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

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Abstract

Introduction: Coronary artery disease (CAD) is on the list of leading causes of morbidity and mortality in the world. Hyperuricemia is no longer a benign disease or metabolic disorder since studies have found an increasing correlation of hyperuricemia and cardiovascular risk and the severity of CAD.

Objective: To identify the relationship that exists between hyperuricemia and the severity and occurrence of CAD among patients who were undergoing coronary angiography in a tertiary care hospital.

Materials and Methods: A cross-sectional study was conducted from July, 2024 to December, 2024 at the Rashid Latif Medical College, Lahore. A sample size of 250 patients who received coronary angiography was involved. The level of serum uric acid and the severity of CAD based on Gensini score were determined. Data analysis was performed using SPSS 26.

Results: The prevalence of hyperuricemia was 41.6 percent. An increased uric acid was linked to increased prevalence of the triple vessel disease and a much higher percentage of mean Gensini scores in the normouricemic patients.

Conclusion: Hyperuricemia was significantly associated with each and severity of CAD which justifies its position as a mere adjunctive risk stratification marker.

Keywords: *Hyperuricemia, Coronary artery disease, Gensini score, Angiography, Cardiovascular risk.*

INTRODUCTION

Coronary artery disease (CAD) remains the primary cause of morbidity and mortality globally, and its incidence has increasingly become prevalent in the South Asian population, including in Pakistan. Risks established by the traditional risk are well known and include hypertension, diabetes mellitus,

dyslipidemia, obesity and smoking. However, there are recent reports that hyperuricemia could also be a significant factor in the pathogenesis and progression of CAD (1, 2). Investigations in different populations have shown that higher levels of serum uric acid can not only be a predictor of CAD but also its severity, as indicated by angiographic results (3). Hyperuricemia has become widely accepted as a cardiometabolic risk factor. High serum uric acid levels have been found to enhance vascular smooth muscle growth, increase oxidative stress, and decrease nitric oxide levels, leading to vascular inflammation and the formation of atherosclerotic plaques (4).

Recent studies on CAD in South Asian countries, such as Pakistan, where CAD develops at an earlier age than in Western nations, are clinically of utmost value when it comes to related risk factors, including hyperuricemia, a novel risk factor (5). Local researchers have reported that elevated serum uric acid is associated with increased angiographic severity of CAD, indicating that it may serve as a complementary risk stratification marker during coronary angiography in patients with a possible benefit (6,7). Mohammed et al. came to a similar conclusion, reporting that hyperuricemia was an independent predictor of poor outcome in patients with non-obstructive acute myocardial infarction (MINOCA), proving that uric acid may act as a prognostic indicator even in atypical manifestations of coronary heart disease (8,9).

Uric acid has been confirmed as having both diagnostic and prognostic value in recent studies. As pointed out by Gao et al., uric acid in serum was highly correlated with the extent of coronary artery stenosis, in addition to other biomarkers such as cystatin C and homocysteine, thereby highlighting its diagnostic importance in clinical cardiology (10, 11). Hyperuricemia has not only been linked to short-term results but also to long-term cardiovascular risk (12). A Japanese cohort study showed that the existence of many patients in Japan with chronic coronary syndrome with high uric acid levels, PCI is accompanied by an increase in the likelihood of cardiovascular developments reoccurring (13). Similarly, Ma et al., hyperuricemia was a negative prognostic indicator in MINOCA patients, which has an impact on prognosis (14). These results indicate that hyperuricemia can be a predictor and a consequence of poor prognosis in CAD in patients in addition to angiographic manifestation.

Similar to China reports, Li et al. demonstrated a strong relationship between high plasma uric acid and CAD in Xinjiang, indicating its clinical application in different ethnic populations (15, 16). In addition to angiographic severity, other emerging imaging modalities have been explored to investigate their ability to characterise plaque (17). Interesting details have also been obtained through gender-based analyses. It is established that higher levels of hyperuricemia correlated with increased Gensini scores of coronary vascular stenosis, some of which were seen in the differences between men and women, and it could imply that sex-specific mechanisms exist for uric acid and the level of CAD (18,19).

