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Study of Serum uric acid levels in patients with Acute Coronary Syndrome admitted to Tertiary Care Centre Karwar, UK District

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Abstract

Background: Cardiovascular disease (CVD) is the number one cause of death in India and accounted for approximately 21% of deaths in theyear 2010, with 10% of all deaths occurring due to CAD. Hyperuricemia has been shown to have a positive association with CV morbidity and mortality. This study helps to establish the role of Hyperuricemia in causation of Acute Coronary Syndrome. **Methodology:** It was a retrospective study conducted at the tertiary hospital Karwar Institute of Medical Sciences. Data of 100 patients were collected.Data of 100 control individuals matching age and gender were taken. After obtaining approval from MRD, the patients details were collected from the case sheets. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were collected. ECG, Trop I and 2D ECHO and serum uric acid levels report was collected. The outcome of hospital stay in form of referral, discharge and death was noted. Data collected was analyzed statistically using descriptive statistics and also appropriate parametric or non-parametric tests were applied. **Results**: A total of 100 consecutive cases of ACS and 100 controls data was collected. Cases and control were matched for age, sex, habits and comorbidities. There were 62 male patients and 38 female patients each in both groups with male to female ratio of 1.6:1. Mean age of study population was 60(±10) years. Out of 100 cases 43 patients were alcoholic and 34 patients were smokers. Among cases 57% patients had Hypertension, 37% had Diabetes and 37% patients had dyslipidemia. Mean Uric Acid level among controls was 5.45 mg/dL whereas, mean among ACS patients was 6.82 mg/dl and the difference was statistically significant with $p < 0.0001$. Among 59 STEMI patients 38(64.4%) had hyperuricemia. Among 27 NSTEMI patients 9) 33.3%) had hyperuricemia and out of 14 Unstable Angina patients 6(42.8%) patients had hyperuricemia. Odds ratio in our study was 4.781 with 95% CI for OR inferring that any person with abnormal uric acid level has 4.781 times more chances (OR= 4.781 with $p < 0.0001$) of suffering from ACS as compared to any person with normal uric acid level. **Conclusion**: Our study suggests that increased risk of Acute coronary Syndrome in patients with Hyperuricemia compared to patients with normal uric acid levels. There are medications available to reduce uric acid levels, which should be made use, to reduce the risk of ACS in patients with Hyperuricemia.However further studies in larger population and study using urate lowering agents need to be performed to establish the role of urate lowering agents in reducing risk of Acute Coronary Syndrome.

Keywords: Hyperuricemia, Acute coronary syndrome, Serum Uric acid.

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Introduction

CAD is a pathologic condition that occurs when there is inadequacy in both blood supply and oxygen to the myocardial tissue. This condition results from luminal plaque formation in the coronary arteries, leading to blood flow hindrance, further leading to arterial occlusion.As per World Health Organisation (WHO) data, the Coronary Artery Disease (CAD) prevalence continues to rise in India with rapid 'epidemiological transition'.The rising incidence of CAD in young Indians is of particular concern. The incidence of CAD in young population in Western countries is 2–5%, whereas it is11–16% in Asian Indians.(1)

Cardiovascular disease (CVD) is the number one cause of death in India and accounted for approximately 21% of deaths in theyear 2010, with 10% of all deaths occurring due to CAD. A study done in Karnataka supported the well established fact that the mean age of occurrence of STEMI in Indians is 5–10 years lower than Western population.(2) This is due to numerous risk factors like hypertension, high cholesterol, low HDL cholesterol, diabetes, truncal obesity and many genetic factors.

Patients with acute coronary syndrome (ACS) commonly are classified into two groups to facilitate evaluation and management, namely patients with acute myocardial infarction with ST-segment elevation (STEMI) on their presenting electrocardiogram (ECG) and those with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). The latter include patients with non-ST-segment elevation myocardial infarction (NSTEMI), who, by definition, have evidence of myocyte necrosis, and those with unstable angina (UA), who do not have evidence of myocyte necrosis.

