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ASSOCIATION OF SERUM URIC ACID IN THE PREVALENCE, SEVERITY, AND PROGNOSIS OF CORONARY ARTERY DISEASE

Cardiology

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ABSTRACT

Objective: Owing to a possible relationship between hyperuricemia and coronary artery disease (CAD), the study was conducted to know the prevalence of hyperuricemia and its relation with the severity and prognosis of CAD. **Methods:** A total of 81 CAD patients of age group 36-83 years were divided in four groups based on serum uric acid (SUA) levels. The prevalence and severity of CAD were assessed by coronary angiography and New York Heart Association (NYHA) scales and their association with SUA level was statistically analyzed. **Results:** The mean age of patients was found to be 54.62±11.03 years. Increasing trends for mean SUA were found across the quartile (P<0.000). With increasing SUA levels, the mean value of Body Mass Index (BMI), Systolic Blood Pressure (SBP), and Diastolic Blood Pressure (DBP) also increased significantly (P<0.01), (P<0.042) and (P<0.019) respectively. Mean SUA significantly increased with NYHA class and the Multivessel disease (MV) showed a significant increase (p<0.051) in CAD patients following the increase in SUA levels. **Conclusion:** The study extends further to support previous findings and draws a link between different levels of SUA and CAD in this intriguing region of the country.

KEYWORDS

coronary artery disease, hyperuricemia, prevalence, severity

INTRODUCTION

In the present world, there is a rapid increase in mortality due to non-communicable diseases like diabetes, cancer, and cardiovascular diseases, when compared to communicable diseases (1). Cardiovascular diseases (CVDs) are of utmost concern in the health sector as they are the leading cause of morbidity and mortality globally (2). Indians, hold the tag of the highest coronary artery disease (CAD) rates, and the conventional risk factors fail to explain the increment (3). The overall burden of conventional risk factors such as diabetes mellitus, hypertension, dyslipidemia, obesity, and smoking could not explain the increased prevalence of CAD in India (3). Risk predictions are the cornerstone of preventive medicine; collecting data on these and intervening in their trends marks a good beginning towards disease surveillance. These efforts to find, track and tackle the probable risk factors of CVD will gradually help to condense the inclusive disease burden and promote health. Amongst the biochemical risk factors, uric acid is the one whose role remains controversial. In humans, the final product of purine metabolism is Uric acid (UA). Apart from dietary factors, neoplastic diseases may influence the concentration of serum uric acid (SUA) (4). Hyperuricemia is elevated levels of SUA due to its physiological imbalance. Normally, the hyperuricemic range for males and females is >7mg/dL and 6mg/dL respectively (5,6). Researchers have established that UA levels lower than the clinical diagnostic criteria, contribute towards cardiovascular mortality (5.6 mg/dL) risk. (6,7). Range of SUA levels with different thresholds as potential risk factors needs to be investigated in diverse regions of the planet. With the emersion of conflicting results regarding the consequences of hyperuricemia on the morbidity and mortality of CAD patients and its independent association, (8) it has become important to evaluate the potential role of chronic hyperuricemia as an important risk factor in postulating appropriate preventive strategies (9). Here, we did a retrospective study to investigate the role of SUA in the prevalence, severity, and prognosis of CAD.

METHODS

Study Design And Patient Population Size

We retrospectively studied 102 consecutive patients with coronary CAD who underwent coronary angiography from January 1st to June 30th, 2022, in our tertiary care hospital in northeast India. Out of these, 81 were selected for the study. Patients who had a myocardial infarction, impaired renal or liver functions, or hematological disorders were excluded from the study. The age group of the patients was 36-83 years. New York Heart Association (NYHA) scoring and vessel diseases were used to access the severity of CAD. Baseline risk factor data and biochemical data were obtained from the hospital records of the patients. SUA level >7.0 mg/dl was considered high. Patients with different ranges of UA were compared to assess the differences in clinical characteristics and angiographic disease patterns.

