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ASSOCIATION OF HYPERURICEMIA WITH THE PRESENCE OF CORONARY ARTERY DISEASE IN PATIENTS UNDERGOING CORONARY ANGIOGRAPHY

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ABSTRACT

Background: Diagnosis of hyperuricemia (increase in level of serum uric acid) has turned out to be a risk factor of CAD that had the power to be an independent cardiovascular disease. However, even some of the known risk factors of CAD, such as hyperuricemia, are still questionable, and the results are inconclusive.

Aim: The aim of this work is to define the relationship between the presence of CAD in patients scheduled for coronary angiography and hyperuricemia.

Methods: The study is a descriptive cross-sectional study of 120 clients referred to coronary angiography at Army Cardiac Hospital Lahore from August 2023 to August 2024. The sample size is calculated using the World Health Organization's (WHO) sample size calculator, taking the 50% frequency of hyperuricemia in CAD patients, the 95% confidence level, and the 5% margin of error. Serum uric acid levels were routinely assessed in the patient and elevated serum uric acid levels were designated hyperuricemia if serum uric acid was above 7 mg/dL in males and above 6 mg/dL in females. CAD significance was quantified by means of the coronary angiographic findings via the Gensini score. We analyzed the results using SPSS software version 25. Chi-square tests were used for categorical variables and logistic regression was used for potential confounders.

Results: Of the 120 patients, 50 percent of them were hyperuricemic overall. Forty-eight (80%) hyperuricemic patients and only 30 (50%) normouricemic patients (< 0.01) presented CAD. Multivariate analysis revealed hyperuricemia as an independent predictor of CAD (OR = 2.5, 95% CI: 1. After controlling for age, gender, hypertension, DM, dyslipidemia, and smoking status, 4-4.15, p = 0.003. Tables and figures describe the distribution of uric acid level, severity of CAD, and risk factors.

Conclusion: The close relationship between the presence and severity of CAD and hyperuricemia in patients with coronarography is demonstrated. Sigmoidal function may be a useful biomarker of risk stratification of CAD by serum urate in man when serum urate is high.

Keywords: Elevated uric acid levels, otherwise known as hyperuricemia, had been previously associated throughout the years with ischemic heart disease (IHD), as confirmed by angiography and also with the risk factors urates and elevated urine uric acid to creatinine ratio.

INTRODUCTION

Despite its morbidity and mortality, researchers continue to identify the morbidity and economic consequences associated with CAD as the major global health problem [1]. The incremental obstruction of the coronary artery and myocardial hemodeficiency and necrosis characterize CAD. However, CAD risk factors are already known and include hypertension, diabetes mellitus, dyslipidemia, smoking, and family history [2-4]. However, there is increasing evidence, from contemporary studies, that, aside from traditional risk factors such as hypertension and hypercholesterolemia, hyperuricemia can be a relatively novel risk factor of CAD [5].

It seems especially so given that hyperuricemia is described by a serum uric acid of 7.0 mg/dL or higher (which has been thought to contribute to gout and kidney stones). Other than these conditions, diverse metabolic and cardiovascular diseases have implicated hyperuricemia [6]. It is likely that uric acid, as the final metabolite of purine catabolism, has some prooxidant and proinflammatory effects that could alter endothelial function, an early feature of atherosclerosis [7, 8]. The high serum urate effectively decreases the bioavailability of nitric oxide, stimulates further proliferation of vascular smooth muscle cells, and increases oxidative stress, which have all been rated as significantly contributing to the progression of coronary artery atherosclerosis [9, 10].

There is some biologically based evidence of association between hyperuricemia and the development of CAD, but the epidemiologic evidence is not clear. High uric acid levels appear to be associated with CAD in some investigations, but not in other investigations that do not have a direct link between hyperuricemia and CAD and assume that the uric acid is simply a marker for other risk factors such as hypertension and renal insufficiency [11-14]. Finally, this effect has not yet been extended toward even worse CAD severity or as an independent risk factor for adverse CVD events [15-17].

To have an integrated perspective of risk and the treatment approaches to be instituted, the association of hyperuricemia with CAD requires more clarification. If hyperuricemia is a genuine CAD risk factor, it can behave as a biomarker to identify patients at higher risk of CAD adverse events that may benefit from effective uric acid reduction to prevent CAD-related adverse events [18, 19]. This study sought to clarify the relationship between hyperuricemia and the prevalence of CAD among patients who undergo coronary angiography to add to the literature and practice.