Moreover, the interaction between hyperuricemia and other lipid indicators has been discussed. Han et al. demonstrated that the combination of hyperuricemia with the atherogenic index of plasma significantly improved the prediction of chronic total occlusion lesions in patients with CAD, which indicates a synergistic effect of uric acid associated with dyslipidemia in enhancing atherosclerosis (20,21). All of this makes a case that hyperuricemia is increasingly understood not only as a byproduct of metabolism but as a potentially modifiable cardiovascular risk factor. In a country like Pakistan, and a high-burden environment with a dearth of healthcare resources, being able to detect biomarkers with easily quantifiable levels, such as serum uric acid, can aid in early detection, risk stratification, and management.

Objective: To identify the relationship between hyperuricemia and the prevalence and grade of coronary artery disease in patients who undergo coronary angiography in a tertiary medical center.

MATERIALS AND METHODS

Study Design: Cross-sectional Observational Study.

Study setting: The research was conducted at the Rashid Latif Medical College, Lahore.

Study duration: This was implemented in a study conducted over six months, from July, 2024 to December, 2024.

Inclusion criteria: Both genders, aged between 30 and 75 years, admitted to elective or emergency angiography, and willing to undergo angiography, were regarded as inclusion criteria. Also accepted were individuals who had recorded procedures on risk factors like hypertension, diabetes, and dyslipidemia.

Exclusion criteria: Patients with chronic illnesses, including kidney disease, gout, cancer, liver disease, haematological disease, or uric acid-lowering medication treatment, were excluded in case they could confound the results.

Methods

Patients who received coronary angiography during the study who were able to give informed consent were recruited. Structured proforma was used to gather detailed demographic, and clinical information such as age, gender, history of hypertension, diabetes, smoking, and dyslipidemia. Standard techniques were used to carry out coronary angiography by qualified cardiologists. The degree of coronary artery disease was estimated by the amount of the involved vessels and the Gensini score was used as the measure. Patients were divided into groups on the basis of the amount of uric acid to determine the relationship between the outcome and angiography. The entry and analysis of data were done with the SPSS version 26. A chi-square test and an independent t-test was used and p-value <0.05 was considered statistically important.

RESULTS

The patients were 250 patients receiving coronary angiography included in this study. The average age of the participants was 56.8 (10.5) having 162 (64.8) males and 88 (35.2) females. A prevalence of 41.6% (104 patients) was discovered on hyperuricemia. In patients with hyperuricemia, males came out the highest (65.4 percent) as opposed to females (34.6 percent).

Table 1: Baseline characteristics of study population (n=250)

Variable	Total (n=250)	Hyperuricemia (n=104)	Normal uric acid (n=146)
Age (years, mean ± SD)	56.8 ± 10.5	58.3 ± 9.8	55.7 ± 11.1
Male, n (%)	162 (64.8)	68 (65.4)	94 (64.4)
Female, n (%)	88 (35.2)	36 (34.6)	52 (35.6)
Hypertension, n (%)	142 (56.8)	67 (64.4)	75 (51.4)
Diabetes mellitus, n (%)	96 (38.4)	47 (45.2)	49 (33.6)
Smoking, n (%)	72 (28.8)	32 (30.8)	40 (27.4)

Stratified by the coronary angiographic results, the patients with hyperuricemia had a higher tendency to have multi-vessel disease than patients with normal uric acid levels.