Statistical Analysis

Patients' SUA values were arranged in four groups by the quartile tool. All data were entered into MS Excel and analyzed using SPSS version 17.0 Chicago, SPSS Inc, IL, USA (10). Categorical data were presented as frequencies (percentages), while continuous data were presented as mean value ± standard deviation (SD). For the comparison of categorical variables, the Chi-square test was used. One-way ANOVA determined the differences in variables among the groups. P <0.05 was considered statistically significant.

Table 1: Age and sex distribution of CAD patients.

Age groups (years)	Male (%)	Female (%)	Total (%)
30-39	3(4.76)	0(0.00)	3(3.7)
40-49	5(7.93)	4(22.22)	9(11.11)
50-59	20(31.74)	4(22.22)	24(29.62)
60-69	16(25.39)	6(33.33)	22(27.16)
70-79	14(22.22)	3(16.66)	17(20.98)
>80	5(7.93)	1(5.5)	6(7.40)
Total	63(100.00)	18(100.00)	81(100.00)

Mean serum uric acid (mSUA) for males and females were 7.31mg/dL and 7.16 mg/dL respectively. In the age group greater than 80 years, the mean serum uric acid was maximum (7.90 mg/dL) followed by those aged between 50-59 years (7.37 mg/dL), Table 2.

RESULTS

A total of 81 CAD patients were included (Male = 63, Female =18) as shown in Table 1, with a male-to-female ratio of 3.5:1. Maximum numbers of patients were in the age group of 50-59 years irrespective of sex with an overall mean age of 54.62±11.03 years.

Table 2: Levels of mSUA according to the age distribution of CAD patients

Age groups (years)	No.of patients (%)	mSUA (mg/dL)
30-39	3(3.70)	7.13
40-49	9(11.11)	7.03
50-59	24(29.62)	7.37
60-69	22(27.16)	7.28
70-79	17(20.98)	7.1
>80	6(7.40)	7.9

Clinical value of SUA quartile and baseline characteristics of patients

The SUA quartiles used in this study are as follows: Q1, 4.7–6.0 mg/dL; Q2, 6.1–7.6 mg/dL; Q3, 7.7–8.0 mg/dL; Q4, 8.1–11.00 mg/dL. Table 3 represents the baseline characteristics of the patients.

Table 3: Baseline characteristics of the study participants according to SUA quartiles.

Characteristics	Q1 (4.7-6 mg/dL)	Q2 (6.1-7.6 mg/dL)	Q3 (7.7-8 mg/dL)	Q4 (8.1-11.0 mg/dL)	p-value
N	21	24	21	15	-
Sex (M/F)	(13/8)	(22/2)	(18/3)	(10/5)	-
Age (years)	59.33 ± 12.23	63.33 ± 11.21	58.81 ± 10.85	64.33 ± 11. 56	0.361
BMI (Kg/m2)	22.39 ± 4.46	25.08 ± 2.81	25.89 ± 4.60	27.30 ± 5.68	0.01
SBP (mmHg)	120.95 ± 20.21	123.33 ± 19.72	132.38 ± 21.80	141.00 ± 28.76	0.042
DBP (mmHg)	73.90 ± 11.71	80.83 ± 9.96	86.66 ± 15.53	83.2 ± 14.02	0.019
UA (mg/dL)	5.50 ± 0.355	7.01 ± 0.501	7.88 ± 0.095	9.37 ± 0.775	0.00
LIPID PROFILE					
HDL (mg/dL)	42.76 ± 14.00	48.45 ± 16.71	50.85 ± 15.89	58.86 ± 17.29	0.039
LDL (mg/dL)	90.95 ± 28.93	90.79 ± 37.42	104.38 ± 33.24	78. 46 ± 32.96	0.157
VLDL (mg/dL)	25.04 ± 10.35	21.32 ± 9.27	26.71 ± 12.52	25.24 ± 9.53	0.385
TG (mg/dL)	65.76 ± 22.01	105.87 ± 45.21	113.28 ± 45.59	110.46 ± 48. 54	0.001
Total Cholesterol (mg/dL)	151.52 ± 47.97	145.79 ± 42.66	153.95 ± 46.47	132.80 ± 45.08	0.561
Traditional coronary risk factors n (%)					
Dyslipidemia	0 (0.00)	3(12.5)	3(14.28)	5(33.33)	
Hypertension	14(66.66)	16(66.66)	14(66.66)	10(66.66)	
Diabetes mellitus	10(47.61)	10(41.66)	11(52.38)	8(53.33)	
Current smoking	1(4.76)	2(8.33)	1(4.76)	2(13.33)	