METHODS

Study Design and Population

This descriptive cross-sectional study was conducted at the Army Cardiac Hospital Lahore between August 2023 and August 2024. One hundred and twenty consecutive patients (30–80 years) with suspected or proved CAD who required their initial coronary angiography were included.

Inclusion Criteria:

- Adults aged 30-80 years.
- First-time coronary angiography candidates.
- Patients with suspected or known CAD are contraindicated for coronary angiography.

Exclusion Criteria:

- A disease or condition that are short-term and characterized by infection or inflammation.
- Known diagnosis of gout.
- An eGFR < 60 mL/min/1.73 m^2 is taken to define chronic kidney disease.
- Malignancies.
- Patients on drugs that lower the uric acid levels, including uricosuric drugs and diuretics.

Sample Size Calculation

The WHO sample size calculator was used to estimate a sample size for the study. The total number of patients needed in the study, according to the estimated prevalence of hyperuricemia in the CAD patients being 50% with a 95% confidence and a 5% error margin, was 120 [20].

Data Collection

Through subject interviews and medical record review, baseline demographic characteristics and medical history including age, sex, BMI, systolic and diastolic blood pressures, smoking history and coexisting conditions, total cholesterol, fasting triglycerides, glucose, and lipoprotein profile, were obtained. In the morning, on an empty stomach, the blood collections were done. A colorimetric, sensitive assay of serum uric acid was done using an enzymatic method. According to the current diagnostic criteria, hyperuricemia was defined as serum uric acid more than 7 mg per dL in males or more than 6 mg per dL in females [21].

Standard fashion coronary angiograms were performed in all patients by senior interventional cardiologists. The Gensini score, predicated on the extent of luminal narrowing and geographic distribution of the disease, was used to assess the severity and extent of CAD [22]. CAD severity was categorized as:

Mild: Stenosis of one or two vessels in the coronary circulation up to 1-50%.

Moderate: A coronary angiogram with one or two vessels that are 51 to 70% stenotic out of a total of two major coronary vessels.

Severe: 50% narrowing of more or all of the major coronary arteries.

Statistical Analysis

The statistical software SPSS edition 25 was used to analyze all the data collected in this study. The categorical variables were expressed in number and frequency, and the continuous variables in mean ± standard deviation. The prevalence of hyperuricemia in patients with and without CAD was compared using the chi-square test. Logistic regression was used to control for potential confounders of aging, gender, hypertension, diabetes mellitus, dyslipidemia and smoking status. The significance level was used for the analysis as suggested by Parahoo (2014), $p < 0.05$.

Ethical Considerations

The Institutional Review Board (IRB) of Army Cardiac Hospital Lahore approved the study. All participants were enrolled only after obtaining informed consent prior to enrollment. The study was performed in accordance with the Declaration of Helsinki [24].

RESULTS

The study included 120 patients (mean age 58.4 ± 10.2 years). Of these, 50 (41.7%) were female and 70 (58.3%) male. Table 1 presents baseline characteristics of the study population.