Table 2: Distribution of coronary artery disease severity by uric acid levels

CAD Severity	Hyperuricemia (n=104)	Normal uric acid (n=146)	p-value
Normal coronaries	12 (11.5)	38 (26.0)	<0.05
Single vessel disease (SVD)	24 (23.1)	51 (34.9)	
Double vessel disease (DVD)	28 (26.9)	30 (20.6)	
Triple vessel disease (TVD)	40 (38.5)	27 (18.5)	

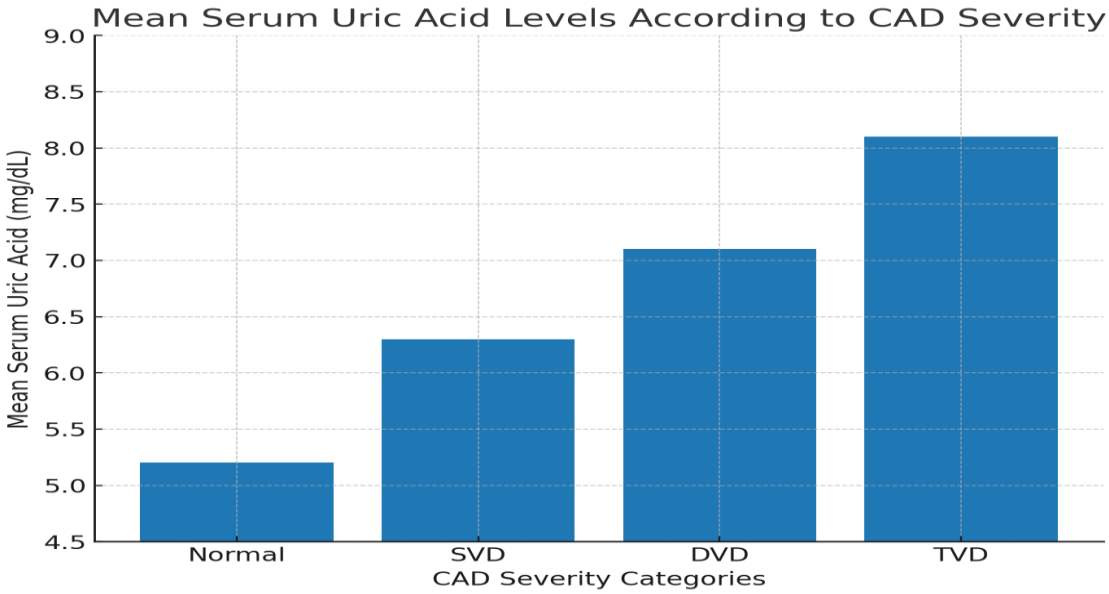
The mean Gensini score was significantly greater in hyperuricemic patients compared to those with normal uric acid levels. Mean score in the hyperuricemia group was 64.5 ± 18.3, whereas in the normal uric acid group, it was 41.2 ±15.7. Comparative Gensini scores as summarised in **Table 3**.

Table 3: Comparison of Gensini score between groups

Group	Mean Gensini score ± SD	Range
Hyperuricemia (n=104)	64.5 ± 18.3	32 – 108
Normal uric acid (n=146)	41.2 ± 15.7	20 – 89

This is seen in **Graph 1**, demonstrating the average serum uric acid values in the various groups of CAD severity groups.

Graph 1: Mean serum uric acid levels according to CAD severity



Other subgroup analyses showed that hyperuricemia occurs more in patients with hypertension and diabetes comorbidities than in other patients. Hyperuricemia prevalence was 47.2 percent in the hypertensive patients and 48.9 percent among diabetics. This is described in the distribution of **Table 4**.

Table 4: Frequency of hyperuricemia in relation to comorbidities

Comorbidity	Total n	Hyperuricemia n (%)	Normal uric acid n (%)
Hypertension (n=142)	142	67 (47.2)	75 (52.8)
Diabetes (n=96)	96	47 (48.9)	49 (51.1)
No HTN/DM (n=92)	92	22 (23.9)	70 (76.1)

In general, the results indicate that there is increased burden and severity of CAD in the hyperuricemia patients versus those with normal uric acid levels in the serum.

