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Evaluate association between of hyperuricemia and cardiovascular diseases

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Introduction: Ischaemic Heart Disease(IHD) causes more death and disability and incurs greater economic costs than any other illness in the developed as well as developing countries. Patients with IHD fall into two groups: patients with Coronary Artery Disease (CAD) who most commonly present with Stable Angina and patients with Acute Coronary Syndrome (ACS). Uric acid is the final oxidation product of purine metabolism, and its elevated levels reflect increased xanthine oxidase activity. For decades, it has been hypothesised that the oxidant properties of uric acid might be protective against ageing, oxidative stress and oxidative cell injury.

MATERIAL AND METHODS: This is a Cross-sectional Study conducted in the General Medicine ward, Cardiology ward, Medical ICU, CCU of MKCGMCH, Berhampur. The study was conducted in 100 cases of ST elevated myocardial infarction patients admitted to our hospital. Patients are selected according to inclusion and exclusion criteria from internal medicine and cardiology departments of MKCG Medical College & Hospital. Diagnosis of ST elevated myocardial infarction is based on chest pain>20 minutes, ECG changes and elevation of cardiac biomarkers (two out of three). Detailed history and physical examination were carried out.

Results: In our study, 9 deaths occurred in the study group of 100 patients. 8 patients had died of ST elevation MI and 1 patient died of Non ST elevation MI. Out of the 9 deaths that occurred, 6 were males and 3 were females. χ^2 value was 0.965 and this was not found to be statistically significant. Most of deaths occurred in the age group 50 to 70 years (77.78%). 54 % of the study group had high levels of troponin and this high values were seen in all 9 cases of myocardial infarction that died. The p value as per fisher's exact test was 0.003 indicating that the result is statistically highly significant. The proportion of hyperuricemics in the study population was

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59%. The presence of hyperuricemia in the patients those died was 100%. 41% had normal serum uric acid levels and there were no death noted in these subgroup.

Conclusion: Serum uric acid levels are elevated in patients with ST Elevated myocardial infarction. There is a strong correlation between serum uric acid levels at the time of admission and in-hospital and short-term mortality in patients with ST elevated myocardial infarction. Patients with elevated SUA levels had higher mortality rates and Major adverse cardiovascular outcomes.

Keywords: Troponin T, Serum uric acid, Ischaemic Heart Disease.

Introduction

Ischaemic Heart Disease(IHD) causes more death and disability and incurs greater economic costs than any other illness in the developed as well as developing countries. Patients with IHD fall into two groups: patients with Coronary Artery Disease (CAD) who most commonly present with Stable Angina and patients with Acute Coronary Syndrome (ACS). [1] The later includes patients with Acute Myocardial Infarction with ST segment elevation (STEMI) on their presenting Electrocardiogram and those with non-ST elevation myocardial infarction (NSTEMI) who have myocardial necrosis and, those with Unstable Angina who do not. [2]

Uric acid is the final oxidation product of purine metabolism, and its elevated levels reflect increased xanthine oxidase activity. For decades, it has been hypothesised that the oxidant properties of uric acid might be protective against ageing, oxidative stress and oxidative cell injury. However recent epidemiological and clinical evidences suggest that hyperuricemia might be a risk factor for cardiovascular disease where enhanced oxidative stress play an important pathophysiological role. [3] It has been recently reported that serum uric acid is an independent predictor of mortality for patient with Coronary Artery Disease and morbidity, including acute myocardial infarction and congestive heart failure[4,5,6].

Hyperuricemia is present frequently in patients with symptomatic heart failure, acute coronary syndromes, arterial hypertension, and atrial fibrillation[7,8,9]. It has been postulated that serum uric acid plays a pivotal role in the pathogenesis of cardiovascular diseases affecting xanthine oxidase pathway that contributes to the production of reacting oxygen species with deterioration of cell membranes[10]. Reactive oxygen species contribute to vascular oxidative stress and endothelial dysfunction, which are associated with the risk of atherosclerosis, damage of both cardiomyocytes and vascular endhothelium inducing disturbances of myocardial contractility and vasoconstriction[11].

The increase in serum uric acid in patients with cardiovascular diseases may reflect a compensatory mechanism to counter the oxidative stress that occurs with tissue hypoxia, thus the higher levels of uric acid corresponding to high risk may reflect response to tissue injury.,

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whereas the higher risk at lower levels of uric acid may be the result of decreased antioxidant capacity[12,13,14]. In this background, my study is intended to correlate the serum uric acid level with severity of STEMI and to find whether there is an association between hyperuricemia and early complication of STEMI or not.

