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ASSOCIATION OF HYPERURICEMIA WITH CRITICAL CORONARY ARTERY DISEASE

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Contribution
GZKN conceived the idea and designed the study. Data collection and manuscript writing was done by GZK, JZ, FA, NA, AA and SS. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: The study was conducted to determine the association of increased serum Uric acid level (SUA) with critical coronary artery disease (CAD) in patients subjected to coronary angiography.

Methodology: 360 patients (180 cases with critical CAD and 180 controls without critical CAD) were enrolled in the study after taking informed consent. Demographic data like age, gender, diabetes mellitus, hypertension, family history of CAD, dyslipidemia, smoking and BMI was collected. Serum uric acid was advised and recorded in the questionnaire.

Results: 360 patients with mean age 51.37 ± 6.5 years were included. 262 patients (72.8%) were male. 54 patients (20.8%) had hyperuricemia. 26.6% cases and 15.0% controls had hyperuricemia. Hyperuricemia was significantly associated with critical CAD (OR=2.06, CI 1.22-3.49, p=0.007). The association persisted after stratification according to age, gender, diabetes, hypertension, dyslipidemia, smoking, family history of IHD and BMI.

Conclusion: There is a positive association between critical CAD and hyperuricemia.

Keywords: Coronary artery disease, Hyperuricemia, IHD

INTRODUCTION

Uric acid which is the end product of purine metabolism was once thought to be linked to gout only because 18% of the patients with hyperuricemia developed gout in five years.[1] Now it has been established as a risk factor for multiple diseases[2-4] like insulin resistance, dyslipidemias, hypertension and cardiovascular diseases.[5-8] Coronary artery disease (CAD) which previously has been an associated with wealthy, developed, industrialized societies, is presently viewed as an epidemic that has travelled from developed word to developing countries.[9] Pakistan is now facing a double burden of disease i.e. both infectious and non-infectious.[10]

The available evidences are contradictory regarding association of hyperuricemia with severity of coronary artery disease. As our population differs from others in terms of lifestyle and meat consumption, if any association is found, patients can be identified and treated for high SUA level along with their critical CAD to slow down the progression of coronary artery disease. It will not only benefit patients in management of their disease but also help physicians to delineate guidelines for diagnosis and management of CAD.

METHODOLOGY

A pilot study was conducted on 30 patients (15 with critical CAD and 15 without critical CAD) to see the association of hyperuricemia with critical CAD in the population of South Punjab as no such study was previously conducted in this region of our country. We found in that pilot study that hyperuricemia was present in 30% cases and 20% controls. On the basis of these results this case control study was done on 360 patients, 180 cases with critical CAD (critical coronary artery disease labeled as more than 90% stenosis in any one of the coronary artery on angiography) and 180 controls without critical CAD and age between 40-60 years from both genders who presented for coronary angiography at Chaudhary Pervaiz Elahi Institute of Cardiology (CPEIC), Multan. Patients with heart failure, hematological disorders or malignancies and chronic infections like tuberculosis, taking diuretics (hydrochlorothiazide and furosemide), multivitamins, uric acid lowering drugs (allopurinol, colchicine) or alcohol and chronic renal failure were excluded from the study.

Under aseptic conditions, blood sample for SUA level was drawn and was determined by using standard chemical analyzer in pathology laboratory of CPEIC, Multan. Hyperuricemia was labeled in patients with SUA level of more than 6.5mg/dl. Patients with unstable angina, non-ST elevation myocardial infarction and ST-elevation myocardial infarction were subjected to coronary angiography and assessed for presence of critical CAD.

Data collected were entered and analyzed in statistical package for social sciences (SPSS) version 17. Odds ratio was calculated to determine the association between hyperuricemia and critical CAD. Outcomes were stratified for age, gender, diabetes, hypertension, smoking, dyslipidemia, family history of IHD and raised body mass index (BMI). Post stratification OR was calculated as well with 95% confidence interval.

RESULTS

The mean age of study population was 51.3 $\pm$ 6.5 years with 173 (48.1%) persons belonging to below 50 years group (83 in cases and 90 in control) and 187 (51.9%) belonging to 50 years or more age group (97in cases and 90 in control). The study included 262 (72.8%) males (135 in cases and 127 in control) and 98 (27.2%) females (45 in cases and 53 in control). Hyperuricemia was found in 75 (20.8%) of total study population (48 in cases and 53 in control). Diabetes was present in 175 (48.6%) (93 in cases and 27 in control), hypertension in 61 (16.9%) (25 in cases and 82 in control), dyslipidemia in 29 (8.1%) (10 in cases and 19 in controls), smoking history in 35 (9.7%) (14 in cases and 21 in control), family history of IHD in 196 (54.5%) (106 in cases and 90 in control) and raised BMI in 217 (60.3%) (107 in cases and 110 in control) of study population.

