23.0 unpaired t-tests were performed to assess the association between serum uric acid level and angiographic severity of CAD patients. The ethical clearance of this study was obtained from the institutional review board (IRB) of Chittagong medical college and hospital.

Inclusion criteria

All patients who underwent elective coronary angiography for their symptoms related to CAD irrespective of age and sex were included in the study.

Exclusion criteria

Individuals who have undergone previous revascularization procedures such as PCI or CABG are excluded, as well as those within the first four weeks of experiencing acute coronary syndrome. Additionally, individuals with heart failure, acute infection, or chronic alcoholism are not eligible to participate. Lastly, individuals who are unwilling to provide their consent are also excluded from the study.

RESULTS

Among the cases, the mean (±SD) serum creatinine was 1.06 (±0.21) mg/dl and random blood sugar was 139.21 (±52.11) mg/dl. The mean (±SD) serum uric acid level was 5.06 (±1.33) mg/dl. The mean (±SD) LVEF (%) of the patients was 57.24 (±7.57). The mean Gensini score was 34.5 (±25.2).

Table 1: Investigation profile of the patients, (n=130).

Parameters	Mean ± SD	Range
Random blood sugar (mg/dl)	139.21±52.11	78-350
Serum creatinine (mg/dl)	1.06±0.21	0.6-1.70
Serum uric acid (mg/dl)	5.06±1.33	2.6-8.2
Left ventricular ejection fraction (%)	57.24±7.57	43-70
Gensini score	34.5±25.2	0-120

Table 2: Association between Serum uric acid and CAG findings of the patients.

Parameters		Mean (±SD) serum uric acid, (mg/dl)	P value
Significant CAD	No	4.22 (±1.03)	0.001#
	Yes	5.26 (±1.32)	
Findings	SVD	5.06 (±1.26)	0.006*
	DVD	5.46 (±1.39)	
	TVD	5.27 (±1.32)	
Gensini score	<20	4.14 (±1.06)	<0.001*
	20-40	5.15 (±1.28)	
	>40	5.64 (±1.19)	

SD: Standard deviation #P values are derived from independent t-test. *P value derived from ANOVA test.

The association between the serum uric acid level of the patients with their angiographic severity, the number of vessel involvement, and the extent are described in Table 2. It shows that serum uric acid level had a significant association with the presence of CAD, number of vessel involvement, and severity of CAD assessed by the Gensini score.

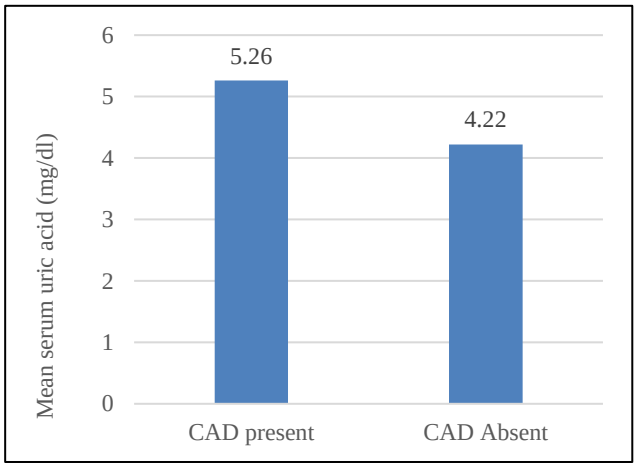

Figure 1: Relationship of serum uric acid level with CAD.

A simple bar diagram shows that the mean SUA level in cases with CAD was significantly higher (5.26±1.32 mg/dl) than in cases without CAD (4.22±1.03 mg/dl), (p=0.001). A mean value range of SUA level (3.94 mg/dl-6.58 mg/dl) was associated with the presence of CAD.

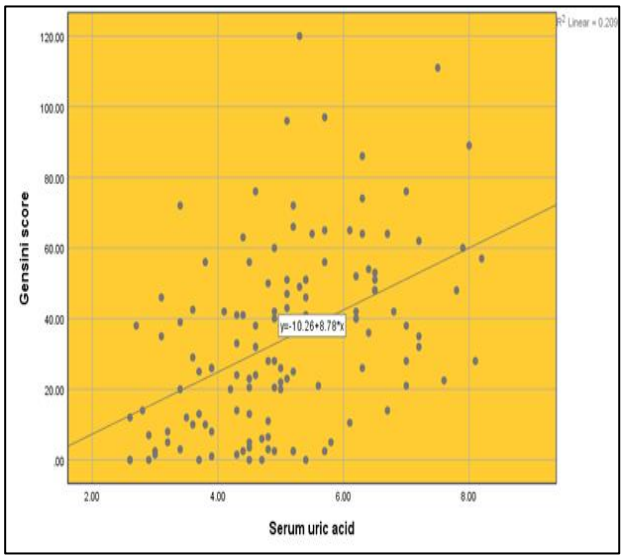

Figure 2: Correlation between serum uric acid level and Gensini score.