Discussion

This study showed that there is a considerable correlation between hyperuricemia and the level of coronary artery disease (CAD) in patients with coronary angiography. The rate of hyperuricemia in CAD patients, as observed, concurs with previous research findings from both local and international settings. Serum uric acid level was also found to be correlated with the degree of coronary involvement, especially the triple vessel disease and increased Gensini scores. It has long been the subject of debate regarding the nature of the relations between hyperuricemia and CAD. Uric acid has long been thought by some researchers to be an innocent bystander or surrogate of more well-recognised cardiovascular risk factors, such as hypertension, diabetes or obesity.

Uric acid increases endothelial dysfunction capacity by inhibiting nitric oxide production, promotes oxidative stress, and stimulates inflammatory pathways, thereby speed up the atherogenic process. Such processes can be one reason why hyperuricemic patients in the study had much angiographic severity (1). Similarly, Padda et al. reported that hyperuricemia correlated with the severity of angiographic lesions, reaffirming its significance in the South Asian community, wherein the risk of cardiovascular disease has already been amplified (2). Another study by Madbouly et al. (2014), conducted in Egypt, found that hyperuricemia had a strong correlation with increased angiographic severity in both males and females, providing global evidence of the association (3). The available results reinforce the contention that hyperuricemia cannot be ignored in clinical practice, particularly within the population who are at risk of early and severe CAD.

Li et al. also highlighted the role of hyperuricemia as a cardiometabolic risk factor, specifically its implication in vascular inflammation and plaque development (4). The current research result regarding the increased prevalence of triple vessel disease in the sample of hyperuricemic patients is in line with the previous findings outlined by Ikramullah et al., who stated that the high levels of uric acid were closely linked to the extent of multi-vessel CAD in Pakistani patients (5). Similar findings were recently established by Kalwar et al., which strengthens the notion that uric acid is both diagnostic and prognostic in assessing patients undergoing coronary angiography (6). All these papers seem to indicate that measuring uric acid could be a simple, inexpensive, and beneficial early risk stratification tool in clinical cardiology. In addition to cross-sectional relations, longitudinal data also support the prognostic relevance of hyperuricemia (7). Similarly, Raza et al. found increased incidence of hyperuricemia as compared to CAD patients, especially in the presence of hypertension and diabetes in patients, which was also observed in our study group (8). They duplicated these results and showed that hyperuricemia was indicative of poorer prognosis even in a group of myocardial infarction patients with non-obstructed coronary arteries, otherwise of lower risk (9).

The Diagnostic Function of uric acid has been confirmed with increasing frequency (12). These results suggest that uric acid provides prognostic information, not only in terms of risk stratification, but also in direct clinical measures. The chronic cardiovascular effect of hyperuricemia was demonstrated in a nationwide cohort study in Japan by Akashi et al., in which patients with chronic coronary syndrome and high uric acid post-PCI were at higher risks of recurrent cardiovascular events (13). The evidence from regional studies can also support these conclusions. The correlation of elevated uric acid with angiographic severity was confirmed in Bengali patients in a study of tertiary care in Bangladesh, as was true in Pakistani patients (15). Similarly, Li et al. in Xinjiang, China, revealed independent links between hyperuricemia and CAD, illustrating its applicability to most Asian ethnic groups (16).

Differences were also pointed out in gender. According to Yang et al., uric acid was correlated with Gensini scores, which were higher in both genders, but to varying extents, indicating sex-specific processes (18). The retreat on the Wang et al. study is susceptible to retraction, but it highlights the pitfalls of conducting methodologically assertive research in this field (19). The correlation between hyperuricemia and lipid indices further substantiates its role as a risk factor. Han et al. demonstrated that hyperuricemia was associated with a strong improvement in chronic total occlusion lesion prediction in patients with CAD when combined with the atherogenic index of plasma (20,21). The advantages of the current study are the targeted high-risk South Asian population and the comprehensive angiographic evaluation that was performed with the Gensini score.

