Original Article

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Risk Factors Associated with Angiographic Severity of Coronary Artery Disease Based on Serum Uric Acid: A Study in a Tertiary Care Hospital, Chattogram, Bangladesh

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ABSTRACT

Background: *Coronary Artery Disease (CAD) is a leading cause of death worldwide, identifying risk factors and severity is crucial for management and prevention. Serum Uric Acid (SUA) has been proposed as a potential marker for the severity of CAD. Elevated SUA levels are associated with endothelial dysfunction, oxidative stress, and inflammation, all of which contribute to the development and progression of atherosclerosis. This study aims to determine the association of risk factors with the severity of CAD using SUA levels.*

Materials and methods: *This was a cross-sectional observational study conducted in the Department of Cardiology at CMCH in Chattogram over one year from October 2020 to September 2021. After case selection demographic data were collected and transthoracic echocardiography was performed on study patients.*

Results: *The study analyzed the association between SUA level and CAD severity in 130 patients undergoing coronary angiography. The mean SUA level was 5.06 mg/dl and was significantly associated with the presence of CAD, number of vessel involvement and severity of CAD assessed by the Gensini score. 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).*

Conclusion: *This study concluded that demographic variables and risk factors are associated with the severity of CAD. The severity of CAD was higher in elderly and male patients. The study suggests that when assessing the risk in a CAD patient, hyperuricemia should be considered.*

Key words : Coronary artery disease; Coronary angiography; Serum uric acid.

Introduction

Coronary Artery Disease (CAD) is one of the leading causes of death worldwide and its prevalence is increasing, particularly in developing countries.[1] CAD occurs due to the formation of plaques in the coronary arteries, which results in a reduction in blood flow to the heart muscles and ultimately leads to angina, myocardial infarction, heart failure and sudden cardiac death.[2] Identifying the risk factors and severity of CAD is essential for the management and prevention of this disease.Several demographic variables and risk factors, such as age, gender, smoking, hypertension, diabetes mellitus and dyslipidemia, have been associated with CAD.[2] The identification of these risk factors has led to the development of various diagnostic and therapeutic strategies for the prevention and treatment of CAD. However, the severity of CAD varies significantly among individuals with similar risk factors and there is a need for more accurate diagnostic and prognostic tools to predict the severity of CAD. Serum Uric Acid (SUA) has been proposed as a potential marker for the severity of CAD.[3] SUA is a natural antioxidant produced in the liver and intestines and is excreted mainly by the kidneys. Elevated SUA levels have been associated with endothelial dysfunction, oxidative stress and inflammation, all of which contribute to the development and progression of atherosclerosis.[4] Recent studies have shown a significant association between elevated SUA levels and the severity of CAD, as determined by angiographic grading.[5,6] Angiographic grading is a widely used tool for assessing the severity of CAD and is based on the degree of stenosis in the coronary arteries. Several studies have investigated the association between demographic variables and risk factors and the severity of CAD using angiographic grading and SUA levels. For example, a study by Sinan et al. found that age, male gender, smoking, hypertension and diabetes mellitus were significantly

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associated with the severity of CAD, as determined by angiographic grading and SUA levels.[7] Similarly, a study by Wang et al. reported that age, male gender, hypertension and dyslipidemia were significant predictors of the severity of CAD, as determined by angiographic grading and SUA levels.[8] In addition to the evaluation of conventional risk factors in daily clinical practice, the measurement of uric acid level might provide significant prognostic benefits in terms of global cardiovascular risk assessment and management of patients.[9,10] Based on the above-mentioned evidence, early assessment of serum uric acid level with the presence and severity of CAD is desirable because it could lead to improved patient or physician adherence to risk-reducing behaviors or interventions and improve clinical outcomes. The study aims to determine the association of risk factors with the severity of CAD using serum uric acid level.

Materials and methods

It was an observational, cross-sectional, descriptive study conducted in the Department of Cardiology at Chittagong Medical College Hospital (CMCH) in Chattogram, Bangladesh over a period of one year from October 2020 to September 2021. The sampling technique used was consecutive sampling 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.

Inclusion criteria

- All patients who underwent elective coronary angiography for their symptoms related to CAD irrespective of age and sex.

Exclusion criteria

- First 4 weeks of acute coronary syndrome
- Acute infection and chronic alcoholism
- Those unwilling to give consent.