MATERIAL AND METHODS

This is a Cross-sectional Study conducted in the General Medicine ward, Cardiology ward, Medical ICU, CCU of MKCGMCH, Berhampur

INCLUSION CRITERIA

1. Age of 18 years or more
2. ST elevated Myocardial Infarction

EXCLUSION CRITERIA

1. Chronic Kidney Disease
2. Patient with prior myocardial infarction
3. Gout
4. Hematological malignancy
5. Patients of drugs like Diuretics, salicylate, ethambutol, pyrazinamide
6. Hypothyroidism
7. Use of corticosteroid and cytotoxic drugs
8. Chronic alcoholism
9. Patients not willing to participate in the study and not giving consent.

PROCEDURE IN DETAIL:

The study was conducted in 100 cases of ST elevated myocardial infarction patients admitted to our hospital. Patients are selected according to inclusion and exclusion criteria from internal medicine and cardiology departments of MKCG Medical College & Hospital. Diagnosis of ST elevated myocardial infarction is based on chest pain>20 minutes, ECG changes and elevation of cardiac biomarkers (two out of three). Detailed history and physical examination were carried out. Patients were followed up till discharge. Uric acid values were measured on days 1 and 3, and other necessary values for exclusion were collected on first day of admission, and mortality/morbidity rates calculated in the first week of admission.

A venous blood sample was collected to measure uric acid by venepuncture, preferably fasting for the last 4 hours, unless told otherwise. Uric acid was measured using autoanalyser, using the modified Trinder technique in our clinical biochemistry laboratory, with value>7mg/dl in male and >6mg/dl in female considered as hyperuricemia. Diabetes was diagnosed according to ADA criteria or if patient is on treatment with oral hypoglycemic agents or insulin. Hypertension was diagnosed by SBP>140 and DBP> 90, average of two readings taken. Smoking at least one

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cigarette per day, for everyday during the year was considered as current smoker. Cardiac biomarker usedfor study was Troponin I

STATISICAL ANALYSIS

The study design was a prospective non interventional observational study. All data collected were noted using a structured proforma, including the investigations. Data was analysed using statistical package and SPSS structured software to find out the significance of serum uric acid as prognostic marker in ST elevated myocardial infarction.

Results

TABLE – 1: AGE AND GENDER DISTRIBUTION

AGE	Males	Females
31 – 40 years	4	2
41 – 50 years	15	8
51 – 60 years	24	12
61 – 70 years	17	7
71 – 80 years	6	5

TABLE-2: MORTALITY IN THE STUDY POPULATION

	Number of survived patients	Number of patients died	Percentage of mortality (%)
MALES	60	6	10%
FEMALES	31	3	9.68%

9 deaths occurred in the study group of 100 patients. 8 patients had died of ST elevation MI and 1 patient died of Non ST elevation MI. Out of the 9 deaths that occurred, 6 were males and 3 were females. χ^2 value was 0.965 and this was not found to be statistically significant. Most of deaths occurred in the age group 50 to 70 years (77.78%)

TABLE – 3: TROPONIN ELEVATION WITH MORTALITY

		Mortality		Total
		No	Yes	
Troponin	HIGH	45	9	54
	LOW	46	0	46
Total		**91**	**9**	**100**

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54 % of the study group had high levels of troponin and this high values were seen in all 9 cases of myocardial infarction that died. The p value as per fisher's exact test was 0.003 indicating that the result is statistically highly significant.

TABLE – 4: HYPERURICEMIA AND MORTALITY CORRELATION

		Mortality		Total
		No	Yes	
Uric acid levels	Normal	41	0	41
	Hyperuricemic	50	9	59
	Total	**91**	**9**	**100**

The proportion of hyperuricemics in the study population was 59%. The presence of hyperuricemia in the patients those died was 100%. 41% had normal serum uric acid levels and there were no death noted in these subgroup.

TABLE - 5 DISTRIBUTION OF URIC ACID IN VARIOUS STEMI LOCATION

Location of infarction	Serum uric acid (mg/dl)				Total
	3.1 - 5.0	5.1 - 7.0	7.1 - 9.0	> 9	
AS	2	8	9	8	27
AW	5	11	17	11	44
IW	4	13	6	2	25
IW+PW	0	0	0	1	1
IW+PW+RV	0	1	0	2	3
Total	**11**	**33**	**32**	**24**	**100**

Hyperuricemia was noted in 17 out of 27 cases of anteroseptal STEMI (63%), 28 out of 44 cases of anterior all STEMI (63.7%), 8 out of 25 cases of inferior wall STEMI (32%) and 3 out of 4 cases of inferoposterior with right ventricular STEMI (75%). The net incidence of Hyperuricemia in inferior wall related STEMI was 28.2%.(11 out of 29 cases). The association of higher serum uric acid levels in majority of anterior wall STEMI cases was not found to have statistically significance (p value 0.162) in table 5.

