

# A study of angiographic severity in patients with coronary artery disease and hyperuricemia

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## ABSTRACT

**Backgrounds:** Hyperuricemia has not yet been established as cardiovascular risk factor. We aimed to study the angiographic severity in patients with coronary artery disease (CAD) and hyperuricemia. **Materials and Methods:** In this observational cross-sectional study we measured serum uric acid level in 82 patients of CAD who underwent coronary angiography in catheterisation laboratory of our Institution. Severity of CAD was determined on the basis of Gensini score, number of diseased vessels, critical lesions and total occlusions. **Results:** The prevalence of hyperuricemia in patients with CAD was 42.68% in our study. Hyperuricemia was associated with higher Gensini score ( $33.33 \pm 10.64$  vs.  $22.90 \pm 6.75$ ,  $p$  value  $< 0.001$ ), number of critical lesions ( $1.03 \pm 0.84$  vs.  $0.63 \pm 0.72$ ,  $p$  value  $0.031$ ), total occlusions ( $0.67 \pm 0.47$  vs.  $0.37 \pm 0.48$ ,  $p$  value  $0.007$ ) and dyslipidemia (63.6% vs. 30.6%,  $p$  value  $0.003$ ) more frequently compared to normouricemic patients. And also the higher serum uric acid level was correlated with higher Gensini score (beta 0.418,  $t$  4.430,  $p$  value  $< 0.001$ , 95% CI 0.036 and 0.094) and frequent number of total occlusion (beta 0.338,  $t$  3.589,  $p$  value  $0.001$ , 95% CI 0.462 and 1.613). **Conclusion:** Hyperuricemia was associated with higher Gensini score, frequent total occlusions and critical lesions in patients with Coronary Artery Disease compared to patients with normal uric acid level and also it was significantly correlated with higher Gensini score and frequent total occlusions.

**Key words:** Hyperuricemia, Angiographic severity, Gensini score, Coronary artery disease (CAD)

## INTRODUCTION

Hyperuricemia induces endothelial dysfunction (ED),<sup>1</sup> the main mechanism by which it promotes atherosclerosis. Kim SY et al observed in their study, an association of increased serum uric acid with an increased risk of CHD incidence and mortality.<sup>2</sup> A Russian study reported that the patients with arterial hypertension of the first-second degree with persistent elevated levels of uric acid in blood serum had significantly higher levels of ED markers: albuminuria, plasmic endothelin concentration.<sup>3</sup> Hyperuricemia also predicts adverse outcomes in patients with heart failure.<sup>4</sup> Hyperuricemia also associated with various components of the Insulin Resistance Syndrome.<sup>5</sup> In this study we aimed to

correlate the angiographic severity in patients with coronary artery disease (CAD) with high serum uric acid levels.

## MATERIALS AND METHODS

In this observational cross-sectional study we measured serum uric acid level in 82 patients of CAD who underwent coronary angiography in catheterisation laboratory of our Institution from May 2013 to December 2014. Informed written consent was taken from every subjects and our study protocol was approved by Institutional Ethics Committee of Burdwan Medical College at the commencement of study. Severity of CAD was determined on the basis of Gensini

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score, number of diseased vessels, critical lesions and total occlusions. Demographic and clinical profile and laboratory data were collected for every patient. Cardiovascular risk factors were recorded according to standard definitions. Patients with history of IHD, heart failure, liver and kidney diseases, haematological or oncological disorders and chronic infections, taking diuretics, multivitamins, alcohol and on drugs interfering with serum uric acid levels were excluded from this study. Serum uric acid level was done after >8 hours of fasting and analysis was done by photometric technique with normal reference range of 3.5-6.5 mg/dl. Coronary angiography was performed through right femoral or right radial route by using Judkin's technique and on Bio-core (Siemens) and Integrus (Philips) machines in catheterization laboratory of Super-Speciality Wing Hospital of Burdwan Medical College in West Bengal, India, by experienced cardiologist unaware of clinical or biochemical profile of patients. The Gensini score was used to evaluate the severity of atherosclerotic lesions on angiogram. The Gensini score was computed by assigning a severity score to each coronary stenosis according to the degree of luminal narrowing (visual assessment) (Table 1). This number is then multiplied by a factor that takes into account the geographical importance of the lesion position in the coronary arterial tree (Table 2). The Gensini score was then expressed as sum of scores of all coronary arteries. Critical lesion was defined as  $\geq 70\%$  stenosis involving proximal part of any of the three main coronary arteries or  $\geq 50\%$  of left main stem stenosis. Total occlusion was defined as 100% occlusion with no ante grade flow of contrast distal to the lesion. A vessel was counted as diseased vessel if it has  $\geq 50\%$  stenosis at any level. Statistical Analysis was performed using SPSS V version 20 for windows with appropriate methods. A 2-tailed P value  $< 0.05$  was considered statistically significant.