Hyperuricemia refers to the elevation of uric acid in the plasma. It has no widely accepted single cut-off value, however, values above 6.8mg/dL are generally considered elevated in adults (3). Hyperuricemia has been shown to have a positive association with CV morbidity and mortality (4,5). Elevated SUA is significantly linked with CV risk factors such as hypertension, abdominal obesity, hyperlipidemia, and insulin resistance (6,7).Hyperuricemia has been described to be associated with cardiovascular (CV) diseases, including hypertension, stroke, and coronary artery disease (CAD). However, the mechanism of how serum uric acid (SUA) is associated with CAD has not been elucidated (8).Pathophysiological mechanisms associating hyperuricemia with CAD have been established, with Serum uric acid being a stimulant to oxidative stress, inducing the production of oxygen free radicals and adhesion of platelets. These processes result in inflammatory reactions and dysfunction of the endothelium, which may explain the correlation between hyperuricemia and CAD .(9)

Objectives

- To estimate the serum uric acid levels in patients with coronary syndrome
- To find the relationship between the serum uric acid levels and acute coronary syndrome.

Methodology

It was a retrospective study conducted at the tertiary hospital Karwar Institute of Medical Sciences. Data of 100 patients were collected.Data of 100 control individuals matching age and gender were taken. Patients with conditions which affect the serum uric acid like CKD and other Kidney problems, Leukemia, Metabolic syndrome, Polycythemia vera Psoriasis, patients on diuretics ,and patients on chemotherapy/ Radiotherapy were excluded from study. After obtaining approval from MRD, the patients details were collected from the case sheets. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were collected. ECG,

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Trop I and 2D ECHO and serum uric acid levels report was collected. All the data collected was compiled and tabulated using MS-Excel. Statistical analyses were carried out using SPSS 16.0. Results are expressed as means with SD and t-test is used to compare continuous variables and chi-square test was used to find the association between the discrete variables. Binary logistic regression analysis was used to carry out univariate and multivariate analyses to find the associated risk factors and the p value <0.05 was considered to be significant.

Results

A total of 100 consecutive cases of ACS and 100 controls data was collected. Cases and control were matched for age, sex, habits and comorbidities. There were 62 male patients and 38 female patients each in both groups with male to female ratio of 1.6:1. Mean age of study population was 60(±10) years.

Out of 100 cases 43 patients were alcoholic and 34 patients were smokers. Among cases 57% patients had Hypertension, 37% had Diabetes and 37% patients had dyslipidemia.

Table1: Baseline variables among case group.

Variable	Male	Female	Total
Hypertension	28	29	57%
Diabetes	19	18	37%
Dyslipidemia	16	21	37%
Alcoholic	43%	0%	43%
Smoker	34%	0%	34%

Depending on ECG changes and cardiac enzyme Trop I levels, cases were classified as patients veith STEMI, NSTEMI and Unstable Angina. 59 patients (35 males, 24 females) had STEMI, 27 patients (20 males, 7 females) had NSTEMI and 14 patients (8 males, 6 females) had Unstable Angina.

