CONCENTRATION OF SERUM URIC ACID AMONG PATIENTS WITH SUSPICION OF SUFFERING FROM CORONARY ARTERY DISEASE

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Abstract:
Objective: The aim of this study is to find out an association between the levels or concentration of serum uric acid in the patients present with the suspicion of suffering from Coronary Artery Disease.
Methodology: The participants of this Study were consisted of 687 patients with suspicion of coronary artery diseases. All these patients underwent coronary angiography. Stenosis of equal or greater than 50.0% luminal diameter defined coronary artery disease. The expression of the severity of the coronary artery disease was performed as 1-vessel, 2-vessel, or 3-vessel disease. We used the standard of NCEP-ATP 3 (National Cholesterol Education Program-Adult Treatment Panel-3) for MS (Metabolic Syndrome). We obtained the aorta-femoral Pulse-Wave Velocity invasively by arterial catheterization.
Results: 395 patients were present with coronary artery disease. The level of serum uric acid was high in the patients suffering from coronary artery disease as compared to the patients present without coronary artery disease (5.50 ± 1.00 vs. 5.20 ± 1.00 mg/dL, P= 0.0040). Additionally, there was significant association of serum uric acid with the coronary artery disease severity (P= 0.0020). However, after the adjustment for important confusing factors including DM (Diabetes Mellitus), age, cholesterol level, smoking, metabolic syndrome, pulse-wave velocity and serum uric acid, we found that there was no independent risk factor for incidence of coronary artery diseases (P= 0.1510). On the basis of analysis of sub-group, there was close association of serum uric acid with incidence of coronary artery disease in females as compared to males and in highest quartile ≥ 6.40mg/dL than in initial quartile < 4.80mg/dL; but these results were not much significant (P= 0.0620, P= 0.0750, respectively). According to multivariate regression analysis, Metabolic Syndrome was the most vital determinant of serum uric acid, which has strong association with the incidence of coronary artery disease.
Conclusions: In suspected patients of coronary artery disease, serum uric acid was not a risk factor for this complication and it may be simply an indicator of resistance to insulin.
KEYWORDS: Coronary Artery Disease, Insulin, Resistance, Serum, Uric, Concentration, Coronary Artery, Metabolic Syndrome.

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INTRODUCTION:

There is frequently encounter of enhanced levels of serum uric acid in the population with renal diseases [1], intolerance to glucose [2], obesity, hyperlipidemia and atherosclerosis [3], and Hypertension [4], these factors play very vital role in the pathogenesis of coronary artery disease. There is uncertain clinical value of serum uric acid for the prediction coronary artery disease. Different research works on the patients suffering from hypertension have showed an important relationship between serum uric acid and cardio-vascular events in future [5, 6]. Additionally, on the basis of the collected data from NHANES-1 (National Health and Nutrition Examination Survey [7], enhanced levels of serum uric acid have association with Ischemic Heart Disease and cardiovascular mortality. Opposite to it, findings of Framingham Heart Study (FHS) and Evans Country Study [8, 9], which are expansively cited epidemiologic investigations, have displayed that there is no recognition of hyperuricemia as an autonomous risk factor for CV events.

Pathophysiologic mechanisms fundamental enhanced concentration of serum uric acid in the disease of atherosclerosis appear to be responsible for insulin resistance [10], which is the most important trait of Metabolic Syndrome and it has positive association with the coronary artery disease. The aim of this research work was to clear the independent clinical serum uric acid value and identification of various determinants accountable of concentration of serum uric acid in the suspected patients of coronary artery disease.

MATERIAL AND METHODS:

This research work carried out in the Cardiology Department of PIMS Hospital Islamabad from June 2016 to December 2019. In this research work, the inclusion of total seven hundred and sixteen patients carried out who underwent coronary angiography for coronary artery disease diagnosis. We excluded 29 patients who fulfilled the excluded criteria as patients with post-cardiac surgery, inefficiency in renal function, aortic dissection, past history of utilization of diuretics for anti-hypertension medication, Acute Coronary Syndrome and heart complications. We took the written consent from 687 patients after explaining them the purpose of this research work.

We performed the hemodynamic examinations and sampling of blood including uric acid with the patients in supine position after taking half an hour rest. The Hypertension diagnosis was based on the measurement of Blood Pressure on three different occasions. The measurement of Diabetes Mellitus carried out by the concentration of the blood glucose in fasting condition. We measured the BMI (Body Mass Index) in accordance with the standard formula. We used the definition for Metabolic Syndrome as prescribed by NCEP-ATP 3) [11]: circumference of waist higher than 102.0 centimeter in males and eighty-eight centimeters in females, level of TG (Triglyceride) in serum at least 150.0 mg/dL (1.690 mmol/L), level of HDL-C (High-Density Lipoprotein Cholesterol) of lower than 40.0 mg/dL (1.040 mmol/L) in males and 50.0 mg/dL (1.290 mmol/L) in females, BP of at least 130.0/85.0 mmHg, or level of serum glucose of minimum 110.0 mg/dL (6.10 mmol/L).

