ORIGINAL ARTICLE

HYPERURICEMIA AS AN INDEPENDENT RISK FACTOR FOR ACUTE CORONARY SYNDROME IN PATIENTS WITHOUT METABOLIC SYNDROME

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ABSTRACT

Background: Hyperuricemia is an excess of uric acid in the blood. Uric acid levels are a function of the balance between purines breakdown and uric acid excretion. Relationship between serum UA levels and acute coronary artery disease (CAD) has been reported in cross-sectional studies. Limited information, however, is available. So, we aimed to conduct this study to find whether UA is associated with CAD.

Objectives: To assess the association between hyperuricemia and acute coronary artery disease in patients without metabolic syndrome

Methods: This present case control study was conducted at North Medical Ward, May Hospital Lahore. Patients of age 40-80years of either gender presenting with coronary artery disease were included. Informed consent was taken from 200 cases. Patients were assessed for presence or absence of coronary artery disease and then patients were divided in two groups.5 cc Blood samples were obtained and samples were sent to assess serum Uric acid level. Odds ratio was calculated to assess the association between Hyperuricemia and coronary artery disease. OR>1 was considered as significant. Data was stratified for gender and type of ACS.

Results: In our study the mean age of the patients was 60.37±11.62 years. 64% patients were males and 36% patients were females. Serum Uric acid Level was noted as 6.94±3.23 mg/dl. The results showed that hyperuricemia was observed in 65.50% patients. Statistically there is significant association was found between hyperuricemia and study groups.

Conclusion: According to the results of our study there is a significant association between the hyperuricemia and acute coronary artery disease in patients without metabolic syndrome.

Keywords: Uric Acid, Hyperuricemia, Coronary Artery Disease, Metabolic Syndrome.

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INTRODUCTION

Uric acid (UA) is by product of purine metabolism, produced by xanthine oxidase, an enzyme increasingly recognized as key contributor to oxidative stress and cardiovascular disease.[1] During ischemia, xanthine oxidase activity rises, while its inhibition has been shown to improve myocardial oxygen consumption and endothelial function.[2]

Several studies have established association between serum uric acid levels and metabolic syndrome.[3] However,

direct link between hyperuricemia and likelihood of developing metabolic syndrome remains poorly understood. Hyperuricemia is strongly associated with cardiovascular risk factors, suggesting it may serve as marker for atherosclerosis rather than independent causative factor.4 Elevated uric acid levels have also been linked to hypertension, metabolic syndrome, abdominal obesity, endothelial dysfunction, inflammation, subclinical atherosclerosis, and increased risk of cardiovascular events.[5] Gender-specific associations have been observed, with uric acid levels showing stronger correlation with metabolic abnormalities in women.[6] Additionally, prevalence of hyperuricemia in women declines with age before increasing between 45 and 54 years, suggesting potential influence of menopausal status.[7]

Hyperuricemia is more prevalent in patients with coronary artery disease (CAD), though its direct impact remains uncertain due to the complex interplay with established cardiovascular risk factors.[8] While significant association between hyperuricemia and CAD has been reported in individuals with metabolic syndrome, data on patients without metabolic syndrome remain scarce, particularly in local populations. Prevalence of hyperuricemia varies globally, with studies estimating it affects approximately 15-25% of general population, while its prevalence in acute coronary syndrome (ACS) patients can be as high as 40-50%.[9,10]

Given the limited local data and the need to clarify whether hyperuricemia is independently associated with ACS in individuals without metabolic syndrome, this study aims to investigate the asociation between hyperuricemia and ACS in this specific population.

METHODS

This present case control study was conducted at North Medical Ward, Department of Medicine, Mayo Hospital Lahore. The study was conducted after the six months of approval of synopsis. The non-probability purposive sampling technique was used in this study. Patients of age 40-80 years of either gender presenting with coronary artery disease were included. Informed consent was taken from 200 cases.

Demographic profile (name, age, gender and contact) was also obtained. Patients were assessed for presence or absence of coronary artery disease and then patients were divided in two groups. Blood samples were obtained from each patient with the help of a staff nurse by using 5cc BD syringe and sample was sent to the pathology laboratory of the hospital to assess the serum Uric acid level. Raised uric acid level i.e. Hyperuricemia was labeled (as per operational definition).

SPSS (v16.0) was used to enter and analyze the data. Quantitative variables like age, BMI & serum uric acid level was presented as Mean±S.D. Qualitative variables like gender, BMI status and hyperuricemia was presented in form of frequency and percentage. Odds ratio was calculated to assess the association between Hyperuricemia and coronary artery disease. OR>1 was considered as significant. Data was stratified for gender and type of ACD. Chi-square test was applied post stratification. p-value ≤ 0.05 was considered significant.

