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Association between hyperuricemia and coronary artery disease severity among patients undergoing coronary angiography

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Abstract---Aim: To determine the association between hyperuricemia and coronary artery disease severity among patients undergoing coronary angiography. Methods: This study was conducted at multi centers including Al- Aleem Medical College (Gulab Devi Teaching Hospital) Lahore and Fatima Memorial Hospital Lahore in the duration from December, 2022 to May, 2023. Total 180 patients were presented with Coronary Artery Disease, Coronary angiography was performed to determine the presence of coronary artery disease, with patients having luminal stenosis of greater than 50% in at least one of the coronary arteries. Relation between hyperuricemia and coronary artery disease was assessed using Chi Square test keeping $P < 0.05$ as significant. Results: The mean age was 49.59 ± 6.11 years. The frequency of hyperuricemia was 120 (66.7%), around 32.3% patients had mild CAD, about 37.2% patients had moderate CAD while 30.6% patients had severe CAD. We found a significant association between

hyperuricemia and severity of CAD. Conclusion: We conclude that hyperuricemia is significantly associated with the severity of coronary artery disease (CAD).

Keywords---hyperuricemia, coronary artery disease (CAD), severity, association.

Introduction

The association between hyperuricemia and cardiovascular disorder, including stroke, and hypertension has long been established in several studies. Serum uric acid (SUA) is linked to coronary artery disease (CAD), however the underlying mechanism is unclear ¹. Although SUA has been linked to an increased risk of CHD, its precise position as a standalone risk factor is still up for debate ². Though it is asserted that there are methods that are both safe and effective procedures that can be utilized to lower Serum uric acid levels and thereby prevent heart disease, these have yet to be thoroughly investigated. In underlining the importance of Serum uric acid levels in relation to CAD, a study discovered that each 1 mg/dl rise in Serum uric acid increases the risk of death from CAD by 12% ².

Furthermore, it is regarded difficult to identify the level of SUA function under this circumstance due to the common presence of additional comorbidities in patients with CAD. With an incidence rate of over 80% among individuals aged than 65 years, CAD is widely regarded as the major cause of death in the senior population ³. Hyperuricemia has been linked to CAD through proven pathophysiological pathways, one of which is that SUA acts as a stimulant to oxidative stress, increasing both oxygen free radical generation and platelet adhesion. The connection between hyperuricemia and CAD may be explained by the inflammatory reactions and endothelial dysfunction that ensue from these events. According to one study, hyperuricemia increases the risk of CAD and its related mortality ⁴⁻⁸.

Both in the industrialized and the developing nations, CAD is the most common cause of mortality ⁹. Finding the risk factors, if mitigated, could make CAD less of a burden has been a focus of research for quite some time. Hyperuricemia has been the subject of discussion associated to an increased risk of coronary artery disease ¹⁰. Patients with cardiovascular risk factors, such as hypertension, should be screened for hyperuricemia and treated early to reduce their chance of developing cardiovascular disease ¹¹. A study found that hyperuricemia is linked to both the severity and presence of coronary artery calcification ¹². However, another research have shown the opposite ¹³.

We set out to investigate not only whether hyperuricemia is associated with the presence of coronary artery disease (CAD), but also whether it is associated with the severity of CAD in the population, which differs in regards to lifestyle, regular activity, fast food, and meat consumption. This finding will aid medical professionals and cardiologists in determining whether hyperuricemia is an

indicator for coronary artery disease and will hopefully inspire more inquiry into the possibility that hyperuricemia management can lessen the risk of CAD.

Material and Methods

This study was conducted at multi centers including Al- Aleem Medical College (Gulab Devi Teaching Hospital) Lahore and Fatima Memorial Hospital Lahore in the duration from December, 2022 to May, 2023. There were 180 patients registered, all of whom were between the ages of 40 and 60. Using the historical frequency of hyperuricemia in CAD patients (64.4%), the margin of error (7%), and the confidence interval (95%) in openepi, the sample size was determined. Patients with coronary artery disease were identified using coronary angiography; those patients had at least one coronary artery with luminal stenosis of more than 50%. Hyperuricemia was defined as a serum uric acid level greater than 7 mg/dl in men and greater than 6 mg/dl in women. Coronary angiography revealed the severity of coronary artery disease (CAD) by measuring the degree of luminal stenosis. Two consultant cardiologists with at least five years of experience beyond fellowship rated the angiograms, and they determined if the CAD was mild, moderate, or severe.