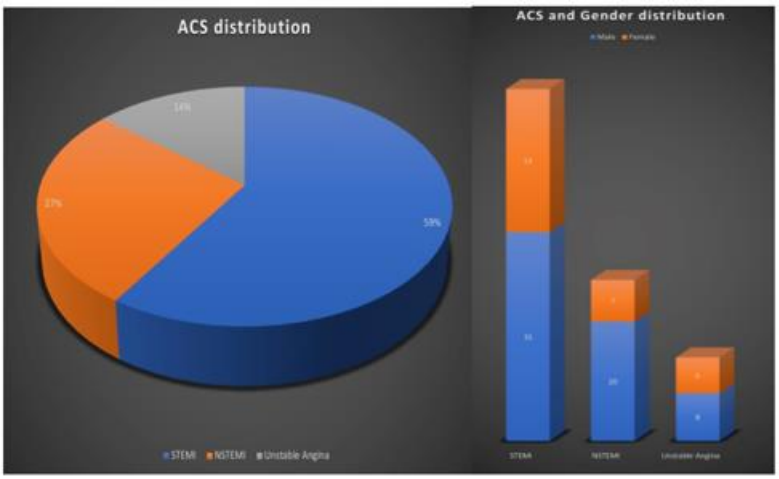

Figure 1: Distribution of ACS among case group and it's gender distribution

Uric acid levels of >7 mg/dl and >6 mg/dl in males and females respectively was taken as hyperuricemia. (10) Mean Uric Acid level among controls was 5.45 mg/dL whereas, mean among ACS patients was 6.82 mg/dl and the difference was statistically significant with p < 0.0001. Among females, 25(65.79%) in case group and 14(36.84%) in control group had hyperuricemia whereas among males, 27(43.54%) in case group and 10(16.13%) in control grouphad hyperuricemia. 52% of cases and 24% of controls had hyperuricemia.

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Table 2: Distribution of Uric acid levels among cases and controls

Group		N	Mean	SD	SE	't' value	p- value
Uric acid levels	Cases	100	5.45	1.6	0.2	4.747	<0.0001
	Controls	100	6.82	2.3	0.2		

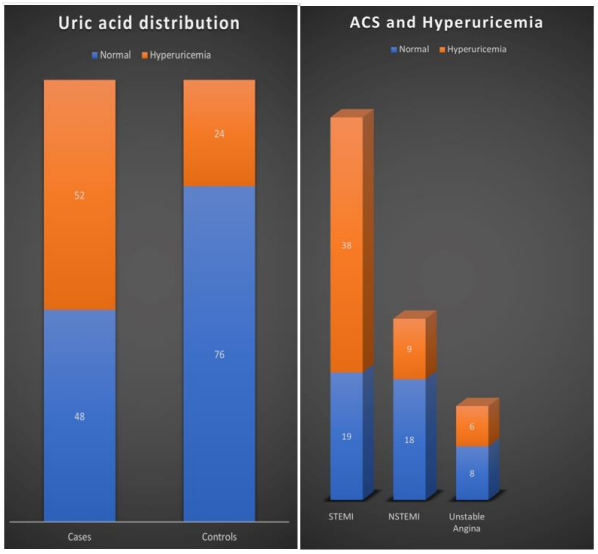

Figure 2: Distribution of Hyperuricemia among case group and control group and it's distribution among ACS patients in case group

Among 59 STEMI patients 38(64.4%) had hyperuricemia. Among 27 NSTEMI patients 9) 33.3%) had hyperuricemia and out of 14 Unstable Angina patients 6(42.8%) patients had hyperuricemia.

Odds ratio in our study was 4.781 with 95% CI for OR inferring that any person with abnormal uric acid level has 4.781 times more chances (OR= 4.781 with $p < 0.0001$) of suffering from ACS as compared to any person with normal uric acid level.

Discussion

Cardiovascular diseases are the leading cause of death globally and in India. There are several risk factors for development of cardiovascular diseases. In this study we are studying uric acid as a risk factor in development of Acute Coronary Syndrome. This was a retrospective case-control study done at tertiary care hospital at Karwar. Study consisted of 100 consecutive cases if ACS and 100 controls admitted from January 2022 to January 2023. Among 100 cases 62% were males and 38% were females with male to female ratio of 1:1.6. Out of 100 cases 43 patients were alcoholic and 34 patients were smokers. Among cases 57% patients had Hypertension, 37% had Diabetes and 37% patients had dyslipidemia.

There were 59% patients with STEMI, 27% patients with NSTEMI and 14% patients with Unstable Angina. CREATE registry(11) for ACS has 60.6% STEMI and 39.4% NTEMI patients. HP ACS registry(12) had 45.5% patients with STEMI and 54.5% patients with NSTEMI. Kerala ACS registry(13) had 37% patients with STEMI, 31% patients with NSTEMI and 32% patients with Unstable Angina. Our results are consistent with study done by CREATE registry, which conducted study in 50 cities across India. STEMI patients were more common among ACS, which had more mortality compared to NSTEMI.