Conclusion

In this study, a distinctive connection between hyperuricemia and the distance and seriousness of coronary artery disease in patients subjected to coronary angiography has been noticed. Higher levels of serum uric acid were associated with a multi-vessel disease, increased Gensini score, and increased frequency of comorbid diseases, including hypertension and diabetes. This finding aligns with local and international research that hyperuricemia is not an incidental finding, but rather an independent cardiovascular risk factor with prognostic value. Given that serum uric acid is inexpensive and easily measurable, it can be utilised as an effective adjunct in the risk stratification of CAD-prone patients

in healthcare systems operating with limited resources. Nevertheless, since a cross-sectional study was employed, the aspect of causality is not present, and it would be desirable to conduct further prospective studies. The recognition of hyperuricemia as a modifiable factor could provide a new area for preventive approaches and management interventions in cardiovascular care.

References

1- Akhtar A, Zaffar MZ, Minhas R, Saeed HY, Niazi GZ. Association of Hyperuricemia with the Presence and Severity of Coronary Artery Disease in Patients Undergoing Coronary Angiography. Pakistan Heart Journal. 2021 Jun 24;54(2):157-61.

2- Padda J, Khalid K, Almanie AH, Al Hennawi H, Mehta KA, Fernando RW, Padda S, Cooper AC, Jean-Charles G. Hyperuricemia in patients with coronary artery disease and its association with disease severity. Cureus. 2021 Aug 13;13(8).

3- Madbouly MA, Boghdady AM, Abd El Hady YA, Abd El Meguid KR. Correlation between Hyperuricemia and Severity of Coronary Artery Disease Detected by Coronary Angiography in Men and Women. Egyptian Journal of Medical Research. 2022 Oct 1;3(4):7-19.

4- Li K, Li K, Yao Q, Shui X, Zheng J, He Y, Lei W. The potential relationship of coronary artery disease and hyperuricemia: A cardiometabolic risk factor. Heliyon. 2023 May 1;9(5).

5- Ikramullah S, Hamid R, Fatima A, Chaudhry ZA, Tareen M, Ahmed F. Association between hyperuricemia and coronary artery disease severity among patients undergoing coronary angiography. International journal of health sciences.;7(S1):2368-74.

6- Kalwar MH, Sahito SH, Hulio AA, Shaikh JK, Phulpoto AA, Balouch IJ. Examining the Link between Serum Uric Acid Levels and Coronary Artery Disease (CAD) Severity in Patients Undergoing Elective Coronary Angiography. International Journal of Pharmacy Research & Technology (IJPRT). 2025 Jul 14;15(2):300-5.

7- Zhang S, Liu X, Song B, Yu H, Zhang X, Shao Y. Impact of serum uric acid levels on the clinical prognosis and severity of coronary artery disease in patients with acute coronary syndrome and hypertension after percutaneous coronary intervention: a prospective cohort study. BMJ open. 2022 Jan 1;12(1):e052031.

8- Raza SA, Anjum N, Ayaz SB, Khalid K, Saleem M, Yousaf MJ. FREQUENCY OF HYPERURICEMIA IN PATIENTS WITH CORONARY ARTERY DISEASE AND ITS ASSOCIATION WITH DISEASE SEVERITY, AGE, GENDER, DIABETES MELLITUS, AND HYPERTENSION. Pakistan Armed Forces Medical Journal. 2021 Apr 30(2):651.

9- Mohammed AQ, Abdu FA, Liu L, Zhang W, Yin G, Xu Y, Che W. Hyperuricemia predicts adverse outcomes after myocardial infarction with non-obstructive coronary arteries. Frontiers in Medicine. 2021 Sep 9;8:716840.