## RESULTS

The prevalence of hyperuricemia in patients with CAD in this study was 42.68% (35 out of total 82 patients). The mean serum uric acid level was high in hyperuricemic group (serum uric acid  $> 6.5$ mg/dL) compared to normouricemic (serum uric acid  $< 6.5$  mg/dL) group ( $7.59 \pm 8.12$  mg/dL vs.  $4.83 \pm 0.66$  mg/dL, p value  $< 0.001$ ) (Table 3). There were no significant difference between two groups regarding mean age ( $53.76 \pm 6.28$  years vs.  $53.45 \pm 6.25$  years, p value 0.828), gender distribution (Male: Female, 63.6%:36.4% vs. 59.2%: 40.8%, p value 0.685), positive family history of heart disease (39.4% vs. 38.8%, p value 0.955), smoker (24.2% vs. 34.7%, p value 0.313), hypertensive (66.7% vs. 49.0%, p value 0.113), diabetes (33.3% vs. 24.5%, p value 0.382), obesity (51.5% vs. 44.9%, p value 0.556), STEMI (57.6% vs. 57.1%, p value 0.969), NSTEMI (27.3% vs. 30.6%, p value 0.744) and unstable angina (15.2% vs.

**Table 1: Gensini number assigned according to degree of luminal narrowing**

Luminal narrowing (%)	Grading of disease	Gensini number
30-50	Mild	01
51-70	Moderate	02
71-90	Severe	04
91-99	Subtotal occlusion	08
100	Total occlusion	16

**Table 2: Gensini multiplying factor assigned according to the location of lesion in the coronary tree**

Location of lesion	Multiplying factor
Left main stem	05
Proximal left anterior descending artery, proximal left circumflex artery	2.5
Mid left anterior descending artery	1.5
Distal left anterior descending artery, first diagonal, mid left circumflex artery, distal left circumflex artery, obtuse marginal, proximal right coronary artery, mid right coronary artery, distal right coronary artery, posterior descending artery	01
Second diagonal and postero-lateral ventricular branch	0.5

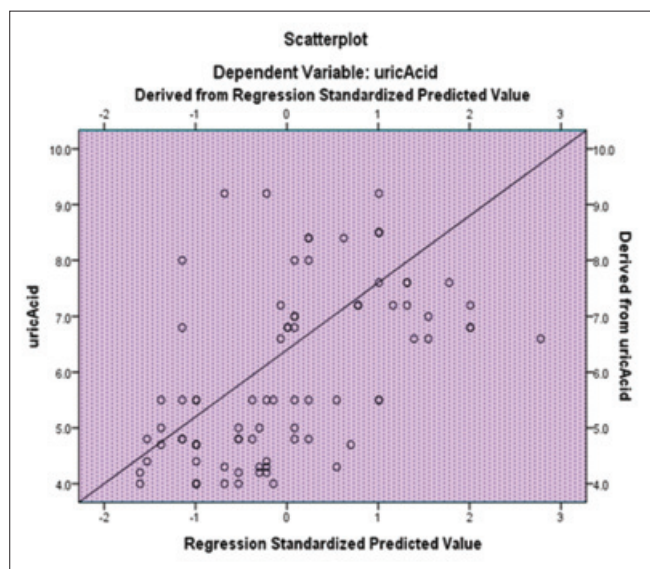
**Table 3: Comparison between normouricemic and hyperuricemic groups**

Parameter	Hyperuricemic (n=35)	Normouricemic (n=47)	P value
Mean uric acid level (mg/dL)	$7.59 \pm 8.12$	$4.83 \pm 0.66$	$< 0.001$
Gensini score	$33.33 \pm 10.64$	$22.90 \pm 6.75$	$< 0.001$
Diseased vessels	$2.36 \pm 1.11$	$2.12 \pm 0.99$	0.319
Critical lesions	$1.03 \pm 0.84$	$0.63 \pm 0.72$	0.031
Total occlusions	$0.67 \pm 0.47$	$0.37 \pm 0.48$	0.007
Mean age (in years)	$53.76 \pm 6.28$	$53.45 \pm 6.25$	0.828
Male:	21 (63.6):	29 (59.2):	0.685
Female (n, %)	12 (36.4)	20 (40.8)	
Family history of CAD (%)	13 (39.4)	19 (38.8)	0.955
Smoker (%)	8 (24.2)	17 (34.7)	0.313
Dyslipidemia (%)	21 (63.6)	15 (30.6)	0.003
Hypertensive (%)	22 (66.7)	24 (49.0)	0.113
Obesity (BMI $> 30$ kg/M <sup>2</sup> )	17 (51.5)	22 (44.9)	0.556
Diabetes mellitus (%)	11 (33.3)	12 (24.5)	0.382
STEMI (%)	19 (57.6)	28 (57.1)	0.969
NSTEMI (%)	9 (27.3)	15 (30.6)	0.744
Unstable angina (%)	5 (15.2)	6 (12.2)	0.705