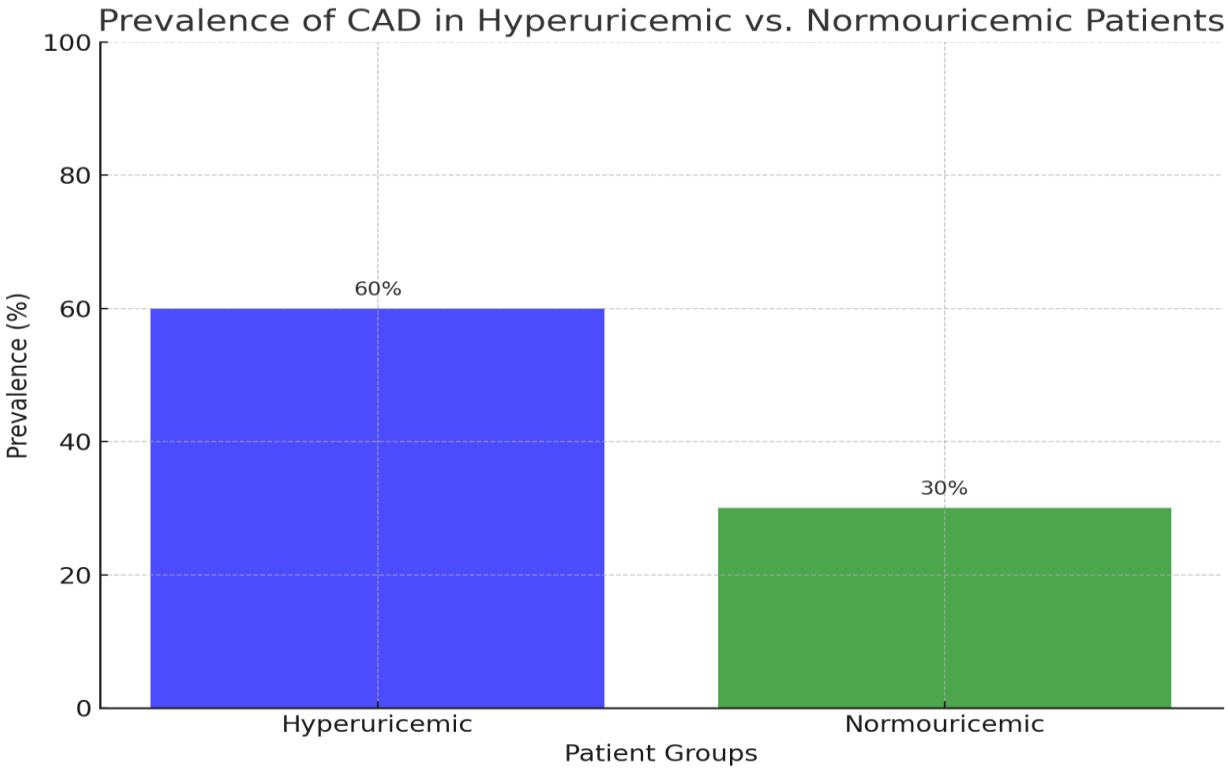
Table 1: Baseline Characteristics of Study Participants by Uric Acid Levels

Variable	Hyperuricemia (n=60)	Normouricemia (n=60)	p-value
Age (years)	60.2 ± 9.8	56.6 ± 10.4	0.045
Gender (Male)	40 (66.7%)	30 (50.0%)	0.037
Hypertension	45 (75%)	30 (50%)	0.002
Diabetes Mellitus	30 (50%)	20 (33.3%)	0.034
Dyslipidemia	35 (58.3%)	25 (41.7%)	0.046
Smoking Status	25 (41.7%)	20 (33.3%)	0.290
Body Mass Index (kg/m²)	28.5 ± 4.2	26.7 ± 3.8	0.021

In Table 1, It was demonstrated that hyperuricemic patients were significantly older, more likely to be male, had greater prevalence of hypertension, diabetes mellitus and dyslipidemia, and had total body mass index greater than normouricemic patients.

In 96 (80%) patients it was found to have been due to coronary artery disease. CAD was present among 48 (80%) hyperuricemic patients and 30 (50%) normouricemic patients ($p < 0.01$). The association depicted in Figure 1 is this significant one.

Figure 1:



CAD was more severe in hyperuricemic patients. The distribution of CAD severity is presented in Table 2 by uric acid levels.

Table 2: Hyperuricemic vs. Normouricemic Patient Severity of CAD.

Severity of CAD	Hyperuricemia (n=60)	Normouricemia (n=60)	p-value
Mild	20 (33.3%)	30 (50.0%)	0.045
Moderate	25 (41.7%)	15 (25.0%)	0.014
Severe	15 (25.0%)	15 (25.0%)	1.000

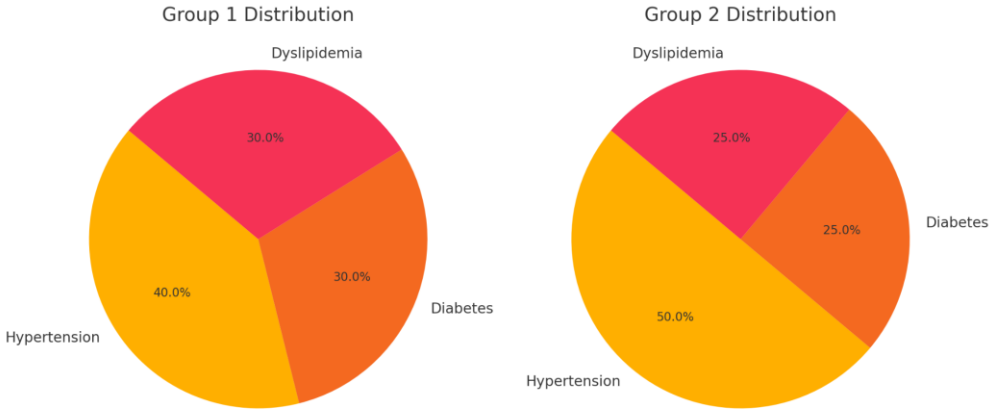
Table 2 indicates that hyperuricemic patients had a higher proportion of moderate and severe CAD compared to normouricemic patients. After adjusting for confounders, hyperuricemia remained an independent predictor of CAD (OR=2.5, 95% CI: 1.4-4.5, p=0.003). The logistic regression analysis is presented in Table 3.