One major epicardial coronary artery with a luminal stenosis of more than 50% was considered to have mild CAD, two major epicardial coronary arteries with a luminal stenosis of more than 50% was considered to have moderate CAD, and three major epicardial coronary arteries with a luminal stenosis of more than 50% was considered to have severe CAD. All the information, including co-morbidities, was recorded into a standard form. IBM SPSS 20 was used for the statistical analysis. Frequencies and percentages were used to illustrate categorical variables, while the mean and standard deviation were used to illustrate numerical ones. We used the Chi-square test for correlation between categories, setting the significance level at 0.05.

Results

This study was conducted on 180 patients. The mean age of the patients was 49.59 ± 6.11 years. There were 62.78% male while 37.22% female patients in our study. Regarding the comorbid we found that 37.8% patients were diabetic, hypertension was seen in 47.8% patients, there were 53.9% obese patients and 31.1% patients were smokers. The frequency of hyperuricemia was 120 (66.7%). In our study 32.3% patients had mild CAD, about 37.2% patients had moderate CAD while 30.6% patients had severe CAD. Regarding the association between hyperuricemia and severity of CAD we found that in patients having mild CAD the prevalence of hyperuricemia was 26.7%, in patients having moderate CAD the prevalence of hyperuricemia was 32.5% while in patients having severe CAD the prevalence of hyperuricemia was 40.8%, we found a significant association between hyperuricemia and severity of CAD.

Table 1
Demographics

Demographics	Statistics
Age (Years)	49.59±6.11
Diabetes	68 (37.8%)
Hypertension	86 (47.8%)
Obesity	97 (53.9%)
Smoking	56 (31.1%)

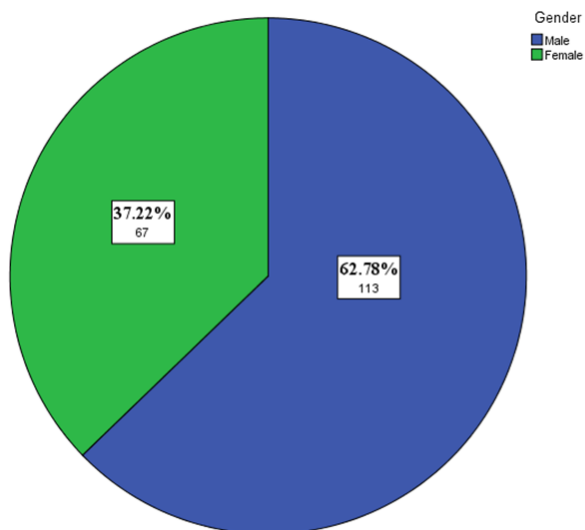


Figure 1. Gender distribution

Table 2
Association of hyperuricemia with severity of CAD

		Severity of CAD			Total	P value
		Mild	Moderate	Severe		
Hyperuricemia	Yes	32 26.7%	39 32.5%	49 40.8%	120 100.0%	0.0001
	No	26 43.3%	28 46.7%	6 10.0%	60 100.0%	
Total		58 32.2%	67 37.2%	55 30.6%	180 100.0%	

Discussion

Angiography confirms the prevalence of hyperuricemia in patients with CAD, which is consistent with reports from the general population. This is true even after controlling for other potential cardiovascular risk factors, a phenomenon known as confounding. The correlation between hyperuricemia and CAD severity was weak. Uric acid levels in the blood were similar in both sexes.¹⁵ Ten hundred

and twenty-nine people who had cardiac angiograms were studied. Eighty-seven percent of the patients were male. They divided them into four categories according to the arteriographic findings. There was no evidence that uric acid caused or contributed to CAD. Several further investigations confirmed the linear relationship between SUA and CAD.^{16, 17}