Results

Table I Distribution of patients according to demographic variables (n=130)

Variables	Mean (±SD) Serum uric acid, mg/dl	p value
Age groups (Years)*		
<40	4.40 (±1.40)	0.136^{NS}
40-60	5.12 (±1.35)	
>60	5.26 (±1.02)	
Gender#		
Male	5.34 (±1.23)	<0.001^{S}
Female	3.97 (±1.13)	
BMI (kg/m2)*		
Normal	4.97 (±1.28)	0.508^{NS}
Overweight	5.03 (±1.39)	
Obese	5.43 (±1.21)	
Smoking#		
Non-smoker	4.91 (±1.42)	0.095^{NS}
Current or Ex-smoker	5.31 (±1.13)	

SD: Standard Deviation, S = Significant, NS = Not Significant.

#p values were derived from the independent test, *p values were derived from the ANOVA test.

No significant difference in SUA levels among different age groups was found in the present study (p.136). Similarly, there were no significant differences in SUA levels concerning BMI and the smoking status of the patients (0.095). On the other hand, SUA level had a highly significant association with gender according to the p value (0.001).

Table II 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 III 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)	

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Parameters	Mean (±SD) Serum uric acid, mg/dl	p value
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)	

#p values are derived from independent t-test, *p value derived from ANOVA test.

Table III shows that serum uric acid level had a significant association with the presence of CAD, number of vessel involvement and severity of coronary artery disease assessed by the Gensini score.

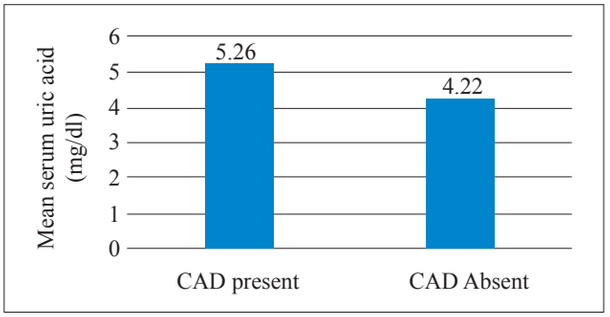

Figure 1 Relationship of serum uric acid level with CAD

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.

Table IV Distribution of the study according to risk factors of CAD (n=130)

Parameters	Mean (±SD) mg/dl (SUA)	p value
Hypertension		
No	4.91 (±1.30)	0.191^{NS}
Yes	5.21 (±1.35)	
Diabetes		
No	5.29 (±1.38)	0.013^{S}
Yes	4.79 (±1.18)	

SD: Standard Deviation, p value was derived from the independent t-test.
S = Significant, NS = Not Significant.

Table IV represents the univariate analysis of serum uric acid levels in comparison to risk factors of CAD. No significant difference in mean serum uric acid level with HTN was found in the present study. But there was a significant difference in mean serum uric acid level with DM.

Table V Univariate association between risk factors and severity of CAD (n=130)

Variables	Severity of CAD			p value
	Gensini score <20 (n=37)	Gensini score 20-40 (n=42)	Gensini score >40 (n=51)	
Age (Years)#	48.16±09.20	51.51±08.41	54.08±08.71	0.009^{S}
Male gender*	22 (57.9%)	34 (79.1%)	47 (95.9%)	<0.001^{S}
HTN*	14 (36.8%)	19 (44.2%)	29 (59.2%)	0.100^{NS}
DM*	11 (28.9%)	17 (39.5%)	23 (46.9%)	0.234^{NS}
Smoker*	13 (34.2%)	16 (37.2%)	19 (38.8%)	0.908^{NS}
BMI (kg/m^2)#	23.98±2.74	24.50±2.53	24.25±2.73	0.674^{NS}

Data are expressed as mean (±SD) or frequency (Percentage), S = Significant, NS = Not Significant.

#p values were derived from the ANOVA test; *P values were derived from the Chi-square test.

The study patients were divided into three groups (Gensini score <20, Gensini score 20-40, and Gensini score >40) according to coronary artery disease severity. Table V describes the association between different risk factors related variables with the severity of CAD. It shows that there was a significant association between gender and age group. Male and elderly patients were more likely to have severe CAD in comparison to their counterparts. On the other hand, HTN, DM, smoking, and BMI had no significant association with the severity of CAD.

Table VI Adjusted Odds Ratio for Risk of Patients having severe CAD by CAG

Variables	Adjusted OR	95% CI		p value
		Lower	Upper	
Male gender	0.308	0.123	0.774	0.010^{S}
HTN	2.454	1.019	5.906	0.042 ^{S}
DM	5.440	1.765	16.765	0.001^{S}
Smoking	0.785	0.337	1.824	0.573^{NS}
SUA	12.40	1.61	95.27	0.003 ^{S}

CI = Confidence Interval, OR = Odds Ratio, S = Significant, NS = Not Significant.