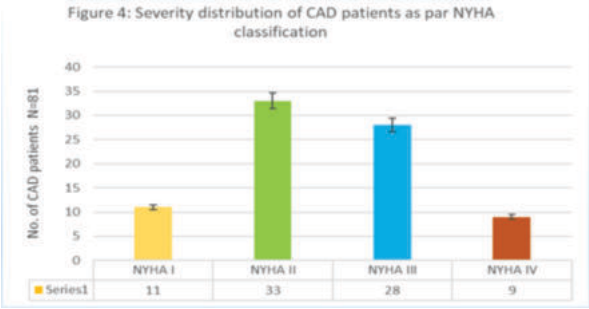
Data is given as Mean ± SD or n (%). P- value obtained from one way ANOVA. BMI, body mass index, SBP, systolic blood pressure, DBP, diastolic blood pressure, UA, uric acid, HDL, high-density protein, LDL, low-density protein, VLDL, very low-density protein, TG, triglycerides.

Increasing trends for mSUA were found across the quartile (P<0.000). With increasing SUA levels, the mean value of BMI, SBP, and DBP also increased significantly (P<0.01), (P<0.042) and (P<0.019) respectively. The mean values for HDL, and TG, also increased significantly with increasing concentration of SUA. On the other hand, along the quartile, the mean value of age, LDL, VLDL, and total cholesterol did not increase significantly. The frequencies of dyslipidemia along the quartile increased to 0%, 12.5%, 14.28%, and 33.33%. The maximum number of Diabetic patients was found in Q4 having an SUA range of 8.1-11.0 mg/dL. Furthermore, current smoking and hypertension showed no significant pattern along the quartiles.

Severity Distribution Of Cad Patients

a. As par NYHA (New York Heart Association) functional classification.

NYHA classification is a system used for patients with heart diseases to classify the extent of the disease as manifested in symptoms and functionality (11). It is a four-category system as NYHA I, NYHA II, NYHA III, and NYHA IV, with NYHA IV being the most severe. In our study, a maximum number of CAD patients fell under NYHA II, Figure 4, with the least being in NYHA IV.



b) NYHA classification of patients along the SUA quartile

In our study, 40.74% of the CAD patients fell under the NYHA II class (p<0.008) having a maximum no. of patients in the SUA quartile: Q2 (14.81%) as depicted in Table 5. The mean serum uric acid (mSUA) level was found to be (7.28 ± 1.40) mg/dL.

Table 5: Serum uric acid levels and severity of CAD patients as par NYHA classification

SUA Quartiles	NYHA I n(%)	NYHA II n(%)	NYHA III n(%)	NYHA IV n(%)	Total (%)	p-value
Q1(4.7-6.0mg/dL)	3(3.70%)	6(7.40%)	9(11.11%)	3(3.70%)	21(25.92%)	0.008
Q2(6.1-7.6mg/dL)	5(6.17%)	12(14.81%)	4(4.93%)	3(3.70%)	24(29.62%)	
Q3(7.7-8.0mg/dL)	1(1.23%)	11(13.58%)	7(8.64%)	2(2.46%)	21(25.92%)	
Q4(8.1-11.0mg/dL)	2(2.46%)	4(4.93%)	8(9.87%)	1(1.23%)	15(18.51%)	
Total n(%)	11(13.58%)	33(40.74%)	28(34.56%)	8(9.87%)	81(100%)	

c) Angiographical findings of CAD patients based on SUA levels

To compare the severity of the CAD patients along the SUA quartile, the angiographical findings indicating single vessel disease (SVD), double vessels disease (DVD), triple vessels disease (TVD), and multivessel disease (MVD) were assessed. The findings in Table: 6 reveales events of multivessel disease increased as the concentration of SUA increased (Q1: 15.78%, Q2: 54.16%, Q3: 66.66%, Q4: 80.00%; P□ =□ 0.051). On the other hand, the events of DVD decreased (Q1: 26.31%, Q2: 4.16%, Q3: 4.76%, Q4: 0.00%: P =0.031) with the increase in the SUA concentration. Whereas the events SVD and TVD showed no strong association across the four quartiles of SUA.