12.2%, p value 0.705) except dyslipidemia (63.6% vs. 30.6%, p value 0.003). Regarding angiographic severity hyperuricemic patients are associated with higher Gensini score ( $33.33 \pm 10.64$  vs.  $22.90 \pm 6.75$ , p value  $< 0.001$ ), frequent number of critical lesion ( $1.03 \pm 0.84$  vs.  $0.63 \pm 0.72$ , p value 0.031) and total occlusion ( $0.67 \pm 0.47$  vs.  $0.37 \pm 0.48$ , p value 0.007); though there was no significant difference in number of involved vessels ( $2.36 \pm 1.11$  vs.  $2.12 \pm 0.99$ , p value 0.319) (Table 4).

**Table 4: Correlation between serum uric acid level and angiographic severity parameters**

Dependent variable: Serum uric acid level	Standardized coefficients	t	Sig.	95% confidence interval for B	
	Beta			Lower bound	Upper bound
Constant		8.331	0.000	2.797	4.552
Gensini score	0.418	4.430	0.000	0.036	0.094
Total occlusions	0.338	3.589	0.001	0.462	1.613

**Figure 1:** Correlation between serum uric acid level and Gensini score ( $p < 0.001$ )

On regression analysis, higher serum level of uric acid was significantly correlated with higher Gensini score (beta 0.418,  $t$  4.430,  $p$  value  $< 0.001$ , 95% CI 0.036 and 0.094) and frequent number of total occlusion (beta 0.338,  $t$  3.589,  $p$  value 0.001, 95% CI 0.462 and 1.613) (Figure 1).

## DISCUSSION

In this observational cross-sectional study we found association of hyperuricemia with the angiographic severity of CAD using Gensini scoring system. The higher serum uric acid levels was associated with higher Gensini score, frequent total occlusions and critical lesions in patients with Coronary Artery Disease compared to patients with normal uric acid level and also correlated with higher Gensini score and frequent total occlusions. Coronary angiography is the gold standard for diagnosis of CAD. Neeland IJ et al compare coronary angiographic scoring systems (Gensini) with intravascular ultrasound derived plaque burden in a CAD population undergoing angiographic evaluation and found strong correlation with each other and also with atherosclerotic plaque burden.<sup>6</sup> Sinning C et al also proposed that both Syntax scoring system and Gensini scoring system in combination with clinical variables could be used to predict the cardiovascular prognosis in CAD patients even during

long-term follow-up.<sup>7</sup> Gensini coring systems therefore appear to be a valid estimate of CAD plaque burden.<sup>6</sup>

Similar to our findings, Sinan DO et al also found association of serum uric acid level with the presence and severity of CAD.<sup>8</sup> Azmat EQ et al also reported the association of hyperuricemia with higher Gensini score, more frequent total occlusions and critical lesions in men presenting with acute coronary syndrome.<sup>9</sup> Duran M et al observed higher Gensini score, high number of diseased vessels, critical lesions, and total occlusion in hyperuricemic patients; serum uric acid level as independent predictor of multi vessel disease; and also the association of hyperuricemia with CAD severity even in non-diabetic and non-hypertensive patients.<sup>10</sup> Xiong Z et al used clinical SYNTAX severity scoring system and also found significant association with the severity and complexity of CAD.<sup>11</sup>

Contrary to our result Gur M et al concluded that uric acid level is associated with the presence but not with the severity of coronary artery disease.<sup>12</sup> Lu P et al observed a higher CAD severity in women having higher uric acid level, although uric acid was not independently associated with CAD or CAD severity either in women or in men.<sup>13</sup>

Ndrepepa G et al concluded that uric acid level predicts an increased risk of cardiac mortality across all subgroups of patients with CAD and the association between uric acid level and cardiac or all-cause mortality had a 'J-shaped' pattern with lowest risk of death in patients with uric acid levels between 5.17 and  $< 6.76$  mg/dL.<sup>14</sup> Kojima S et al suggest that hyperuricemia after AMI is associated with the development of heart failure.<sup>15</sup> Tamariz L et al found greater risk of atrial fibrillation in patients with elevated serum uric acid levels, particularly among blacks and women.<sup>16</sup> Demir B et al observed a positive correlation between severity of calcific aortic stenosis and serum uric acid levels.<sup>17</sup> A large scale prospective study is needed to determine the prognostic significance of hyperuricemia over cardiovascular events.

## CONCLUSION

In conclusion, we found association of Hyperuricemia with severity of CAD. The higher serum uric acid levels

was associated with higher Gensini score, frequent total occlusions and critical lesions in patients with Coronary Artery Disease compared to patients with normal uric acid level and also correlated with higher Gensini score and frequent total occlusions. We suggest large scale prospective study to determine prognostic significance of Hyperuricemia.

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### Authors Contribution:

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