RESULTS

Total 200 patients were enrolled in this study. The mean age of the patients was noted as 60.37±11.62 years with minimum and maximum ages of 40 & 60 years respectively. The study results showed that the male patients were 64% whereas the female patients were 36%. In this study, out of 100 ACS patients, NSTEMI was found in 36 (36%) patients, STEMI was found in 28 (28%) patients and unstable angina was found in 36 (36%) patients.

Table-1: Association of hyperuricemia with coronary artery disease

Hyperuricemia	Study Group		Total
	Cases	Control	
Yes	50 (50%)	19 (19%)	69 (34.5%)
No	50 (50%)	81 (81%)	131 (65.5%)
Total	100 (100%)	100 (100%)	200 (100%)

Odds ratio = 4.263, p-value = 0.000

Table-2: Distribution of hyperuricemia in accordance with type of acute coronary syndrome

Hyperuricemia	ACS (n=100)			Total
	NSTEMI	STEMI	UA	
Yes	16 (44.4%)	16 (57.1%)	18 (50%)	50 (50%)
No	20 (55.6%)	12 (42.9%)	18 (50%)	50 (50%)
Total	36 (100%)	28 (100%)	36 (100%)	100 (100%)

Chi-square = 1.016, p-value = 0.6017

In this study, the mean value of Serum UA Level was noted as 6.94±3.23 mg/dl with minimum and maximum values of 3 & 15 mg/dl respectively. The study results showed that hyperuricemia was observed in 65.50% patients whereas it was not observed in 34.50% patients. In this study the hyperuricemia was observed in 69 patients in whom 50 were cases and 19 were controls, similarly it was not observed in 131 patients in whom 50 were cases and 81 were controls. The calculated OR was 4.263 which was statistically significant (P<0.05).

The study results showed that hyperuricemia was observed in 50 ACS patients in whom 16 had NSTEMI and STEMI respectively, 18 had UA type of ACS. Similarly, hyperuricemia was not observed in 50 ACS patients in whom 20 had NSTEMI, 12 had STEMI and 18 had UA type of ACS. Statistically there is insignificant difference was found between the hyperuricemia and type of ACS of the patients i.e. p-value>0.05.

Among male patients, in case group, hyperuricemia was found in 25 (41%) patients while 10 (14.9%) in controls. The odds ratio was calculated as 3.958 (P<0.05). Among female patients, in case group, hyperuricemia was found in 25 (64.1%) patients while 9 (27.3%) in controls. The odds ratio was calculated as 4.762 (P<0.05).

Table-3: Association of hyperuricemia with coronary artery disease in accordance with gender of patients

Hyperuricemia	Male		Female	
	Cases	Control	Cases	Controls
Yes	25 (41%)	10 (14.9%)	25 (64.1%)	9 (27.3%)
No	36 (59%)	57 (85.1%)	14 (35.9%)	24 (72.7%)
Total	61 (100%)	67 (100%)	39 (100%)	33 (100%)

Odds ratio (Male) = 3.958	Odds Ratio (Female) = 4.762
95% CI=[1.703, 9.203]	95% CI= [1.739, 13.04]
p-value=0.001	p-value=0.002

DISCUSSION

This study was conducted at North Medical Ward, Department of Medicine, Mayo Hospital Lahore to determine the association between hyperuricemia and acute coronary artery disease in patients without metabolic syndrome.

An association between high levels of serum urate and cardiovascular disease has been proposed for many decades. However, it was only recently that compelling basic science data, small clinical trials, and epidemiological studies have provided support to the idea of a true causal effect. Hyperuricemia and gout are closely related conditions that are prevalent worldwide. Hyperuricemia and gout are closely related conditions that are prevalent worldwide.[9-10] The associations between hyperuricemia and cardiovascular diseases have not been described to be as strong as associations of cardiovascular disease with smoking, hyperlipidemia, diabetes, and hypertension.[11]

Angelo L Gaffo et al concluded in their study that the paradigm of the causative association of hyperuricemia and cardiovascular diseases seems to have progressed from one of skepticism to one of increasing evidence of a true relationship.[12]

Thus, we conducted a case control study with 200 patients. The mean age of the patients was noted as 60.37±11.62 years. There were 64% males whereas 36% were females. In our study, 18% presented with NSTEMI, 24% were presented with STEMI and 18% had unstable angina unstable angina UA type ACS was found in 36(18%) patients.

In this study the mean value of Serum UA Level was noted as 6.94±3.23 mg/dl. Thus, hyperuricemia was observed in 65.5% patients. The hyperuricemia was observed in 50 (50%) patients' cases and 19 (19%) controls. The calculated OR was 4.263 which was statistically significant (P<0.05). This showed that the patients who have CAD will have 4 times more risk of developing hyperuricemia which further can cause renal failure as compared to controls.