10- Gao Y, Guo Y, Hao W, Meng J, Miao Z, Hou A, Luan B. Correlation analysis and diagnostic value of serum homocysteine, cystatin C and uric acid levels with the severity of coronary artery stenosis in patients with coronary heart disease. International Journal of General Medicine. 2023 Dec 31:2719-31.

11- Prasetyo DH, Nasution SA, Alwi I, Abdullah M. Correlation between Serum Uric Acid Level and Severity of Coronary Artery Stenosis in Patients with Acute Coronary Syndrome. Majalah Kedokteran Bandung. 2021 Mar 20;53(1):1-6.

12- Nakahashi T, Sakata K, Masuda J, Kumagai N, Higuma T, Ogimoto A, Tanigawa T, Hanada H, Nakamura M, Takamura M, Dohi K. Impact of hyperuricemia on coronary blood flow and in-hospital mortality in patients with acute myocardial infarction undergoing percutaneous coronary intervention. Journal of Cardiology. 2022 Sep 1;80(3):268-74.

13- Akashi N, Kuwabara M, Matoba T, Kohro T, Oba Y, Kabutoya T, Imai Y, Kario K, Kiyosue A, Mizuno Y, Nochioka K. Hyperuricemia predicts increased cardiovascular events in patients with chronic coronary syndrome after percutaneous coronary intervention: A nationwide cohort study from Japan. Frontiers in cardiovascular medicine. 2023 Jan 10;9:1062894.

14- Ma W, Gao S, Huang S, Yuan J, Yu M. Hyperuricemia as a prognostic marker for long-term outcomes in patients with myocardial infarction with nonobstructive coronary arteries. Nutrition & Metabolism. 2021 Dec 20;18(1):107.
15- Ismail KM, Sadaf A, Das S, Latif SB, Rahman MM, Eva TE. Risk Factors Associated with Angiographic Severity of Coronary Artery Disease Based on Serum Uric Acid: A Study in a Tertiary Care Hospital, Chattogram, Bangladesh. IAHS Medical Journal. 2023;6(2):48-52.
16- Li HY, Ji HY, Maimaitituersun G, Ma YT, Fu ZY. Correlation of elevated serum uric acid with coronary artery disease in Xinjiang, China: A retrospective case-control study. Medicine. 2023 Mar 31;102(13):e33256.
17- Lacaita PG, Schoegl S, Barbieri F, Widmann G, Held J, Haschka D, Weiss G, Klauser A, Feuchtner GM. The influence of serum uric acid on coronary atherosclerosis plaque phenotypes by computed tomography angiography: The missing link?. Nutrition, Metabolism and Cardiovascular Diseases. 2025 Apr 1;35(4):103828.
18- Yang B, Ma K, Xiang R, Yang G, Luo Y, Wu F, Mao M. Uric acid and evaluate the coronary vascular stenosis gensini score correlation research and in gender differences. BMC Cardiovascular Disorders. 2023 Nov 8;23(1):546.
19- Wang X, Yu D, Wang J, Huang J, Li W. [Retracted] Analysis of Coronary Artery Lesion Degree and Related Risk Factors in Patients with Coronary Heart Disease Based on Computer-Aided Diagnosis of Coronary Angiography. Computational and Mathematical Methods in Medicine. 2021;2021(1):2370496.
20- Han H, Liu X, Zhao Q, Wang Z, Sun Y, Ma X, Li M, Ma H, Liu Y, Shi D, Cheng Y. The synergistic effect of the atherogenic index of plasma and hyperuricemia on the prediction of coronary chronic total occlusion lesion: an observational cross-sectional study. Frontiers in Cardiovascular Medicine. 2024 Jul 23;11:1437096.
21- Çakmak EÖ, Bayam E, Çelik M, Kahyaoğlu M, Eren K, Imanov E, Karagöz A, İzgi İA. Uric acid-to-albumin ratio: a novel marker for the extent of coronary artery disease in patients with non-ST-elevated myocardial infarction. Pulse. 2021 Mar 4;8(3-4):99-107.