Uric acid levels of >7 mg/dl and >6 mg/dl in males and females respectively was taken as hyperuricemia. (10) Mean Uric Acid level among controls was 5.45 mg/dL whereas, mean among ACS patients was 6.82 mg/dl and the difference was statistically significant with $p < 0.0001$.Among 59 STEMI patients 38(64.4%) had hyperuricemia. Among 27 NSTEMI

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patients 9) 33.3%) had hyperuricemia and out of 14 Unstable Angina patients 6(42.8%) patients had hyperuricemia. Among the ACS patients uric acid levels were higher in patients with STEMI compared to NSTEMI/ Unstable Angina. STEMI occurs when there is near total or complete blicy in the coronary vessels. So, increased levels of uric acid is seen among STEMI patients alarms us to the role of uric acid in causing coronary vessel block. The exact mechanism of this is unknown however Serum uric acid being a stimulant to oxidative stress, inducing the production of oxygen free radicals and adhesion of platelets results in inflammatory reactions and dysfunction of the endothelium. This inturn accelerates the process of atherosclerosis resulting in coronary vessels blockage and in turn development of Acute Coronary Syndrome.

Odds ratio in our study was 4.781 with 95% CI for OR inferring that any person with abnormal uric acid level has 4.781 times more chances (OR= 4.781 with $p < 0.0001$) of suffering from ACS as compared to any person with normal uric acid level. Various others studies also show relationship between uric acid levels and development of ACS, where they have compared the uric acid levels with the percentage of coronary vessel blockade, determined by coronary angiogram. However this could not be established in our study due to lack of coronary angiogram facilities at our institution. A multivariate study on 771 participants with 37% participants having high uric acid levels (defined as >6 mg/dl in females and >7 in males) showed high uric acid levels as an independent risk factor in CAD severity. Incidence of CAD is rare but rising in the age group less than 35 years. This study has shown hyperuricemia as an independent risk factor for acute coronary syndrome in the 18-35 age group(14). A total of 8,529 CAD patients with available serum uric acid data were studied by Ce Zhang et al. Hyperuricemia was present in 1,207 (14.2%) patients on their study. During the median follow-up of 7.5 years, significantly more deaths occurred in hyperuricemic patients compared with normouricemic patients (22.5% vs 13.7%; $p < 0.001$). Multivariable analyses showed that hyperuricemia was associated with an increased risk of mortality (hazard ratio 1.33; 95% confidence interval 1.15 to 1.53; $p < 0.001$).(15)

Furthermore there are studies which have shown administration of urate lowerng agents to reduce the cardiovascular risk and it's complications. An observational study suggested protective effects of allopurinol for MI in elderly people supporting earlier Medicare claims (16). Allopurinol benefits are not only limited to CAD; the possible blood-pressure reduction was also evident. Compared to placebo/no treatment, allopurinol $\leq$ 300 mg daily was associated with insignificant reduction of major adverse cardiovascular events (MACE) and mortality, however, reduced risks of hypertension (Odds Ratio (OR) 0.54, 95% CI 0.370.80) and total events (OR 0.60, 95% CI 0.44-0.82) were observed (17). Xanthine oxidase (XO) inhibition was also shown to enhance endothelial function and subsequent vasodilation and larger blood flow in patients with HF achieved by allopurinol in normouricemia and hyperuricemia patients suggesting a crucial effect of oxidative stress inhibition in such cohort (18). Hence the administration of urate lowering agents should be encouraged in patients with CAD and Hyperuricemia to prevent further complications and reduce mortality risk.

Conclusion

Our study suggests that increased risk of Acute coronary Syndrome in patients with Hyperuricemia compared to patients with normal uric acid levels. There are medications available to reduce uric acid levels, which should be made use, to reduce the risk of ACS in patients with Hyperuricemia. However further studies in larger population and study using urate lowering agents need to be performed to establish the role of urate lowering agents in reducing risk of Acute Coronary Syndrome.

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