ORIGINAL ARTICLE
FREQUENCY OF HYPERURICEMIA IN SUBJECTS WITH UNSTABLE ANGINA/MYOCARDIAL INFARCTION AND THEIR PROGNOSIS

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Background: Suppression of nitric oxide synthesis and stimulation of smooth muscle proliferation by increased serum levels of uric acid has a pathogenetic contribution towards accelerated atherogenesis of blood vessels of subjects with hyperuricemia. The objective of this work was to find out the prevalence of hyperuricemia in subjects who presented with unstable angina/myocardial infarction and their prognosis. **Methods:** This cross-sectional study was carried out in the Cardiology unit of Ayub Teaching Hospital, Abbottabad from 1st September, 2018 to 28th February, 2019. One hundred and ninety-nine subjects who were diagnosed with acute coronary syndrome (ACS) were enrolled in this study using non-probability consecutive sampling. ACS was diagnosed on the basis of history, electrocardiogram (ECG) findings and on the presence of elevated cardiac biomarkers. Uric acid levels were checked in less than 24 hours of presentation and subjects were grouped into hyperuricemic and normouricemic groups according to their serum levels of uric acid. After those patients in both groups were observed by comparing the presence or absence of complications between the two groups. The data was collected on a structured proforma and was statistically assessed with the help of version 16 of SPSS software. **Results:** Among 199 study participants, there were 146 (73.37%) male and 53 (26.63%) female patients. The mean age of patients in this study was 57.99±6.07 years with a range of 48–68 years. Hyperuricemia was diagnosed in 50 (25.13%) study participants. Among complications, 15 patients (7.94%) had cardiogenic shock, 27 (13.57%) had heart failure, 10 (5.03%) had cardiac arrhythmias, 16 (8.04%) had conduction defects and hyperuricemia was diagnosed in 50 (25.13%) patients. Cardiogenic shock was more common in patients with hyperuricemia (p<0.05). **Conclusion:** Hyperuricemia can result in multiple complications in patients who have an acute coronary event. Regular screening / monitoring of serum uric acid level in general population can prevent the direct as well as indirect morbidity associated with hyperuricemia.

Keywords: Acute coronary Syndrome; Hyperuricemia; Cardiogenic shock; ST elevation myocardial infarction (STEMI)

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INTRODUCTION

The term acute coronary syndrome (ACS) is used for two conditions which are unstable angina and acute myocardial infarctions. These conditions occur because of a sudden decrease in the flow of blood through the coronary arteries.[1] In patients with acute myocardial ischemia, there could be two different changes on the electrocardiogram (ECG). Those patients who have ST segment elevation in the ECG are said to have ST segment elevation myocardial infarction (STEMI) and the patients who do not have ST segment elevation in ECG are said to have Non-ST-segment elevation acute coronary syndrome (NSTE-ACS).[2] Non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA) are embodied in NSTE-ACS.[3] NSTEMI is diagnosed when symptoms of ischemia are coupled with an increase in the level of cardiac enzymes suggesting myocardial necrosis whereas UA is characterized by transitory ischemia in which cardiac enzymes are not elevated.[4]

A cardinal presentation of ACS is acute chest pain for which a large number of patients get admitted in hospitals worldwide that causes a significant load on healthcare resources.[5] Approximately ten lac people suffer from ACS in United States each year and among this number, three-quarters are those with NSTE-ACS.[6] Keeping in view the global population's rising age and the increasing rates of diabetes mellitus and obesity worldwide, it is speculated that there will be a rise in the complications of atherosclerosis which will have a major detrimental influence on the economy and the standard of life.[7] Coronary artery disease (CAD) is one of the leading causes of ill health and deaths throughout the world. Pakistan is one of those Southeast Asian countries, which has a relatively

higher prevalence of CAD.[8] Besides the conventional risk factors of CAD like hypertension, diabetes mellitus, hyperlipidaemia and smoking, hyperuricemia has also been linked to the development of coronary artery disease in numerous studies.[9] Raised serum uric acid levels are quite common in industrialized world. According to an estimate almost 21% of people in the United States who are above 20 years of age have raised serum uric acid levels.[10]

It has been proved that the production of nitric oxide is hindered when uric acid in soluble form interacts with the endothelial cells of vessels, moreover, higher the concentrations of uric acid more would be the multiplication of vascular smooth muscle cells. The decrease of nitric oxide's vasodilatory effects, along with the growth of the smooth muscles of vessels, plays a significant role in accelerated atherosclerosis in patients with hyperuricemia.[11] Hyperuricemia was found to be present in 24.7 percent of patients with ACS in a study conducted by Abdullah *et al*. and was significantly associated with the development of heart failure, conduction defects, lower ejection fraction, and increased length of hospital stay.[11] The aim of this research is to determine the frequency of hyperuricemia in patients of ACS from our population and to find its relation, if any to in-hospital outcome of patients so that measurement of serum uric acid, a simple and reasonable biochemical tool can serve as a valuable marker for risk stratification of ACS patients and also for implementing primary preventive measures.