In our study the hyperuricemia was observed in 34.50% patients, the odds ratio of hyperuricemia in accordance with study groups was noted 0.235 in our study. A highly significant difference was found between the hyperuricemia and ACS types of patients i.e. p-value=0.000. whereas Frequency of hyperuricemia was significantly higher in patients with (68.5%) of coronary artery disease.[8]

Qureshi et al concluded that Hyeruricemia is associated with higher Gensini score and more frequent total occlusions and critical lesions in men presenting ACS.[13]

Recent studies have shown that early diagnosis of atherosclerosis is an important step in prevention of cardiovascular diseases.[14]

In a recent study by Ndrepepa G et al, of over 5000 patients with ACS undergoing PCI, raised serum UA was associated with increased 1 year mortality; with 12% increase in the adjusted risk for every 1 mg/dl increase in serum UA level. And this increased risk was observed in all ACS groups (STEMI, NSTEMI and USA).[15]

Kojima S et al also showed that serum UA predicted the development of heart failure and long-term mortality in acute MI. This risk was even stronger in women.[16]

Eswar Krishnan et al confirmed the independent risk relationship between hyperuricemia and acute MI. Gouty arthritis is associated with an excess risk of acute MI, and this is not explained by its well-known links with renal function, metabolic syndrome, diuretic use, and traditional cardiovascular risk factors.[17]

Li Chen et al demonstrated in their study that Hyperlipidemia was more common in hyperuricemia patients than in non-hyperuricemia patients (43.7% vs. 33.7%, P=0.047), and serum triglyceride level was significantly higher in hyperuricemia patients (2.11±1.24 vs. 1.78±1.38, P=0.014). But no significant

association was observed between serum UA level and one or more diseased vessels (P>0.05).[18]

In our study a significant difference was observed between the gender and hyperuricemia status i.e. p-value=0.005. The studies discussed below supports the results of our study.

The prevalence of hyperuricemia decreased with age before the age group 45 through 54 years and then increased with age for female participants, which indicated that menopausal status might influence UA level.[6] Several observational studies reported that gout was associated with multiple risk factors for cardiovascular disease and with cardiovascular morbidities and mortalities.[17,21-22]

Whether gout directly or indirectly through hyperuricemia increases the risk of cardiovascular disease remains uncertain, but current data suggest more aggressive cardiovascular risk management in patients with gout.[23]

We stratified data on the basis of type of ACS and found that hyperuricemia was observed in 16 (44.4%) NSTEMI patients, in 16 (57.1%) STEMI patients and in 18 (50%) patients with unstable angina. Statistically there is insignificant difference was found between the hyperuricemia and type of ACS of the patients i.e. p-value>0.05. This showed that overall, ACS is associated with hyperuricemia. The type of ACS does not alter the extent of hyperuricemia.

We stratified data on the basis of gender of patients and found that in male patients, in case group, hyperuricemia was found in 25 (41%) patients while 10 (14.9%) in controls. The odds ratio was calculated as 3.958 (95% CI; 1.703, 9.203, P<0.05). This showed that among male cases of CAD, the risk of developing hyperuricemia is 3 times greater as compared to controls. Among female patients, in case group, hyperuricemia was found in 25 (64.1%) patients while 9 (27.3%) in controls. The odds ratio was calculated as 4.762 (95% CI; 1.739, 13.04, P<0.05). This showed that among male cases of CAD, the risk of developing hyperuricemia is 4 times greater as compared to controls.

Gender might be an important effect modifier in the association between hyperuricemia and CAC because of differences in (a) the distribution of sUA and (b) the prevalence of CAC. Iribarren and colleagues analyzed data from the Atherosclerosis Risk in Communities study and concluded that an association between sUA and cardiovascular risk is evident in men but not women.[19]

In contrast, a similar study by Ishizaka and colleagues reported that gender was not a factor. Since the prevalence of hyperuricemia and CAC are both lower among women, a greater sample size would be needed to detect a given effect size of hyperuricemia-CAC association.[20]

CONCLUSION

According to the results of our study there is an association between the hyperuricemia and acute coronary artery disease in patients without metabolic syndrome. Thus, we have got local magnitudes as well as now in future we will implement to check uric acid level regularly in ACS patients to prevent hazardous events.