All the patients had to undergo coronary angiography with the utilization of the Judkins procedure with digital coronary angiography equipment. At least 3 angiographers visually evaluated the coronary angiograms. We also expressed the coronary artery disease severity. We expressed different values in averages and standard deviations. The comparison of categorical variables carried out with the utilization of the Chi-square test. The comparison of the differences in average values between groups carried out with the utilization of unpaired T-test. P value of less than 0.050 was significant statistically. We used the logistic regression analysis for the identification of the independent coronary artery disease risk factors. SPSS V. 20 was in use for the statistical analysis of the collected information.

RESULTS:

Table-1 shows the clinical traits of the population of this research work. There were 288 males and 399 female's patient. Total 57.50% (n: 395) patients were present with coronary artery disease. The average age of the patients was 59.30 ± 10.40 years. Patients of the coronary artery disease were much older as compared to subjects without coronary artery disease (62.70 ± 10.20 vs. 56.80 ± 9.60, P< 0.0010). Diabetes mellitus (31.90 vs. 22.90%, P= 0.010) and metabolic syndrome (35.20 vs. 28.10%, P= 0.0490) were more frequent in the patients of coronary artery disease. The coronary artery disease patients were present with high ratio of waist to hip, increases Triglyceride, LDL-C level and pulse wave velocity and enhanced level of serum uric acid. There was not significant difference in the sex, smoking status, TC, Blood Pressure and HDL-C in both groups. When we expressed the coronary artery disease severity as 1, 2, 3-vessels disease, or without coronary artery disease, there was strong association examined between level of serum uric acid and coronary artery disease severity.

Table 1. Clinical Characteristics Of Subjects With And Without Coronary Artery Disease

Parameters	Coronary Artery Disease	No Coronary Artery Disease	p value
(n = 395)	(n = 292)		
Age, yr.	62.7 ± 10.2	56.8 ± 9.6	< 0.001
Male	177 (44.8)	111 (38.0)	0.074
Cigarette smoking	114 (28.9)	68 (23.3)	0.102
Body mass index, kg/m2	24.9 ± 3.6	24.7 ± 3.4	0.679
Waist-to-hip ratio	0.92 ± 0.06	0.90 ± 0.09	0.006
Diabetes mellitus	126 (31.9)	67 (22.9)	0.01
Metabolic syndrome	139 (35.2)	82 (28.1)	0.049
Hypertension	234 (59.2)	171 (58.6)	0.858
Systolic blood pressure, mmHg	158.6 ± 16.9	157.9 ± 17.0	0.773
Diastolic blood pressure, mmHg	98.9 ± 12.8	96.2 ± 11.3	0.112
Ejection fraction, %	63.7 ± 7.1	64.5 ± 6.5	0.717
Total cholesterol, mg/dL	189.2 ± 45.6	182.6 ± 32.4	0.073
HDL-C, mg/dL	45.7 ± 14.3	49.4 ± 14.2	0.098
Triglyceride, mg/dL	152.4 ± 82.5	129.1 ± 75.5	0.031
LDL-C, mg/dL	113.1 ± 39.9	106.7 ± 32.0	0.048
Serum creatinine, mg/dL	0.8 ± 0.3	0.8 ± 0.2	0.897
Serum uric acid, mg/dL	5.5 ± 1.0	5.2 ± 1.0	0.004
Calcium channel blockers	158 (40.0)	108 (37.0)	0.423
ACEIs or ARBs	162 (41.0)	111 (38.0)	0.427
â-blockers	86 (21.8)	52 (17.8)	0.2

Values are presented as mean ± SD or number (%) of patients. coronary artery disease, coronary artery disease; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers.

The most important risk factors of coronary artery disease were age of patient (P= 0.0010), diabetes mellitus (P= 0.0210) and pulse wave velocity (P= 0.0480). In opposition, ratio of waist to hip (P= 0.0890), Triglyceride (P= 0.1140), level of LDL-C (P= 0.1670), Metabolic Syndrome level (P= 0.2780) and concentration of serum uric acid (P= 0.1510) were not associated to coronary artery disease. In specific sex analysis, age (P= 0.0020) and diabetes (P= 0.0450) were present with association to coronary artery disease in females and males. Detection of a trend performed toward metabolic syndrome and level of serum uric acid being autonomous risk factors of incidence of coronary artery disease in females (P= 0.0590, P= 0.0620, respectively), but not in males (P= 0.4230, P= 0.2990, respectively). Table-2 represents the findings of adjusted ORs. In multivariate regression analysis, important determinants accountable for the modulation of the Metabolic Syndrome induced by levels of serum uric acid (P< 0.0010), diabetes mellitus (P= 0.0180) and sex (P= 0.0390). In analysis specific to age, the only independent factors of risk were Metabolic Syndrome for the levels of serum uric acid in both genders (P= 0.0010, P= 0.0390, respectively).