The Gensini score and serum uric acid level are correlated in this scatter dot graphic. The correlation between the two variables was positive, and the level of connection was statistically significant (Spearman rho 0.489; p<0.001).

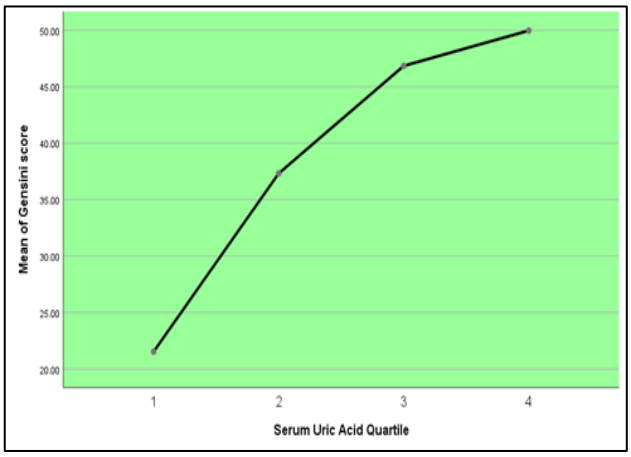

Figure 3: Correlation between serum uric acid quartiles and Gensini score.

A line graph demonstrating the relationship between the Gensini score and the quartiles of serum uric acid. A statistically significant difference was detected across the groups, and the Gensini score was shown to have grown considerably across the quartiles (p<0.001).

Table 3: Association between serum uric acid and demographic behavioral variables.

Parameters	Mean (±SD) serum uric acid, (mg/dl)	P value
Age groups (Years)		
<40	4.40 (±1.40)	0.136NS
40-60	5.12 (±1.35)	
>60	5.26 (±1.02)	
Gender		
Male	5.34 (±1.23)	<0.001S
Female	3.97 (±1.13)	
BMI (kg/m^2)		
Normal	4.97 (±1.28)	0.508NS
Overweight	5.03 (±1.39)	
Obese	5.43 (±1.21)	
Smoking		
Non-smoker	4.91 (±1.42)	0.095NS
Current or ex-smoker	5.31 (±1.13)	
Hypertension		
No	4.91 (±1.30)	0.191NS
Yes	5.21 (±1.35)	
Diabetes		
No	5.29 (±1.38)	0.013S
Yes	4.79 (±1.18)	

SD: Standard deviation; #P values were derived from the independent t-test, *P values were derived from the ANOVA test, S=Significant, NS=Not significant.

The results show that serum uric acid levels increase with age, but this association is not statistically significant. There is a significant difference in serum uric acid levels between males and females, with males having higher levels. BMI is not significantly associated with serum uric acid levels. There is a non-significant trend towards higher serum uric acid levels in current or ex-smokers compared to non-smokers. Hypertension is not significantly associated with serum uric acid levels, but there is a significant association between serum uric acid levels and diabetes, with non-diabetics having higher levels.

Table 4: Association between serum uric acid and risk factors of CAD.

Parameters	Mean (±SD) serum uric acid, (mg/dl)	P value
Hypertension		
No	4.91 (±1.30)	0.191NS
Yes	5.21 (±1.35)	
Diabetes		
No	5.29 (±1.38)	0.013S
Yes	4.79 (±1.18)	

SD: Standard deviation; P value was derived from the independent t test, S=Significant, NS=Not significant.

Table 4 represents the univariate analysis of serum uric acid levels in comparison to risk factors of CAD. There was no discernible difference between HTN and mean blood uric acid levels. Nevertheless, the mean serum uric acid level with DM differed significantly from that without.

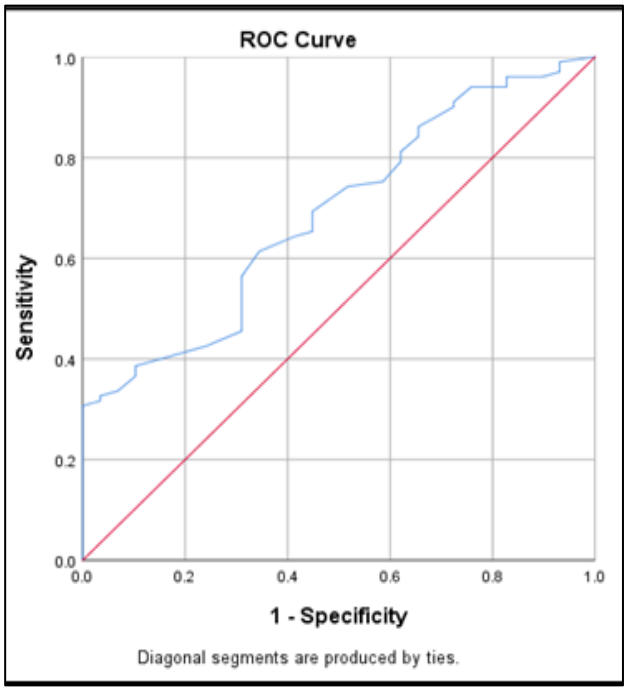

Figure 4: Receiver operating characteristic (ROC) curve for serum uric acid level concerning the presence of CAD.

