Original Research Article

Hyperuricemia as a risk factor for increase severity of coronary vessel occlusion disease: a cross-sectional study in North Indian population

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ABSTRACT

Background: Cardiovascular disease (CVD) is the most common cause of death worldwide. The present study was conducted to study uric acid as a potential biomarker in predicting the severity of CVD in terms of vessel involvement.

Methods: A cross-sectional study, conducted at Rajiv Gandhi Super Speciality Hospital, Tahirpur, Delhi. A total of 52 consecutive male and female patients age between 30 to 70 years was included in this study. Written informed consent was obtained from all the enrolled patients. Automated analysers were used for the analysis of blood glucose, lipid profile and serum uric acid level. IBM SPSS Statistics (Version 20.0, IBM SPSS, IL, USA) was used for the statistical analyses.

Results: In this study, a total of 52 consecutive patients were divided into three groups: single-vessel disease (n=19), double vessel disease (n=19) and triple vessel disease (n=14). Biochemical profile of all the groups was calculated. A group of triple vessel disease patients showing higher amount (164±42 mg/dl) of cholesterol level as compared to the other two groups (157±34 mg/dl). The mean level of serum uric acid levels significantly differed and its mean levels increases as the severity of vessel diseases increases. The receiver operating characteristic curve shows the uric level has 71% sensitivity and 52.5% specificity for detecting the severity of coronary vessel disease.

Conclusions: This study demonstrated an increased serum uric acid levels were associated with increased severity of vessel disease, and serum uric acid is an independent risk factor for coronary artery disease.

Keywords: Coronary vessel occlusion, Cardiovascular disease, Hyperuricemia, Serum uric acid

INTRODUCTION

Cardiovascular disease (CVD) is a complex multifactorial disease of a medium and large-sized coronary artery resulting from atherosclerosis. The etiopathogenesis of coronary artery occlusion is complex, and many known and unknown environmental and genetic factors are involved.¹ The adverse outcome of occlusion of the coronary artery is myocardial infarction (MI) due to sudden blockage in the blood supply of myocardial tissue.² CVD is one of non-communicable disease which causes major morbidity and mortality worldwide. CVD once thought to be a disease of obese and high socioeconomic individuals, but now it is prevalent even in non-obese and middle and lower socioeconomic status individuals.³ Most of CVD patients present in an emergency for the first time with signs and symptoms of MI without any known risk factors.³ Scientists have been working on biomarkers which can help in its early detection and diagnosis of CVD so that timely interventions could be done to prevent the adverse outcome. The severity of CVD can be assessed by the
involvement of a number of coronary artery blockage. Subclinical inflammation has been considered, one of the important factors in developing atherosclerosis and finally blocking coronary arteries. Serum uric acid has been shown to be associated with inflammation in the endothelium of many vessels such as coronary artery. Increases uric acid could also be a risk factor for assessing the severity of CVD. Therefore, the present study was conducted to study uric acid as a potential biomarker in predicting the severity of CVD in terms of vessel involvement.

METHODS

This was a cross-sectional, hospital based study of 52 consecutive male and female patients (age 30-70 yrs) presenting with CVD conducted at Rajiv Gandhi Super Specialty Hospital, Tahirpur, Delhi between April-2019 and March-2020. Written informed consent was taken, and the study was approved by the ethical review committee. Demographic, clinical, procedural, and laboratory data were collected. The patients with a history of IHD, heart failure, liver and kidney diseases, hematological or oncological disorders and chronic infections were excluded. Patients taking diuretics, multivitamins, alcohol and on drugs interfering with serum uric acid levels were also excluded. Serum uric acid level including blood glucose and lipid profile were performed on dry chemistry analyser (vitos 5600, ortho clinical diagnostics pvt ltd). Angiography was performed during hospital admission for all the patients with raised hsTropI levels >10ng/l, suggestive of MI.

Statistical analysis

All Statistical analyses were performed using IBM SPSS Statistics (Version 20.0, IBM SPSS, IL, USA). Data are presented as mean±SEM.

Comparison of means between the study groups was done by the analysis of variance (ANOVA) followed by Tukey's post hoc test. A p-value <0.05 was considered to be statistically significant. Pearson correlation analysis was done to assess the serum uric acid with study variables.

RESULTS

Demographic and biochemical characteristics of the subjects in all groups

The study populations were age and sex-matched, as shown in Table 1. The biochemical characteristics of the study population are shown in Table 2.

| Parameters | SVD (n=19) (mean±SD) | DVD (n=19) (mean±SD) | TVD (n=14) (mean±SD) | p-value |
|------------|---------------------|---------------------|---------------------|---------|
| Age (year) | 53±14               | 54±10               | 60±15               | 0.384   |
| Sex         | 16/4                | 16/3                | 10/4                | 0.818   |

*p-value<0.05 is considered statistically significant

Table 2: Biochemical profile of the study population

| Parameters             | SVD (n=19) (mean±SD) | DVD (n=19) (mean±SD) | TVD (n=14) (mean±SD) | p-value |
|------------------------|---------------------|---------------------|---------------------|---------|
| HbA1c (mg%)            | 6.5±1.8             | 6±0.9               | 7.2±2.5             | 0.390   |
| hsTropI (ng/dl)        | 9.3±2.3             | 7.8±4               | 7.5±4               | 0.398   |
| Total Cholesterol (mg/dl) | 157±34            | 157±34              | 164±42              | 0.519   |
| HDL Cholesterol (mg/dl) | 37±10              | 35±10               | 68.7±108            | 0.360   |
| LDL Cholesterol (mg/dl) | 92±29              | 80±28               | 84±41               | 0.626   |
| Non-HDL Cholesterol (mg/dl) | 119±33            | 110±34              | 124±40              | 0.678   |

*p-value<0.05 is considered statistically significant. SVD- Single vessel disease; DVD- Double vessel disease; TVD- Triple vessel disease; HbA1c-Hemoglobin A1C; hsTropI- High sensitivity troponins; HDL- High-density lipoprotein; LDL-Low- density lipoprotein

Serum uric acid levels in study population

As shown in Table 3, the mean level of serum uric acid levels significantly differed and its mean levels increases as the severity of vessel diseases increases. It shows that increase serum uric acid might cause oxidative stress and free radical injury prevailing in the cases of cardiovascular disease. Table 4 shows correlation analysis of serum uric acid with study parameters.

