Original Article

Acute Coronary Syndrome with Serum with Serum Uric Acid

The Association of Risk Factors and Severity of Acute Coronary Syndrome with Serum Uric Acid Levels in Female Population Younger Than 45 Years

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ABSTRACT

Objective: The study aimed to evaluate Uric Acid levels in the female population younger than 45 years and to demonstrate if its levels are correlated with severity and risk factors of Coronary Artery disease in Acute Coronary Syndrome patients.

Study Design: A Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the Cardiology ward of Ch.Pervaiz Elahi Institute of Cardiology Multan from July 2020 to Dec 2020 for a period of six months.

Materials and Methods: A total of 60 women aged less than 65 years old were included in the study following inclusion and exclusion criteria. Patients were evaluated for their family history and coronary artery risk factors such as hypertension, diabetes, dyslipidemia, family history, smoking, and body mass index. Blood samples were collected for evaluation of serum uric acid and two groups were formed: hyperuricemia and non-hyperuricemia. Coronary angiography was performed to determine the number of coronary arteries involved. Each risk factor and extent of severity of disease was compared for mean serum uric acid level between two groups. Statistical analysis was conducted on SPSS using version 23.

Results: Among analyzed 60 female patients, 31% had STEMI, 48% were diagnosed with NSTEMI, and 21% had unstable angina. 75% of patients were aged between 30-45 years. Among risk factors, hypertension (mean value=7.55± 1.72), diabetes (7.62±2.13), and dyslipidemia (7.77±1.78) were found to be significantly associated with hyperuricemia. Similarly, the higher number of involved coronary arteries was significantly related to higher uric acid levels (p=0.0001).

Conclusion: Shortly, serum UA is correlated with risk factors of coronary artery disease (CAD) like diabetes, hypertension, and dyslipidemia in the young female population. Similarly, it is a significant predictor of the severity of Coronary artery disease.

Key Words: Acute coronary syndrome, Coronary artery disease, Hyperuricemia, Female cardiac disease patients, Serum uric acid

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INTRODUCTION

Acute coronary syndromes (ACS) are one of the major causes of mortality and morbidity across the world [(1)].

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Though several types of research have already been conducted on risk assessment of ACS [(2)], many risk aspects remain poorly understood. Uric acid (UA) is produced as a result of purine catabolism in man and is a part of regular clinical testing. Although uric acid has been associated with cardiovascular diseases (CVD) for the last 130 years, its correlation with CVD as a risk factor is still under exploration. The association between raised uric acid and magnified mortality risk has already been explored in the general population with CVD [(3)], hypertension [(4)], coronary artery disease [(5)], and diabetes [(6)]. Elevated UA level in serum is a frequent finding in patients with hypertension, obesity, CVD, and diabetes.

Multiple epidemiological studies have demonstrated deranged Uric acid levels in patients with CVD to establish their relationship. However, in some studies, independent relations between the two diseases couldn't be found [(7)]. It is predicted that lack of independent

relation could be due to the likely association of UA with other risk factors of CVD such as obesity, decreased high-density lipoprotein cholesterol, hyperinsulinemia, hypertension, hypertriglyceridemia, and increased insulin resistance. Similarly, other clinical outcomes of atherosclerosis, including oxidative stress, endothelial dysfunction, and inflammation, have also been related to higher UA levels.

The young population specifically those less than 45 years is ignored when studies on risk factors and diagnosis of CVD are conducted. However, ascending trend of the incidence rate of CVD has also been demonstrated among the young population in some studies [8]. Pakistan has a high incidence rate of hyperuricemia, especially among the female segment. According to certain epidemiological studies, the reported prevalence rate is 30-39% [9]. The rationale of the present study is to evaluate hyperuricemia in the younger female population with coronary vessel disease in ACS so that UA could be established as a viable biomarker for risk analysis and severity assessment of CVD in the young population. Moreover, to our knowledge, no such study has been conducted to address this aspect, especially in the Pakistani setting. The study aimed to evaluate UA levels in the female population younger than 45 years and to demonstrate if its levels are correlated with severity and risk factors of CAD in ACS patients.

MATERIALS AND METHODS

A cross-sectional analytical study was conducted in the Department of Cardiology at Ch. Pervaiz Elahi Institute of Cardiology Multan, for the period of 6 months from 21st July 2020 to 21st Dec 2020. A total of 60 consecutive female patients who were under 45 years old, admitted with the diagnosis of ACS, which includes ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable Angina, and undergoing coronary angiography were included in the study. Whereas, those with renal disorders, gout, know malignancy, any inflammatory disorder, those on hyperuricemia medication, and those not undergoing coronary angiography were excluded from the study.