MATERIAL AND METHODS

From September 1, 2018 to February 28, 2019, a cross-sectional study was done at the Cardiology Department of Ayub Teaching Hospital in Abbottabad. Through non-probability consecutive sampling, a total of 199 patients were enrolled. Sample size was determined using the WHO program for sample size calculation in health research by retaining the Confidence level at 95 percent, expected population of hyperuricemia in ACS at 24.7 percent[11] and an absolute precision of 6 percent.

The research included patients with ACS who were 20–70 years old and of both genders. Patients having a history of myocardial infarction, prior cardiac procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), valvular heart disease, cardiomyopathies and gout were all excluded from the study. Patients who were using pyrazinamide, thiazide diuretics, aspirin, or alcohol, which raise blood uric acid concentrations, were also excluded. The research also excluded people with chronic renal and liver problems. Patients with characteristic cardiac chest pain lasting more than 20 minutes who were admitted to the cardiology department with or without ECG alterations or increased cardiac biomarkers were diagnosed with ACS. Patients were regarded as hyperuricemic when blood uric acid levels were more than 7 mg/dl in men and more than 6 mg/dl in women.

Before collecting data, the Hospital Ethical Committee gave its approval. A systematic proforma was used to collect data. Before collecting data, patients gave their informed consent and data confidentiality was ensured. The research recruited all patients who were hospitalized to the cardiology department with an ACS diagnosis and who met the inclusion criteria. Within 24 hours of presentation, serum uric acid levels were examined, and patients were divided into hyperuricemic and normouricemic groups based on uric acid levels. The presence or absence of cardiogenic shock, development of heart failure, cardiac arrest, the ejection fraction of the left ventricle assessed by echocardiography and the development of conduction abnormalities were then compared between the two groups.

SPSS version 16 was used to analyze the gathered data statistically. Quantitative variables such as age, BMI and left ventricular ejection fraction were reported as mean ± standard deviation. Gender, hypertension, diabetes, cardiogenic shock, the development of heart failure, cardiac arrest and the development of conduction abnormalities were all reported as percentages and frequencies. According to blood uric acid levels, patients were divided into hyperuricemic and normouricemic groups, and in-hospital outcomes were compared between the two groups, as well as the existence of co-morbidities such as hypertension, diabetes, and a high Body mass index.

RESULTS

This descriptive cross-sectional research included 199 individuals with ACS. The research participants' mean±SD age was 57.99±6.07 years, with a range of 48–68 years. In the same way, the research population's mean±SD ejection fraction and body mass index were 41.47±5.34 percent and 27.15±2.66 respectively. (Table-1). In the study population, there were 146 (73.37%) males and 53 (26.63%) females (Table-2). In 50 (25.13%) of the research subjects, hyperuricemia was discovered (Table-3). 97 (48.74%) patients were found to be hypertensive while 61 (30.65%) had diabetes mellitus. There were 15 (7.53%) cases of cardiogenic shock, 27 (13.56%) cases of heart failure, 10 (5.02%) cases of cardiac arrhythmias, and 16 (8.04%) cases of conduction abnormalities among the sequelae. Except for cardiogenic shock ($p<0.05$), no statistically significant relationship was seen ($p>0.05$) when hyperuricemia was stratified by various complications of ACS and factors such as hypertension, diabetes mellitus and body mass index (Table-4, Table-5 and Table-6).

Table-1: Descriptive statistics of study population

	Mean	Standard Deviation	Minimum	Maximum
Age (years)	57.99	6.07	48	68
Ejection Fraction (%)	41.47	5.34	30	51
Body Mass Index	27.15	2.66	22.53	31.70

Table-2: Gender distribution of study population

Sex	Frequency	Percentage (%)
Male	146	73.37
Female	53	26.63
Total	199	100.0

Table-3: Frequency of hyperuricemia in study population

Hyperuricemia	Frequency	Percentage (%)
Present	50	25.13
Absent	149	74.87
Total	199	100.0

Table-4: Cross-tabulation of hyperuricemia with Hypertension and Diabetes mellitus in the study participants

Hyperuricemia	Hypertension (*p* value 0.84)			Diabetes mellitus (*p* value 0.24)		
	Present	Absent	Total	Present	Absent	Total
Present	25	25	50	12	38	50
Absent	72	77	149	49	100	149
Total	97	102	199	61	138	199

Table-5: Cross-tabulation of hyperuricemia with body mass index and cardiogenic shock in the study participants.

Hyperuricemia	Body mass index (*p* value 0.76)			Cardiogenic shock (*p* value 0.009)		
	<25	>25	Total	Present	Absent	Total
Present	12	38	50	8	42	50
Absent	39	110	149	7	142	149
Total	51	148	199	15	184	199

Table-6: Cross-tabulation of hyperuricemia with heart failure, conduction defects and cardiac arrhythmias in the study participants.