By receiver operating characteristic (ROC) curve analysis, the AUC for the presence of CAD was 0.689 for serum uric acid level (p=0.002). A serum uric acid level of 4.65 mg/dl was found most appropriate cut-off point with a sensitivity of 65.3% and a specificity of 44.8% for the detection of CAD.

DISCUSSION

The current study was conducted in the department of cardiology, Chittagong medical college hospital to evaluate the association of serum uric acid level with the angiographic severity of CAD. A total of 130 consecutive patients underwent elective coronary angiography due to symptoms related to CAD. In the present study, the mean (±SD) serum uric acid level was 5.06 (±1.33) mg/dl and 303.46 (±79.77) mol/L. There was a statistically significant difference between the mean uric acid levels of patients with and without CAD (5.26±1.32 mg/dl vs. 4.22±1.03 mg/dl respectively, p=0.001). Similar to this, another study found that those with CAD had substantially higher SUA levels than people without CAD (7.35 1.61 mg/dl vs. 4.08 0.83 mg/dl, p<0.001.[11] Another study also reported that there was a statistically significant difference between the mean uric acid levels of patients with and without CAD (358.23±71.11 µmol/l vs. 251.32±54.92 µmol/l respectively, p<0.001).[14] For patients with and without CAD, there was a statistically significant difference in the mean uric acid concentrations [380±121 mol/l (6.39±2.04 mg⁄dl) vs 323.5±83.2 l mol⁄l (5.44±1.40 mg⁄dl).[13] The association between serum uric acid of the patients with severity of CAD shows that serum uric acid level was significantly higher among the patients with severe CAD in comparison to their counterparts (p<0.001). In addition to the evaluation of conventional risk factors in daily clinical practice, the measurement of uric acid levels might provide significant prognostic benefits in terms of global cardiovascular risk and management of the patients. The coronary angiographic finding revealed that most of the patients had triple vessel disease (29.3%), significant CAD (80%), and Gensini score >40 (39.2%). Hyperuricemia had a significant association with the extent, number of vessel involvement, and severity of CAD assessed by the Gensini score. Figure 2 shows that serum uric acid level and Gensini score were positively correlated and the degree of association was highly strong (Spearman rho 0.489; p<0.001). Similarly, another study described that a direct correlation between serum uric acid levels and Gensini score was also found to be statistically significant using a 2-tailed Spearman correlation (p=0.032).[15] Spearman correlation analysis demonstrated a positive correlation between the serum uric acid level and the severity of CAD (p<0.001, r=0.541).[13] Most of the study population (76.9%) was within the 40 to 60 years of age group. The mean age of the patients was 51.50±09.02 years (range: 34-80 years). Mean ± SD age (years) was 48.16±09.20 in the <20 Gensini score group, 51.51±08.41 in the 20-40 Gensini score group, and 54.08±08.71 in the>40 Gensini score group. Elderly patients were more

likely to have severe CAD in comparison to their counterparts in the present study. Gender distribution of the study subjects depicts that, there was male predominance, a total of 103 (79.2%) with male to female ratio of about 3.8:1. In another study total of 80 cases were included in study among them 48 were males and 32 females with male preponderance by male to female ratio of 1.5:1. And total 39 cases were diagnosed with CAD, of which 31 (79.4%) were male and 8 (20.5%) were female and those without CAD were 41 of which 17 (41.5%) were male and 24 (58.5%) were female. By using transthoracic echocardiography, the mean LVEF was calculated to be 57.24±7.57. The left ventricular ejection fraction and serum uric acid level were correlated.[11] Many studies have been done to look at the connection between various elements of cardiovascular illnesses and serum uric acid.[7] It is generally known that uric acid is connected to CAD risk factors as hypertension, type 2 diabetes, the metabolic syndrome, dyslipidemia, and obesity.[16] Clinically, this study might indicate that the presence of serum uric acid level is a useful marker for predicting severe CAD and that more attention should be paid to SUA-level management in such patients. Clinical implications of the present study are that in patients who had conventional cardiovascular risk factors with hyperuricemia, more severe CAD may be found, and the global cardiovascular risk may be increased. Thus, the suggestion can be given that when assessing this risk in CAD patient, hyperuricemia should be considered. Identification of high-risk CAD patients might be useful in clinical practice, leading to more intensive treatment of modifiable cardiovascular risk factors and early and frequent diagnostic checks.

Limitations

The study was a single-center study and conducted with small sample size. So, the results may not represent the whole community.

CONCLUSION

A strong positive association has been found between serum uric acid level and the severity of CAD. The findings of this study approve the effectiveness of hyperuricemia as an emerging risk factor for CAD.

Recommendations

Further studies with advanced imaging may provide more accurate information on the amount of coronary atherosclerosis. Although a significant association was detected, further prospective studies are needed to confirm this association and clarify the mechanisms behind it. However, larger-scale randomized studies are needed to show the effects of serum uric acid levels on the severity of CAD.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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