After acquiring informed consent from patients and approval from the ethical committee of the hospital, detailed physical examination, family history of the participants, and baseline laboratory analysis, including CBC, renal function tests, electrolytes, and cardiac enzyme level, was conducted. Blood samples were then collected on an empty stomach for the analysis of serum UA and the lipid profile. For lipid profile following levels were regarded as normal: total cholesterol less than 200 mg/dl, serum HDL-C less than 40mg/dl, serum LDL less than 100mg/dl, and serum triglyceride less than 150 mg/dl. Women were declared of having hyperuricemia if the serum levels were ≥6.0 mg/ dL in women. Based on serum UA level, patients were divided into two groups: hyperuricemia and non-hyperuricemia. The severity of CAD was characterized based on the number of coronary arteries: absent, 1 vessel, 2 vessels, and 3 vessels. The extent of stenosis was determined by comparing the reduction in luminal diameter with the closest normal segment. Besides patients were also assessed for established CAD risk factors: smoking, hypertension, diabetes mellitus, obesity (body mass index> 30kg/m^2).

Statistical Analysis: Statistical analysis was conducted on SPSS (version 23). Mean serum UA of the patients from two studied groups was compared for different risk factors of CAD and coronary angiographic results using the student's t-test. The statistical significance between two groups for different variables was found using the chi-square test. P-value less than 0.05 for any variable was considered statistically significant.

RESULTS

A total of 60 females complied with inclusion and exclusion criteria and were included in the study. Among the studied subjects, 31% had STEMI, 48% were diagnosed with NSTEMI, and 21% had unstable angina. Upon classifying patients in terms of their ages, it was found that only 10% of women were between 21-25 years, 15% were between25-30 years old, while 75% were between 30-45 years old (data not shown). In the study, 49% of females had hyperuricemia with a mean serum UA level (mg/dl) 7.10± 2.11. The association of serum UA was assessed with every CAD risk factor. The hypertensive patients had a mean serum UA level of 7.55± 1.72 whereas non-hypertensive had 6.1± 1.55 and this difference was found to be statistically significant. A significant association was also found between hyperuricemia and hypertension. Similarly, a significant difference was found in the mean serum UA level of diabetics (7.62±2.13) and that of non-diabetics (6.3±1.7). A significant difference was observed between the mean values of those who had dyslipidemia (7.77±1.78) than those had normal lipid profile (6.21±1.1). Furthermore, positive correlation was found between serum UA and triglycerides ($r = 0.687$, $p<0.001$) while UA was negatively correlated with low density lipoproteins ($r = .079$, $p>0.01$) (Table I). Thus, a significant association was interpreted between diabetic status and UA. However, no statistical difference was found between UA levels and family history ($p=0.72$), smoking (0.08), and BMI (0.67) (Table I). The patients with hyperuricemia had higher involvement of coronary vessels. Those with no coronary lesion were found to have mean serum UA level of 3.1mg/dl, while significantly different mean serum UA level of 5.53, 6.93, and 11.01 was found in those with involvement of 1, 2, and 3 vessels respectively. Hence, hyperuricemia was significantly associated with the severity of CVD (Table 2).

Table No.1: Association of Coronary Artery Risk Factors with Uric Acid Level of Patients (N=60)

Variables		Mean serum uric acid ±SD(mg/dl)	Hyper Uricemia (%)	Non-hyperuricemia (%)	P-value
Hyper Tension	Yes (N= 40)	7.55± 1.72	29/40 (72.5)	11/40 (27.5)	P=0.001
	No (N= 20)	6.1± 1.55	16/20 (80)	4/20 (20)	
Diabetes mellitus	Yes (N=25)	7.62±2.13	17/25 (68)	8/25 (22)	P=0.02
	No (N=35)	6.3±1.7	15/35 (42.8)	20/35 (57.1)	
Dyslipidemia	Yes (N=38)	7.77±1.78	29/35 (82.8)	6/35 (17.1)	P=0.005
	No (N=22)	6.21±1.1	5/22 (22.7)	17/22 (77.2)	
Family history	Yes (N=18)	7.26± 2.15	7/18 (38.8)	11/18 (61.1)	0.72
	No(N=42)	7.08 ± 1.64	20/42 (47.6)	22/42 (52.3)	
Smoking	Yes (N=8)	6.99±1.53	3/8 (37.5)	5/8 (62.5)	0.08
	No (N=52)	7.51± 2.322	23/52 (44.2)	29/52 (55.7)	
BMI<30kg/m2	Yes (N=15)	7.092 ± 1.54	8/15 (53.3)	7/15 (46.6)	0.67
	No (N=45)	7.341 ±2.44	22/45 (48.8)	23/45 (51.1)	