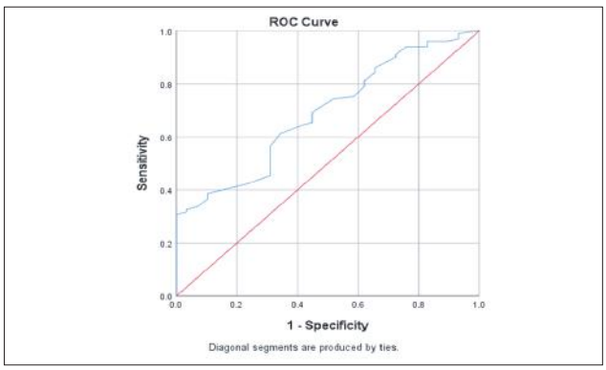

Figure 2 Receiver operating characteristic (ROC) curve for SUA level in relation to presence of CAD

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

Discussion

The Gensini scoring system was used to assess the coronary atherosclerotic disease burden in 130 consecutive patients undergoing elective coronary angiography due to symptoms related to CAD. The patients were classified into three groups based on their Gensini score.The Gensini scoring system (Gensini, 1983) was used in this study for assessing the coronary atherosclerotic disease burden. Gensini score was chosen because of its simplicity and widely accepted as a CAD burden marker and its prognostic value has been demonstrated in different clinical situations. The patients were classified into three groups according to their Gensini score.[9] In this study, 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±08.42 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. A similar study described that among 1012 patients (Mean age, 59.4 ± 10.24 years), 680 were men (Mean age, 58.7 ± 10.5 years) and 332 were women (mean age, 61.0 ± 9.51 years). CAD was present in 689 (68%) patients.[9] Patients with or without CAD were similar in terms of age (59.5 ± 9.7 years vs. 60.7 ± 10.1 years). Another study reported cases with CAD was 56.71 ± 10.36 years.[11] In another study, patients with and without CAD were similar in terms of age (53.46 ± 9.95 years vs. 47.16 ±7.73 years, p=0.003) and a significant age difference was found between patients.[10] 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. Male patients were more likely to have severe CAD in comparison to their counterparts and serum uric acid levels had a highly significant association with gender according to P value. Another study found a total of 80 cases were included in the study. Among them 48 were males and 32 were females with a male preponderance by a male to female ratio of 1.5:1. And a total of 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.[11] Another study showed, among 1012 patients, 680 were men and 332 were women.[9] Patients with or without CAD were similar in terms of gender (66% man vs. 68% women). Several studies have been performed to investigate the different aspects of cardiovascular diseases.[12,13] It is well-documented that uric acid is related to risk factors for CAD such as hypertension, diabetes mellitus, metabolic syndrome, dyslipidemia, and obesity.[14] A comparison of baseline characteristics was done in patients with and without CAD by Gensini score; age and sex were associated with CAD significantly.After controlling potential risk factors, only smoking and serum uric acid were significant predictors for CAD.[11] Another study also reported that serum uric acid level and risk factors associated with the CAD (age, gender, DM, hypertension, smoking, BMI, total cholesterol, LDL, HDL) were evaluated in a stepwise multivariate logistic regression analysis.[9,10] Age, male gender, DM and increased serum uric acid level were found to be independent risk factors for the presence of CAD in all groups (for uric acid hazard ratio 1.31, 95% CI: 1.19–1.43, $p < 0.001$).[9] Clinical implications of the present study are that in the 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 a CAD patient, hyperuricemia should be considered. The 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.

Limitation

The study was conducted on a relatively small sample size, which might not represent the entire population and limit the generalizability of the findings.

Conclusion

The present study concluded that the severity of CAD was higher in elderly patients and male patients. Serum uric acid level was significantly associated with gender and severity of CAD. The study suggests that when assessing the risk in a CAD patient, hyperuricemia should be considered.

Recommendation

Future research is advised with larger sample size and more confounding variables like family history and lifestyle factors. Moreover, longitudinal investigations may shed light on the connection between SUA levels and the onset and evolution of CAD. Practically, doctors should consider SUA levels when treating CAD patients, especially those with traditional risk factors, to determine the patient's overall cardiovascular risk and guide treatment choices.

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Disclosure
There is no conflict of interest as declared by any author.

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