Hyperuricemia was found in 48 (26.6%) of cases and 27 (15%) of controls. Hyperuricemia was positively associated with presence of critical CAD (Table 1)

Table 1: Association of Hyperurecemia with Critical CAD

	Hyperuricemia		Total
	Yes	No	
Cases	48	132	180
Controls	27	153	180
Total	75	285	360

Odds ratio 2.06 [95% CI 1.22 to 3.49]
P-value 0.007

Table 2 shows the outcomes stratified for age, gender, DM, hypertension, smoking, family history of IHD and BMI. Post stratification odds ratio was also calculated for each group showing hyperuricemia has association with critical CAD.

Table 2: Stratification of results for different risk factors of ischemic heart disease

Stratification category	Frequency (Percentage)	Frequency of hyperuricemia	Frequency of CAD with hyperuricemia	Odds Ratio
Age				
Below 50 years	173(48%)	21 (12.1%)	17 (20.48%)	5.5
50 years or more	187(52%)	54 (28.9%)	31 (31.96%)	1.36
Gender				
Male	262 (72.8%)	54 (20.6%)	37 (27.40%)	2.44
Female	98 (27.2%)	21 (21.4%)	11 (24.44%)	1.39
Diabetes Mellitus				
Diabetic	175 (48.6%)	35 (20%)	22 (23.66%)	1.64
Non-Diabetic	185(51.39%)	40 (21.66%)	26 (29.88%)	2.55
Hypertension				
Hypertensive	61 (16.9%)	15 (24.5%)	8 (32%)	1.94
Non-hypertensive	299 (83.05%)	60 (20%)	40 (25.80%)	2.15
Dyslipidemia				
Dyslipidemia	29 (8.1%)	8 (27.5%)	3 (30%)	1.20
Normal lipid profile	331 (91.94%)	67 (20.2%)	45 (26.47%)	2.27
Smoking Status				
Smokers	35 (9.7%)	13 (37.1%)	6 (42.86%)	1.50
Non-smokers	325 (90.28%)	62 (19%)	42 (25.30%)	2.35
Family History of ischemic heart disease				
Positive	196 (54.5%)	34 (17.3%)	20 (18.87%)	1.38
Negative	165 (45.55%)	41 (25%)	28 (37.84%)	3.62
Body mass index (BMI)				
Raised	217(60.3%)	46 (21.2%)	29 (27.10%)	2.03
Normal	143 (39.72%)	29(20.2%)	19 (26.03%)	2.11

DISCUSSION

As we know Framingham Heart Study and ARIC study showed no relationship between uric acid and CAD, but numerous recent studies have shown that uric acid may have been linked with the presence of coronary artery disease.[11] In a study conducted in Japan it was shown that even 1.0 mg/dl increase in serum uric acid (SUA) level after 6 months had caused significantly higher cardiovascular events than the group in which SUA level did not change (70.6 vs. 58.8/1,000 patients-year, p=0.042).[12] In a local cross sectional survey, mean Gensini score (a validated indicator of severity of coronary disease) was significantly different in group with normal SUA (22.15 ± 21.52 mg/dl) and group with increased SUA levels (35.69 ± 26.80 mg/dl) (p<0.006). Similarly critical lesions were more frequent in hyperuricemic group than in normouricemic group (0.66 ± 0.82 vs. 1.04 ± 1.09) (p=0.046) respectively.[13] NHANES I epidemiologic follow-up study on a representative sample of the United States adult population showed that hyperuricemia is linked to increased cardiovascular morbidity and mortality.[14] Kuwabara concluded that hyperuricemia in patients with cardiovascular risk factors like hypertension is considered as a risk factor for cardiovascular disease and appropriate intervention must be done at an early stage.[15] Another study showed association of asymptomatic hyperuricemia with coronary artery disease independently and it should not be considered biologically inert.[16] Biscaglia et al. also showed similar results.[17] Our results are comparable to national and international studies revealing there is an association with CAD and SUA. However Our results contradict with the Italian study, which concluded that there is no relationship is present between hyperuricemia and severity of coronary artery disease (Odds Ratio at 95% CI, [0.93 to 1.21], p=0.35) and extent of CAD (Odds Ratio at 95% CI, [0.87-1.15], p=0.96).[18] Li et al. also shown that hyperuricemia may be a risk factor for CAD but concluded that further workup for developing hyperuricemia as an independent risk factor is needed and whether to modify it or not.[19]

No doubt our study added evidence to the association of increased SUA levels with the critical CAD but it has few limitations too. Our study was observational and it was difficult to analyze all confounders. Secondly our study depends on only one measurement of SUA level and changes in uric acid level are likely to occur with time. Due to complex relationship of SUA levels with many other established cardiovascular risk factors like raised BMI, diabetes mellitus, metabolic syndrome and chronic renal disease it is still unknown whether hyperuricemia is an independent risk factor, a consequence of some other risk factor, or merely a marker for coronary artery disease.

CONCLUSION

Frequency of hyperuricemia in patients with critical coronary artery disease is higher as compared to controls without critical coronary artery disease (26.6% vs. 15%). It may be concluded that there is an association between critical coronary artery disease and hyperuricemia (odds ratio = 2.06). The association persisted after stratification according to age, gender, diabetes, hypertension, dyslipidemia, smoking, family history of IHD and BMI.

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