Table No.2: Comparison of Angiographic Findings between Two Study Groups (N=60)

Coronary angiographic findings	Mean SUA±SD (mg/dl)	Hyperuricemia (%)	Non-hyperuricemia (%)	P-value
0 vessel, n=1	3.1 ± 1.543	0/1 (0)	1/1(100)	P=0.001
1 vessel, n=15	5.53± 2.11	6/15 (40)	10/15 (60)	
2 vessel, n=35	6.93± 1.87	24/35 (68.5)	9/35 (31.5)	
3 vessel, n=9	11.01± 2.01	9/9 (100)	0 (0)	

DISCUSSION

The study aimed at targeting the female young population with ACS and tried to build a correlation between their serum Uric acid levels and risk factors and severity of the disease. Our study was conducted on 65 female patients diagnosed with ACS (including STEMI, NSTEMI, and unstable angina). The mean serum UA level of the patients was 7.10± 2.11 mg/dl. In recent times, studies have been conducted to assess the significance of UA as a biomarker in acute myocardial infarction (MI), but only a few have demonstrated its role in causing the severity of CAD and correlated it with ACS. Similarly, to the best of our knowledge, very few studies have specifically targeted the female population in this regard.

Our study has developed a significant relationship between high serum UA levels and the number of the coronary artery involved. In a study conducted by Sun et al, hyperuricemia was found to be an independent risk factor in the occurrence of CAD in more than 80% of the assessed women, when compared to men. However, the study didn't address the correlation with the severity of the disease[10]. In another Japanese study, both male and female patients with acute MI were assessed and correlation was analyzed between serum UA levels and Killip classification. The results found out high reports of short-term adverse effects in patients with hyperuricemia[11]. Similarly, Nadkar et al conducted a cross-sectional study and reported higher serum UA concentration in patients with acute MI [12].

In a study conducted by Culleton et al, serum UA was not only found to be significantly related to the incidence of CAD but a higher rate of adverse effects reported was reported in women than men, after age adjustment[7]. Zhang et al reported serum UA as a valuable predictor of CVDs in premenopausal women[13].

We also assessed the association of serum UA with different CAD risk factors. It was found that the majority of hypertensive were hyperuricemia and the relation was tending to be significant. Similar results were reported by Schmidt et al, who compared normotensive participants with hypertensive patients and found significantly higher serum UA in the later participants[14]. The Framingham Heart Study has established serum UA as an independent predictor of incidence and progression of hypertension. Similarly, hyperuricemia was found to be significantly correlated with diabetic status (p=0.002). Similar results were found in another cohort study where the majority of diabetic patients were having higher UA concentrations and were later involved in CVD-related morbidities [15]. Similar to the positive correlation between UA level and triglycerides found in our study, Desai et al, reported independent and linear relation between UA and TG and HDL [16]. Although the underlying mechanism between the association of two variables, it is predicted that the two metabolic disorders might have common genetic alteration.

Our study demonstrated the association of hyperuricemia with angiographic findings. We found higher involvement of coronary arteries in hyperuricemic patients (p=0.001). Similar results were found by Goodarzynejad et al who conducted a study on angiographically approved patients with atherosclerosis. It was shown that hyperuricemia might be linked with the severity of CAD (p=0.05). It is anticipated that higher serum UA leads to the formation of uric acid crystals and consequently atherosclerosis.

In compliance with our results, Tuttle and his colleagues found a linear correlation between the severity of CAD and serum Uric acid level in women when compared to men [17].

CONCLUSION

Shortly, serum Uric acid is correlated with risk factors of coronary artery disease (CAD) like diabetes, hypertension, and dyslipidemia in the young female population. Similarly, it is a significant predictor of the severity of CAD.

Author's Contribution:

Concept & Design of Study:	Kashif Ali Hashmi
Drafting:	Tariq Mehmood Khan
Data Analysis:	Amir Shahzad
Revisiting Critically:	Kashif Ali Hashmi, Tariq Mehmood Khan
Final Approval of version:	Kashif Ali Hashmi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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