Table 6: Angiographical findings of vessel involvement along the SUA quartile

	Q1(4.7-6.0 mg/dL) n=19	Q2 (6.1-7.6 mg/dL) n=24	Q3 (7.7-8 mg/dL) n=21	Q4(8.1-11mg/dL) n=15	p-value
SVD	3(15.78%)	4(16.66%)	1(4.76%)	2(13.33)	0.684
DVD	5(26.31)	1(4.16%)	1(4.76%)	0(0.00)	0.031
TVD	8(42.10%)	6(25.0%)	5(23.80%)	1(6.66)	0.241
MV	3(15.78%)	13(54.16%)	14(66.66%)	12(80.00%)	0.051

DISCUSSION

The association between SUA and CAD has always attracted the researcher's focus due to its controversial findings. The relationship between SUA and CAD has been considered 'epiphenomenal' and not causal because of many documentations establishing a correlation between SUA levels and cardiovascular risk factors age, male sex, hypertension, dyslipidemia, obesity, diabetes mellitus (8, 12, 13,14). However, some studies found that CAD patients have elevated SUA levels compared with those not diagnosed with CAD (15, 8). It was also noticed that stable CAD patients had lower SUA levels when compared with unstable ones (16); hence indicating the role of SUA in CAD severity. These correlations support the impression that hyperuricemia may be a potential marker and/or independent risk factor for CAD. In an attempt to elucidate the causal role of SUA in CAD more clearly, the present study was conducted for people in this region. Concordant results with previous studies of male preponderance in arteriosclerosis patients were also found in our study (16). The age group (50-59 years), with a mean age of 54.62 ± 11.03 years had the maximum number of patients. We found two peaks of mSUA -7.9mg/dL and 7.37mg/dL in the age groups >80 years and 50-19 respectively. Along the SUA quartile, consistent results with previous studies of statistically significant characteristics for BMI, SBP, DBP, HDL, and TG were found (17). In the present study, the prevalence of hypertension was 66.66% along the quartiles whereas dyslipidemia showed an increasing pattern along the SUA quartile. With no increase in the number of diabetic and currently smoking patients, in the quartiles, the NYHA scale showed the maximum patients in Q2. Furthermore, it was also found that mSUA significantly increased with NYHA class. The above findings hint towards SUA being a potential biomarker in response to medication or surgical intervention therapies during follow-ups. A study by Tuttle et al (18) reported a correlation between CAD severity and uric acid levels in women but not in men. In our study, CAD severity was also evaluated

according to the involvement of the number of coronary vessels for both men and women. Occurrence of Multivessel disease (MV) showed a significant increase($p<0.051$) in CAD patients following the increase in SUA levels. At the same time, DVD was found to decrease significantly ($P<0.031$) along the SUA quartile. The ability of the previous studies to elucidate a causal role between uric acid and CAD has been limited. Accordingly, our study further supports previous findings and draws a link between different levels of SUA and CAD, with special reference to this part of the country.

CONCLUSION

Our study revealed a high prevalence of hyperuricemia in North Eastern Indian patients with CAD. In the present study, we found that serum uric acid levels correlated with NYHA class. After controlling potential conventional risk factors, BMI, SBP, DBP, uric acid, and TG were significant predictors for CAD. However, probably statistically significant correlations could not be found between other potential parameters and uric acid due to the small sample size. Consequently, serum uric acid can be well-thought-out as a low-priced and effective predictive indicator in CAD patients, though a larger sample study would be more decisive. Further research eventually can contribute towards a better understanding of SUA's role in CAD and in providing new therapeutic targets for the prevention and treatment of CAD.

Limitations Of The Study

Firstly, the study sample size was relatively small due to some unavoidable constraints. Again, this was a retrospective study and not a randomized one. Hence the association between SUA and the degree of severity of CAD patients cannot be said precisely and categorically.

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