Hyperuricemia	Heart failure (*p* value 0.92)			Conduction defects (*p* value 0.99)			Cardiac arrhythmias (*p* value 0.92)		
	Present	Absent	Total	Present	Absent	Total	Present	Absent	Total
Present	7	43	50	4	46	50	5	45	50
Absent	20	129	149	12	137	149	5	144	149
Total	27	172	199	16	183	199	10	189	199

DISCUSSION

Hyperuricemia has been more common during the last several years all around the world. High-income countries have elevated blood uric acid levels, and the numbers are rising in emerging and underdeveloped countries as well.[12] Hyperuricemia and gout are becoming more common as a result of our westernized lifestyle and surroundings.[13] Higher blood uric acid levels have been linked to coronary artery calcification[14] as well as reduced flow-mediated dilation, indicating vascular endothelial dysfunction in hyperuricemics, according to clinical studies[15]. These findings point to a link between hyperuricemia and arteriosclerosis. In our study, 25.13 percent of patients had hyperuricemia, and there was no statistically significant link between hyperuricemia and the various complications that developed after an acute coronary syndrome in our patients, except for cardiogenic shock, which was more common in patients with hyperuricemia ($p<0.05$).

Despite the fact that hyperuricemia has been linked to serious cardiovascular events[16], we couldn't discover any evidence of such a link. He and colleagues found that hyperuricemia predicts major adverse cardiac events (MACEs) and mortality in ACS patients in a meta-analysis. The researchers looked at nine trials with a total of 8776 ACS patients. After adjusting for traditional risk variables, ACS patients with hyperuricemia had a higher risk of cardiovascular mortality (RR: 1.74; 95 percent CI: 1.36-2.22), all-cause mortality (RR: 1.86; 95 percent

CI: 1.49–2.32) and MACEs (RR: 1.86; 95 percent confidence intervals [CI]: 1.47–2.35).[16]

Hyperuricemia is linked to a greater risk of medium/long-term mortality and severe cardiovascular events in individuals who have had an acute coronary syndrome, according to a recent study.[17] 1119 subjects were involved in that cohort study and for a mean of 36 months these participants were followed-up. It was discovered that raised serum uric levels were linked with higher major cardiovascular event rates (HR: 1.36; 95 percent CI: 1.11–1.67; $p<0.01$), higher cardiovascular mortality (HR: 1.91; 95 percent CI: 1.32-2.76; $p<0.01$) and higher all-cause mortality (HR: 1.59; 95 percent CI: 1.18–2.15; $p<0.01$).

In our research population, we found a statistically significant link between hyperuricemia and cardiogenic shock, whereas Pagidipati and colleagues found that heart failure was more prevalent in individuals with ACS who had increased serum uric acid levels.[18] According to the researchers, subjects with higher levels were more likely to be male and had a previous history of heart failure, diabetes and myocardial infarction as opposed to those who had serum uric acid levels less than 6.0 mg/dL. The authors found that rising blood uric acid levels, regardless of a clinical diagnosis of gout, are linked with an increased risk of cardiovascular events in individuals with ACS.

Individuals with elevated blood uric acid levels had lengthy stays in the hospital and considerably increased mortality within the hospital, according to research by Bhattacharya and colleagues. Over a quarter of the research participants (27.45%) had high blood uric acid levels (>7.0 mg/dL). Increasing blood uric acid levels were directly proportional to the length of stay within the hospital (9 days for blood uric acid levels greater than 7 mg/dL as opposed to 6 days for blood uric acid levels less than 4 mg/dL). This study showed that the overall death rate was 9.8% within the hospital and among the patients who died, the largest percentage (70%) comprised of those who had blood uric acid levels higher than 7 mg/dL ($p=0.03$).[19]

Although only the incidence of cardiogenic shock was observed to be increased in patients with hyperuricemia in our cohort, Li and colleagues showed that in patients with STEMI, hyperuricemia could be associated with complications in the short-term. Patients with hyperuricemia had considerably increased rates of postoperative angina pectoris, overall adverse cardiovascular events and heart failure.[20]

The results of this study cannot be applied to the entire population because it was a single-center study with a limited sample size. Moreover, no comparison was made between the association of hyperuricemia in patients with STEMI and NSTEMI.

CONCLUSION

Hyperuricemia is significantly associated with the adverse outcomes following an acute coronary event and all patients presenting with myocardial infarction should be screened for hyperuricemia. Regular screening / monitoring of serum uric acid level in general population can prevent the direct and indirect morbidity associated with hyperuricemia.

AUTHORS' CONTRIBUTION

ARQ: Concept, data collection, data analysis, manuscript writing, manuscript review. SAA: Data collection, data analysis, manuscript writing, manuscript review. MJD: Data analysis, manuscript writing, manuscript review. SIA: Data analysis, manuscript writing, manuscript review. AG: Manuscript writing, manuscript review. Wahaj: Manuscript writing, manuscript review.

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