ETHICAL APPROVAL

Ethical approval was granted by the Institutional Review Board King Edward Medical University, Lahore vide reference No 639/RC/KEMU dated: 10/09/2020

CONFLICT OF INTEREST:

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

ND: Data collection and manuscript writing
MSA, SH: Data collection & analysis and critical review
SR: Data analysis and interpretation
AS, SK: Data collection & data analysis and manuscript writing
ALL AUTHORS: Approval of the final version of the manuscript to be published

REFERENCES

1. McQuade C, Skugor M, Brennan DM, Hoar B, Stevenson C, Hoogwerf BJ. Hypothyroidism and moderate subclinical hypothyroidism are associated with increased all-cause mortality independent of coronary heart disease risk factors: a PreCIS database study. Thyroid. 2011;21(8):837-843.
2. Sui X, Church TS, Meriwether RA, Lobelo F, Blair SN. Uric acid and the development of metabolic syndrome in women and men. Metabolism. 2008;57(6):845-852.
3. Chiou W-K, Wang M-H, Huang D-H, Chiu H-T, Lee Y-J, Lin J-D. The relationship between serum uric acid level and metabolic syndrome: differences by sex and age in Taiwanese. Journal of epidemiology/Japan Epidemiological Association. 2009;20(3):219-224.
4. Krzystek-Korpacka M, Patryn E, Kustrzeba-Wojcicka I, Chrzanowska J, Gamian A, Noczynska A. Gender-specific association of serum uric acid with metabolic syndrome and its components in juvenile obesity. Clinical Chemistry and Laboratory Medicine. 2011;49(1):129-136.

5. Zhang Q, Lou S, Meng Z, Ren X. Gender and age impacts on the correlations between hyperuricemia and metabolic syndrome in Chinese. Clinical rheumatology. 2011;30(6):777-787.
6. Lu W, Song K, Wang Y, Zhang Q, Li W, Jiao H, et al. Relationship between serum uric acid and metabolic syndrome: an analysis by structural equation modeling. Journal of clinical lipidology. 2012;6(2):159-167.
7. Neogi T. Asymptomatic hyperuricemia: perhaps not so benign? Journal of rheumatology. 2008;35(5):734-737.
8. Sama PK, Bari MS, Kabir MS, Ahmed AF, Alam MM. Risk of Coronary heart disease with Raised Serum Uric Acid. Dinajpur Med Col J 2008;1(1):18-20.
9. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part II. Arthritis & Rheumatism. 2008;58(1):26-35.
10. Klemp P, Stansfield SA, Castle B, Robertson MC. Gout is on the increase in New Zealand. Annals of the rheumatic diseases. 1997;56(1):22-26.
11. Ridker PM, Libby P. Risk factors for atherothrombotic disease. Libby, Bonow, Braunwald A Textbook of cardiovascular medicine. 2005:946-957.
12. Gaffo AL, Edwards NL, Saag KG. Hyperuricemia and cardiovascular disease: how strong is the evidence for a causal link? Arthritis Research and Therapy. 2009;11(4):240.
13. Qureshi AE, Hameed S, Noeman A. Relationship of serum uric acid level and angiographic severity of coronary artery disease in male patients with acute coronary syndrome. Pakistan journal of medical sciences. 2013;29(5):1137.
14. Butler R, Morris AD, Belch JJ, Hill A, Struthers AD. Allopurinol normalizes endothelial dysfunction in type 2 diabetics with mild hypertension. Hypertension. 2000;35(3):746-751.
15. 15.Ndrepepa G, Braun S, King L, Fusaro M, Tada T, Cassese S, et al. Uric acid and prognosis in angiography-proven coronary artery disease. European journal of clinical investigation. 2013;43(3):256-266.
16. Kojima S, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Yamagishi M, et al. Prognostic usefulness of serum uric acid after acute myocardial infarction (the Japanese Acute Coronary Syndrome Study). The American journal of cardiology. 2005;96(4):489-495.
17. Krishnan E, Baker JF, Furst DE, Schumacher HR. Gout and the risk of acute myocardial infarction. Arthritis & Rheumatism. 2006;54(8):2688-2696.
18. Chen L, Li X-l, Qiao W, Ying Z, Qin Y-l, Wang Y, et al. Serum uric acid in patients with acute ST-elevation myocardial infarction. World. 2012;3(1):35-39.
19. Iribarren C, Folsom AR, Eckfeldt JH, McGovern PG, Nieto FJ. Correlates of uric acid and its association with asymptomatic carotid atherosclerosis: the ARIC Study. Annals of epidemiology. 1996;6(4):331-340.
20. Ishizaka N, Ishizaka Y, Toda E-I, Nagai R, Yamakado M. Association between serum uric acid, metabolic syndrome, and carotid atherosclerosis in Japanese individuals. Arteriosclerosis, thrombosis, and vascular biology. 2005;25(5):1038-1044.
21. Choi HK, Curhan G. Independent impact of gout on mortality and risk for coronary heart disease. Circulation. 2007;116(8):894-900.
22. Cohen SD, Kimmel PL, Neff R, Agodoa L, Abbott KC. Association of incident gout and mortality in dialysis patients. Journal of the American Society of Nephrology. 2008;19(11):2204-2210.
23. 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. 2010;62(2):170-180.