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Research Article

Examining the Link between Serum Uric Acid Levels and Coronary Artery Disease (CAD) Severity in Patients Undergoing Elective Coronary Angiography

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ABSTRACT

Background: High serum uric acid (SUA) is prevalent in subjects with obesity, renal disease, glucose intolerance, hyperlipidemia, hypertension, and atherosclerosis, all of which are established risk factors for coronary artery disease (CAD). Uric acid is a significant antioxidant in the initial atherosclerosis but can potentially switch to a pro-oxidant in advanced cases, depending on the factors like tissue acidity and oxidative stress. This paradoxical behavior, in addition to its association with inflammation and insulin resistance—a characteristic of metabolic syndrome—requires further investigation. Therefore, the aim of this study was to examine the relationship between SUA levels and the presence and severity of CAD.

Study design: An observational cohort study

Duration and place of study: This study was conducted in People's University of Medical and Health Sciences Nawabshah (PUMHS) from January 2023 to January 2024

Objective: To explore the relationship between serum uric acid level and the presence and seriousness of coronary artery disease (CAD) in individuals undergoing elective coronary angiography

Methodology: This cohort study of 200 consecutive hospitalized patients with CAD symptoms, all undergoing elective coronary angiography, was observational. Patients were divided into CAD-positive (with stenosis) or CAD-negative (without stenosis) groups according to their angiographic findings. CAD severity was graded using the Gensini grading system, and two blinded cardiologists assessed the angiograms. Risk factors like age, gender, smoking, diabetes, hypertension, hyperlipidaemia, family history, and hyperuricemia were documented and biochemical tests such as lipid profiles, fasting glucose, and uric acid were performed employing routine methods after 10 hours.

Results: Observational cohort study included 200 patients who underwent coronary artery disease (CAD) assessment via coronary angiography. Out of these, 175 had CAD, whereas 25 did not. CAD patients had significantly higher levels of blood uric acid compared to non-CAD patients (358.23 μmol/L vs. 251.32 μmol/L, $p < 0.001$). In accordance with logistic regression analysis, elevated levels of uric acid, smoking, decreased levels of HDL-C, and hypertension were all significantly related with the presence of CAD. These findings reflect a significant correlation between elevated serum uric acid and the presence and seriousness of CAD.

Conclusion: In short, serum uric acid level was significantly correlated with the presence and seriousness of coronary artery disease (CAD).

INTRODUCTION

Individuals with glucose intolerance, obesity, renal disease, atherosclerosis, hyperlipidaemia, and hypertension—all of which are established risk factors for coronary artery disease (CAD)—often present with an elevated serum uric acid (SUA) level [1]. The clinical utility of SUA as a prognostic marker for CAD is currently unknown, however [2]. Future cardiovascular events have been reported to be strongly related to serum uric acid (SUA) levels in various cohort studies among individuals with hypertension (HTN) [3]. Furthermore, ischaemic heart disease and cardiovascular death are independently and strongly related to elevated SUA levels, as per the results of the First National Health and Nutrition Examination Survey (NHANES I) [4]. Yet findings from the Evans County Study and the highly publicized Framingham Heart Study suggest that hyperuricemia is not independently a risk factor for cardiovascular disease [5].

Approximately 60% of human serum free radicals are neutralized by uric acid, a purine metabolism product with great antioxidant properties [6]. Uric acid is a potent extracellular antioxidant but also stimulates the production of reactive oxygen species like peroxide and superoxide free radicals and granulocyte adhesion to endothelial cells [7]. Hyperuricemia has been shown to be highly associated with various inflammatory markers like tumour necrosis factor-alpha, C-reactive protein, interleukins, and total leukocytes and neutrophils [8]. Uric acid acts as an antioxidant and plays a major role in the plasma antioxidant capacity in the initial stages of atherosclerosis [9]. This antioxidant activity is paradoxically reversed in the later phases of atherosclerosis when uric acid exhibits pro-oxidant action [10]. Several environmental and physiological factors, including stage of the disease, tissue acidity, availability of oxidative chemicals and enzymes, and local depletion of other antioxidants, appear to influence this shift [11,12].

Insulin resistance, a key feature of metabolic syndrome (MS) and a condition with an inextricable link to coronary artery disease (CAD), is thought to be a primary stimulus of the pathophysiologic pathways underlying elevated serum uric acid (SUA) levels in atherosclerotic disease [13]. Therefore, the aim of the present study was to explore the relationship between serum uric acid level and the presence and seriousness of coronary artery disease (CAD) in individuals undergoing elective coronary angiography.

METHODOLOGY

This is an observational cohort study and had a total of 200 individuals. All the people were those patients who were experiencing symptoms of CAD and were being admitted consecutively to the hospital. All the participants underwent elective coronary angiography. Their informed written consent was obtained. The Ethical Review Committee approved the study.

A complete clinical history was elicited on the day of evaluation of the patients for coronary angiography. Patients were classified as having CAD and assigned to the CAD-positive (case) group if they had evidence of stenosis in a coronary artery or in a large epicardial coronary branch by angiogram. CAD-negative (control) patients were those with no evidence of stenosis. All subjects provided their informed consent according to the study protocol, which had been approved by the local ethics committee.

Exclusion criteria: Those patients experiencing acute coronary syndrome in the first four weeks were excluded. Also excluded were individuals who had a history of coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), or stent implantation. Other exclusions included chronic liver disease, neoplastic disease, alcoholism, heart failure, and significantly impaired renal function.