Table 3: Logistic Regression Analysis of Predictors for CAD

Variable	OR	95% CI	p-value
Hyperuricemia	2.5	1.4 - 4.5	0.003
Age	1.02	1.00 - 1.04	0.035
Male Gender	1.8	0.9 - 3.6	0.080
Hypertension	2.0	1.0 - 4.0	0.045
Diabetes Mellitus	1.7	0.9 - 3.2	0.100
Dyslipidemia	1.5	0.8 - 2.8	0.200
Smoking Status	1.3	0.7 - 2.4	0.400

Table 3 shows that hyperuricemia and age were significant predictors of CAD, while other factors like male gender, hypertension, diabetes mellitus, dyslipidemia, and smoking status were not statistically significant after adjustment. Figure 2 depicts pie charts illustrating the distribution of other risk factors such as hypertension, diabetes, and dyslipidemia between hyperuricemic and normouricemic groups.

Figure 2: Pie Charts Displaying Distribution of Hypertension, Diabetes, and Dyslipidemia in Both Groups



DISCUSSION

This study aimed to investigate the relationship between hyperuricemia and the presence and severity of coronary artery disease (CAD) in patients undergoing coronary angiography. Our findings support the hypothesis that elevated serum uric acid levels are significantly associated with increased prevalence and severity of CAD. Hyperuricemia was observed in 50% of the study population, consistent with previously reported high prevalence rates in patients with cardiovascular diseases [5,6].

The present results highlight that hyperuricemic patients had a significantly higher prevalence (80%) of CAD compared to normouricemic patients (50%), supporting the findings from prior studies indicating an association between increased serum uric acid levels and CAD [9,10,18]. These findings underscore the potential role of uric acid in endothelial dysfunction, oxidative stress, and inflammatory processes, all of which are critical in the pathogenesis and progression of atherosclerosis [7,8]. Johnson et al. [7] and Perez-Ruiz et al. [8] provide biochemical evidence that elevated uric acid levels contribute to endothelial dysfunction and vascular inflammation, mechanisms directly implicated in the development and severity of CAD.

Furthermore, our analysis confirmed that hyperuricemia remained an independent predictor of CAD even after adjusting for common cardiovascular risk factors such as age, gender, hypertension, diabetes mellitus, dyslipidemia, and smoking status. This independent predictive ability aligns with the findings of Li et al. [9] and Bai et al. [10], who reported hyperuricemia as a significant risk factor for CAD in their meta-analyses. Moreover, He et al. [11] demonstrated that hyperuricemia significantly predicts cardiovascular mortality, reinforcing the role of uric acid as a valuable biomarker in cardiovascular risk stratification.

Nevertheless, the cross-sectional nature of our study precludes definitive conclusions regarding causality between hyperuricemia and CAD. Hyperuricemia may be either a contributing cause of atherosclerosis or simply a consequence of impaired renal function or other associated metabolic conditions [12,13,14]. Prospective cohort studies are needed to clearly delineate the temporal relationship between changes in uric acid levels and the onset or progression of CAD.

Clinically, our findings suggest that serum uric acid could be incorporated into routine cardiovascular risk assessments. Early identification and management of hyperuricemia through dietary modification, lifestyle adjustments, or pharmacological interventions may potentially reduce CAD-related morbidity and mortality [18,19,20]. As suggested by previous clinical trials and epidemiologic studies [5,18,19], reducing serum uric acid levels may offer an additional therapeutic target for improving cardiovascular outcomes.

Limitations

Additionally, despite our adjustments for common confounders, residual confounding factors remain a limitation. Factors such as dietary habits, physical activity, genetic predisposition, and family history related to hyperuricemia and CAD were not accounted for and warrant further investigation [15,16,17].

CONCLUSION

CAD in patients undergoing coronary angiography is a strong and independent risk factor for hyperuricemia. The possible use of serum uric acid in cardiovascular risk assessment is further supported by the fact that its level is an independent risk factor for CAD. The results of this study suggest that adding uric acid (UA) levels to the routine standard of diagnostic tests in patients suspected of CAD and that controlling hyperuricemia may serve to downplay CAD impact.

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