Table 2. Odds Ratio Of Coronary Artery Disease According To Prognostic Variables

Variable		Number of subjects	Coronary Artery Disease, n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age	≤ 59 yr.	324	149 (46.0)	1	1
	> 60 yr.	363	246 (67.8)	2.88 (1.69 - 4.92) b	2.96 (1.62 - 5.42) b
Gender	Female	399	218 (54.6)	1	1
	Male	288	177 (61.5)	1.76 (1.34 - 3.32)	1.52 (1.08 - 2.89)
Diabetes	No	494	269 (54.5)	1	1
	Yes	193	126 (65.3)	2.64 (1.37 - 5.07) b	2.09 (0.95 - 4.61) a
Hypertension	No	282	153 (54.3)	1	1
	Yes	405	242 (59.8)	1.55 (0.90 - 2.68)	1.46 (0.76 - 2.82)
Metabolic syndrome	No	466	256 (54.9)	1	1
	Yes	221	139 (62.9)	1.98 (0.96 - 4.38) a	1.65 (0.97 - 2.81)
Serum uric acid	Quartile 1 (2.6 - 4.7, mg/dL)	171	93 (54.4)	1	1
	Quartile 2 (4.8 - 5.6, mg/dL)	172	94 (54.7)	1.25 (0.59 - 2.65)	0.56 (0.18 - 1.72)
	Quartile 3 (5.7 - 6.3, mg/dL)	171	96 (56.1)	1.62 (1.22 - 5.60)	1.16 (0.37 - 3.57)
	Quartile 4 (6.4 - 9.2, mg/dL)	173	112 (64.7)	2.42 (1.12 - 5.20) a	1.88 (0.91 - 3.84)

Adjusted for age, gender, diabetes, hypertension, and metabolic syndrome. Coronary Artery Disease, coronary artery disease; OR, odds ratio; CI, confidence interval. a$p < 0.05$. b$p < 0.01$.

DISCUSSION:

The results of this research work supposed that Serum Uric Acid level was not risk factor of incidence of coronary artery disease after the adjustment of different potential variables. The analyses of the sub-groups, however, stated that there was strong association of serum uric acid with enhanced risk of coronary artery disease in females (P =0.0620) as compared to males (P= 0.2990). These results are much consistent with the findings of many other previous research works [8, 12,13]. In contrast, FHS [14,15] identified no relationship between concentration of serum uric acid and CV incidents after the adjustment of age, BP, TC, smoking status and diuretics treatment. NHANES-1 epidemiologic research work [16] also stated no relationship between CV events and serum uric acid in males; however, among females, level of serum uric acid was indicator of IHD and all-cause mortality. 3rd NHANES [17,18] discovered that people with hypertension having levels of serum uric acid in 2nd (5.0-5.90 mg/dL) and 3rd quartiles (6.0-6.90 mg/dL) have a significant high risk for both stroke and heart attack [19].

Mechanisms underlying levels of serum uric acid increases among patients suffering from atherosclerosis remain unidentified. Laboratory evidences states that uric acid performs an important role in the adhesiveness of platelets [20,21], production rate of free radicals as well as oxidative stress [22]. Currently, different research works [23,24] linked the Metabolic Syndrome with serum uric acid which is abnormality of metabolism with insulin resistance as main trait. Most important limitation of this research work is that the suspected population of coronary artery disease in comparison with the population-based specimen, were evaluated [25]. As a result, there was high observed rate of Metabolic Syndrome and Diabetes Mellitus (28.10%, 32.20%, correspondingly) as compared to research works conducted in past.

CONCLUSION:

The findings of this current research work demonstrate a positive relationship between the coronary artery disease severity and levels of serum uric acid in the suspected patients with coronary artery disease. Concentration of serum uric acid was not an independent factor of risk after the adjustment for the associated risk factors for coronary artery disease. Important determinant of concentrations of serum uric acid was Metabolic Syndrome, which is associated with the insulin resistance and Metabolic Syndrome also has association with the incidence of coronary artery disease. So, serum uric acid is merely an indicator of the insulin resistance, which performs very vital causative role in the pathogenesis of coronary artery disease.

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