Standard technique was employed for coronary angiography, and the Gensini scoring system, as a measure of the site and severity of stenosis, was employed to assess the severity of CAD. Two blindfolded cardiologists interpreted the angiograms. Age, sex, smoking, hyperlipidaemia, diabetes, hypertension, family history, and hyperuricemia were some of the CAD risk variables that were studied. Definitions for each of the risk factors were based on laboratory findings and clinician consensus. After 10 hours of fasting, biochemical tests were conducted in order to determine lipid profiles, fasting blood glucose, and uric acid by conventional methods.

RESULTS

There were a total of 200 patients who were a part of this study. All the participants were

divided into 2 groups. One group had only 25 patients and it was represented as the group without CAD. It included individuals with a Gensini score of 0. The rest 175 patients were in the other group which was represented as the group with CAD. It included individuals with scores more than 1. Both groups had individuals with similar ages. Table number 1 shows the age, distribution of Gensini scores, and uric acid levels in both the groups. Note that all the values in table number 1 are in terms of mean.

Table No. 1

Features	Group with CAD (n=175)	Group without CAD (n=25)	p-value
Age (yrs)	52.99	47.15	0.003
Total cholesterol (mg/dl)	178.12	163.20	0.186
HDL-C (mg/dl)	36.21	36.68	0.702
LDL-C (mg/dl)	102.10	95.63	0.464
Systolic blood pressure (mmHg)	138.89	141.20	0.585
Diastolic blood pressure (mmHg)	82.77	83.60	0.691
Uric acid (mol/l)	357.99	251.32	<0.001
Ejection fraction	54.50	63.16	<0.001

Table number 2 shows the demographic characteristics and risk factors in both the groups.

Table No. 2

Characteristics	Group with CAD (n=175)		Group without CAD (n=25)	
	N	%	N	%
Gender				
• **Female**	17	9.8	12	48.0
• **Male**	158	90.2	13	52.0
Smoking	89	50.8	4	16.0
Family history	65	37.1	6	24.0
Diabetes	67	38.2	8	32.0
Hypertension	79	45.1	14	56.0

Table number 3 shows the distribution of Gensini scores, demographic features, and risk factors according to the serum uric acid quartiles. Note that the values in table number 3 are in terms of mean and percentage

Table No. 3

Features	1st Quartile (<288 µmol/l)	2nd Quartile (289-339 µmol/l)	3rd Quartile (340-406 µmol/l)	4th Quartile (>406 µmol/l)
Age (yrs)	49.78	54.54	50.30	56.49
Total cholesterol (mg/dl)	180.00	163.39	179.89	181.39
HDL-C (mg/dl)	36.78	35.66	35.40	36.76
LDL-C (mg/dl)	108.61	91.20	104.89	101.07
Systolic blood pressure (mmHg)	137.98	137.21	144.78	136.40
Diastolic blood pressure (mmHg)	82.93	80.73	85.34	82.51
Gender (%)				
• **Female**	33	12	4	9
• **Male**	67	88	96	91
Smoking (%)	35	39	64	50
Family history (%)	41	23	40	37
Diabetes (%)	37	38	38	37
Hypertension (%)	45	36	60	46

Table number 4 shows the outcomes of logistic regression analysis.

Table No. 4

Features	β	p-value	Odds Ratio
Age	-0.009	0.698	0.991
Diabetes	0.964	0.155	2.623
Hypertension	-1.930	0.002*	0.145
Gender	0.363	0.635	1.437
HDL-C	-0.078	0.011*	0.925
LDL-C	0.003	0.639	1.003
Smoking	1.767	0.011*	5.850
Uric acid	0.016	0.001*	1.016

DISCUSSION

The primary outcome of the study indicates that patients with CAD had significantly higher serum uric acid concentration compared to those who did not have the disease. In addition, serum uric acid concentration was found to be positively related to CAD presence and severity. Moreover, the prevalence and seriousness of CAD were greater in individuals with the highest quartile of serum uric acid in comparison to patients in the lowest quartile.

In our research, CAD patients had significantly higher mean serum uric acid levels compared to non-CAD patients. The difference was statistically significant. A positive correlation ($p < 0.001$) between serum uric acid and severity of CAD was observed using Spearman's correlation analysis. Logistic regression analysis indicated that patients who had higher levels of uric acid had a 1.01 times greater risk of developing CAD compared to those who had lower levels, which was also significant.

The MONICA Augsburg trial, including 1,044 men, identified that high serum uric acid was an independent risk factor for total and cardiovascular mortality [14]. Similarly, a substudy of the LIFE experiment ascertained that baseline serum uric acid was highly associated with a composite endpoint of cardiovascular death, fatal or nonfatal myocardial infarction, and nonfatal stroke in the whole study population [15].

In a case-control study, there was no relationship between serum uric acid level and CAD severity in 1,029 consecutive patients undergoing coronary angiography and divided into four groups based on the outcome of their angiogram [16]. Two other studies demonstrated that the concentration of uric acid did not have an independent relationship with the occurrence or CAD severity [17,18]. Although several studies have explored the correlation between serum uric acid and CAD presence, fewer studies have explored its correlation with CAD severity [19]. However, one study that used the Gensini score as an index of CAD severity found a correlation between elevated serum uric acid levels and CAD presence and severity [20].

CONCLUSION

Serum uric acid level was significantly correlated with the presence and seriousness of coronary artery disease (CAD).

Funding Source

This study was conducted without receiving financial support from any external source.

Conflict in the Interest

The authors had no conflict related to the interest in the execution of this study.

Permission

Prior to initiating the study, approval from the ethical committee was obtained to ensure adherence to ethical standards and guidelines.

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