Researchers in the United States surveyed a cross-section of the senior population. The results of this study demonstrate a more definitive association between elevated uric acid levels and CAD. Male and female mortality rates were calculated after accounting for variables such as age, cholesterol levels, body mass index, and smoking history. Individuals with severe CAD (coronary angiography reveals stenosis of more than 70%) had high SUA levels associated with poor outcomes and mortality.¹⁸ Uric acid levels in the blood were correlated with total mortality, coronary artery disease incidence, and the number of CAD cases. They looked at 117,376 people and found that 617 had a connection to CAD, 1460 to all deaths, and 429 to CV. No association between SUA and increased CAD risk, total mortality, or cardiac mortality was seen in this analysis.¹⁹

Hyperuricemia is not only linked to a higher likelihood of developing coronary arteries disease (CAD), but it also has complex associations with many other independent CV risk factors, including type 2 diabetes, obesity, the metabolic syndrome, chronic renal disease, and others. This complicates the ability of separate investigations to establish a causal relationship between uric acid levels and CAD. Many studies have linked elevated uric acid to CAD, but some have also linked the severity of the condition to the development of CAD.²⁰ High uric acid levels were a sole predictor for the level of severity of CAD in a multivariate analysis of 771 individuals, 37% of whom had increased levels of uric acid. Although CAD is still uncommon, it is on the rise among those under the age of 35. Acute cardiac syndrome was found to be predicted by hyperuricemia in this research of adults aged 18 to 35.²¹

The future is uncertain for someone with CAD who also has significant atherosclerosis in all three arteries. A total of 8529 participants were included in a cohort research to determine the incidence of all-cause mortality. In order to evaluate the two cohorts, a propensity score match was performed. High levels of uric acid were found in the blood of 14.2% of all patients.²¹ More preexisting conditions were present in patients with hyperuricemia. Over the course of the average 7.5-year follow-up period, patients with hyperuricemia had a 39.11% higher mortality rate than those with normal uric acid levels ($p < 0.001$). Multivariate analysis demonstrated a statistically significant link between hyperuricemia and an increased mortality risk (1.3 HR, 95% CI 1.15 to 1.53, $p = 0.001$).²²

We recruited 180 patients presenting with Coronary artery disease (CAD). The mean age of our patients was 49.59 ± 6.11 years. There were 62.78% male while 37.22% female patients. Regarding the comorbid we observed that 37.8 patients were diabetic while 47.8% patients were hypertensive. Similar to the above discussion we also observed that hyperuricemia was significantly associated with severity of CAD. In patients having mild CAD we observed that 26.7% had

hyperuricemia, in patients having moderate CAD about 32.5% had hyperuricemia and in patients with severe CAD we observed that 40.8% had hyperuricemia. Our results are in comparison with a study which reported that hyperuricemia was significantly associated with the severity of CAD¹⁴. The also noted a significant progression of hyperuricemia in mild, moderate and severe CAD patients. They reported that 52.4% patients had hyperuricemia who had mild CAD, in moderate CAD patients they reported 60.7% hyperurecemia while in severe CAD patients they reported that 79.2% had hyperuricemia.

Conclusion

We conclude that hyperuricemia is significantly associated with the severity of Coronary artery disease (CAD). Hyperuricemia seemed to be more predominant in severe Coronary artery disease.