Table 3: Serum uric acid level in the study population

| Parameters | SVD (n=19) | DVD (n=19) | TVD (n=14) | p-value |
|------------|------------|------------|------------|---------|
| Serum Uric Acid | 5.3±1.9   | 6.3±1.4   | 8±3.4    | 0.028* |

*p-value<0.05 is considered statistically significant. SVD- Single vessel disease; DVD- Double vessel disease; TVD- Triple vessel disease
Table 4: Correlation analysis of serum uric acid with study variables.

| Parameters         | Serum uric acid |        |        |
|--------------------|-----------------|--------|--------|
|                    | r value         | p-value|        |
| HbA1C              | 0.069           | 0.636  |        |
| hsTropI            | -0.110          | 0.428  |        |
| Total Cholesterol  | -0.171          | 0.220  |        |
| HDL Cholesterol    | -0.097          | 0.488  |        |
| LDL Cholesterol    | -0.160          | 0.252  |        |
| Non-HDL Cholesterol| -0.146          | 0.298  |        |

p-value ≤0.05 is considered statistically significant. r = Pearson’s correlation coefficient. SVD- Single vessel disease; DVD- Double vessel disease; TVD- Triple vessel disease; HbA1c-Hemoglobin A1C; hsTropI- High sensitivity troponins; HDL- High-density lipoprotein; LDL-Low- density lipoprotein

Figure 1 shows ROC curve of serum uric level which predicts that at the cut of 5.7%, the uric level has 71% sensitivity and 52.5% specificity for detecting the severity of coronary vessel disease (Triple vessel disease).

**Figure 1: ROC curve of serum uric acid.**

**DISCUSSION**

The present study with diagnosed and suspected cases of mi showed that serum uric acid levels were correlated with coronary vessel disease severity. Uric acid is the byproduct of purine metabolism. The enzyme xanthine oxidase catalyses the essential reactions of conversion of hypoxanthine to xanthine and then uric acid. The final degradation product of uric acid metabolism, allantoin is then excreted freely in the urine. After filtration through the glomeruli, uric acid is completely reabsorbed in the PCT. Elevated levels of uric acid in serum can be either due to overproduction or under secretion. Previous studies have reported that a positive correlation between serum uric acid and cardiovascular conditions including hypertension, coronary artery disease, pre-eclampsia, metabolic syndrome, cerebrovascular disease, dementia. The stipulated mechanisms for the association of uric acid with these pathological cardiovascular events could be attributed to either increased oxidative stress due to oxidants being generated by xanthine oxidase, which then impairs nitric oxide synthesis and mediated vasodilation. Studies also suggest that uric acid induces proliferation of vascular smooth muscle cells, and induces expression of pro-inflammatory molecules like C-reactive protein in endothelial cells. Genetic causes of hyperuricemia have been linked with derangement of nitric oxide synthesis, and thus, endothelial dysfunction acts as a harbinger for inflammation and cardiovascular compromise.

The results of this study reveal that serum uric acid levels significantly rises with the severity of the disease, from a single vessel to triple vessel involvement. High sensitivity troponins levels were elevated in all the patients and based on that the diagnosis of MI was made. Angiography was done, which showed the extent of vessel involvement and further grouping was done into patients with single, double and triple vessel disease. A causal role for uric acid in coronary artery disease has been suggested in several studies, including a follow-up study of patients hospitalized for coronary angiography and for patients at high cardiovascular risk. On the basis of present study, it may be hypothesized that uric acid is involved in the process of myocardial injury by accentuating progression of atherosclerosis and occlusion of the vessel due to its role in the imbalance between myocardial oxygen supply and demand. The beneficial effect of allopurinol treatment coincides with the postulated mechanism. Increased low-density lipoprotein levels may also enhance atherosclerosis due to its oxidative effect, but in this study, authors couldn’t find a significant association with vessel disease. Larsen et al, found that on further subgrouping of MI patients in type-1 and type-2, uric acid levels were found to be significantly higher in type-2 MI patients where a pathophysiological imbalance between vasodilators and constrictors play the important role.

Another study by Prasad et al, revealed an association between increased uric acid levels and cardiovascular risk in postmenopausal women. According to them, endogenous estradiol plays a role in preserving endothelial function and in lowering serum uric acid level independent of cardiovascular risk factors, and with menopause, decreased estrogen levels and increased serum uric acid levels may promote endothelial dysfunction and development of the cardiovascular disease. Studies have shown that xanthine oxidase inhibition is associated with improved endothelial function, cardiovascular risk, and plaque progression. Thus, xanthine oxidase activity and increased oxygen free radicals may play a key role in the initiation and progression of atherosclerosis, even independent of uric acid.
severity of vessel disease are consistent with these observations. The current study has some limitations which suggest it to be considered as a preliminary report. One, large size data would help in stratification based on changes in trop I levels with the severity of vessel disease. Second, the findings are based on cross-sectional data only as angiography could not be performed in an asymptomatic population.

CONCLUSION

Authors observed that increased serum uric acid levels were associated with increased severity of vessel disease, and serum uric acid is an independent risk factor for coronary artery disease.

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