References

1. Zhang S, Wang Y, Cheng J, Huangfu N, Zhao R, Xu Z, et al. Hyperuricemia and cardiovascular disease. *Curr Pharm Des.* 2019;25(6):700-9.
2. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. *Arthritis Care & Research: J Am Coll Rheumatol.* 2010;62(2):170-80.
3. Wu J, Lei G, Wang X, Tang Y, Cheng H, Jian G, et al. Asymptomatic hyperuricemia and coronary artery disease in elderly patients without comorbidities. *Oncotarget.* 2017;8(46):80688.
4. Zuo T, Liu X, Jiang L, Mao S, Yin X, Guo L. Hyperuricemia and coronary heart disease mortality: a meta-analysis of prospective cohort studies. *BMC Cardiovasc Disorder.* 2016;16(1):1-0.
5. Palazzuoli A, Hashemi H, Jameson LC, McCullough PA. Hyperuricemia and Cardiovascular Disease. *Rev Cardiovasc.* 2017;18(4):134-45.
6. Borghi C, Palazzuoli A, Landolfo M, Cosentino E. Hyperuricemia: a novel old disorder relationship and potential mechanisms in heart failure. *Heart Fail Rev.* 2020;25:43-51.
7. Chazova IE, Zhernakova JV, Kisliak OA, Nedogoda SV, Podzolkov VI, Oshchepkova EV, et al. Consensus on patients with hyperuricemia and high cardiovascular risk treatment. *Systemic Hypertension.* 2019;16(4):8-21.
8. Shahin L, Patel KM, Heydari MK, Kesselman MM, Heydari-Kamjani M. Hyperuricemia and cardiovascular risk. *Cureus.* 2021;13(5):e14855
9. Li M, Hu X, Fan Y, Li K, Zhang X, Hou W, et al. Hyperuricemia and the risk for coronary heart disease morbidity and mortality a systematic review and dose-response meta-analysis. *Sci Rep.* 2016;6(1):1-11.
10. Chiang KM, Tsay YC, Vincent Ng TC, Yang HC, Huang YT, Chen CH, et al. Is hyperuricemia, an early-onset metabolic disorder, causally associated with cardiovascular disease events in han Chinese?. *J Clin Med.* 2019;8(8):1-19.
11. Kuwabara M. Hyperuricemia, cardiovascular disease and hypertension. *Pulse.* 2015;3(1)242-52.
12. Gagliardi AC, Miname MS, Santos MD. Uric acid: A marker of increased cardiovascular risk. *Atherosclerosis.* 2009;202(1):11-7.

13. Larsen TR, Gerke O, Diederichsen AC, Lambrechtsen J, Steffensen FH, Sand NP, et al. The association between uric acid levels and different clinical manifestations of coronary artery disease. *Coron Artery Dis.* 2018;29(3):194-203.
14. Akhtar A, Zaffar MZ, Minhas R, Saeed HY, Niazi GZK. Association of Hyperuricemia with the Presence and Severity of Coronary Artery Disease in Patients Undergoing Coronary Angiography. *Pak Heart J.* 2021;54(02):157-161.
15. Goodarzynejad H, Anvari MS, Boroumand MA, Karimi A, Abbasi SH, Davoodi G. Hyperuricemia and the presence and severity of coronary artery disease. *Lab Med.* 2010;41:40-45.
16. Alderman M, Aiyer KJ. Uric acid: role in cardiovascular disease and effects of losartan. *Curr Med Res Opin.* 2004;20:369-379.
17. Culleton BF, Larson MG, Kannel WB, Levy D. Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study. *Ann Intern Med.* 1999;131:7-13.
18. Lv S, Liu W, Zhou Y, et al. Hyperuricemia and severity of coronary artery disease: an observational study in adults 35 years of age and younger with acute coronary syndrome. *Cardiol J.* 2019;26:275-282.
19. Zhang C, Jiang L, Xu L, et al. Implications of hyperuricemia in severe coronary artery disease *Am J Cardiol.* 2019;123:558-564.
20. Krishnan E, Pandya BJ, Lingala B, Hariri A, Dabbous O. Hyperuricemia and untreated gout are poor prognostic markers among those with a recent acute myocardial infarction. *Arthritis Res Ther.* 2012;14:0.
21. Casiglia E, Tikhonoff V, Virdis A, et al. Serum uric acid and fatal myocardial infarction: detection of prognostic cut-off values: the URRAH (Uric Acid Right for Heart Health) study. *J Hypertens.* 2020;38:412-419.
22. Tardif JC, Kouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. *N Engl J Med.* 2019;381:2497-2505.