TABLE – 6: SERUM URIC ACID CORRELATION WITH EJECTION FRACTION %

		Serum uric acid	
		Normal	Hyperuricemia
Ejection Fraction	≤ 25 %	0	5
	26 – 30 %	1	10
	31 – 35 %	0	12
	36 – 40 %	1	16
	41 – 45 %	14	15
	46 – 50 %	18	0
	51 – 55 %	7	1
	Total	**41**	**59**

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Serum uric acid levels were correlated with the ejection fraction done by 2-D echocardiogram. There was an inverse relationship between serum uric acid levels and the ejection fraction. Higher serum uric acid levels correlated with lower ejection fractions. The result was statistically significant (p value 0.0005)

Discussion

The study included 66% males and 34% females. Male predominance was observed in all the age subgroups included in the study. According to Viola Vaccarino et al, increased early mortality was seen in women after acute myocardial infarction, probably due to their old age; however on controlling the risk factors, females had better survival rates than males in the long run[15]. Our study showed no significant association between gender and mortality. Similarly, there is no significant association between elevated uric acid levels and male gender, though the mean uric acid levels were higher in males compared to females. This is in accordance with the studies done by Dharma[16] et al.

Peter Stubbs et al had come to the conclusion that elevated Troponin I in patients with STEMI at the time of admission, increased the risk of subsequent cardiac events as compared to those with normal values[17]. This correlates well with our study, in which 100% of the patients who expired, had elevated Troponin I values and this was found to statistically highly significant.

The proportion of hyperuricemics in the study population was 59%. Out of the 9 patients who succumbed to death following ST elevated myocardial infarction, all of them were hyperuricemic at presentation. This establishes a strong significant association between elevated serum uric acid levels and mortality rates in ST elevated myocardial infarction. According to Vladimir Trkulja et al, higher serum uric acid on admission was independently associated with thirty day mortality[18]. The Framingham Heart study which compared serum uric acid with the risk for cardiovascular mortality, established a strong association between baseline serum uric acid levels and coronary artery disease and death. However, a causal association could not be established.

In our study 42% of the study group was diabetics. No significant association was observed between diabetes mellitus and serum uric acid levels($p=0.119$). D M Cook et al described that uric acid levels were significantly reduced in insulin dependent patients, in those on oral antidiabetic agents as well as non-diabetic population with random glucose level>10 mmol/L, but such a negative association was not seen in our study[19].

Studies done previously suggest that uric acid levels are low in smokers due to chronic exposure to cigarette smoke, which causes oxidative stress[20]. However significant association was found between smoking and hyperuricemia in this study($p=0.003$). The prevalence of hyperuricemia in

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smokers in our study was foundto be 74.47%.
Studies done by Li Chen et al showed a positive correlation between triglyceride level and hyperuricemia[21]. However no statistically significant association could be elicited between dyslipidemia and hyperuricemia in this study. The proportion of hyperuricemics in the dyslipidemic subgroup was 63.6%.

91.67% of patients with a prior history of cerebrovascular event, had elevated serum uric acid levels. The association between the two is statistically significant with a p value of 0.025. According to Ioana Mozos et al, the mortality was higher in stroke patients with hyperuricemia[116]. This association was not seen in our study.

In a study done by Laurens P et al in 158 patients with isotopic pacemaker implantations, he described that the frequency of hyperuricemia is more in such patients[22]. 93.94% of the patients with heart blocks following ST elevated myocardial infarction in our study, were found to be hyperuricemic. Hence significant association exists between heart blocks and hyperuricemia (p=0.003).

Higher serum uric acid levels were seen in cases of anterior wall and anteroseptal wall STEMI, when compared to inferior and inferoposterior wall STEMI. However, no association could be established between the location of myocardial infarction and uric acid levels, owing to lesser number of inferior and inferoposterior wall STEMI cases.

LV dysfunction is an important prognostic indicator in myocardial infarction. In our study, there exists an inverse relation between serum uric acid levels and ejection fraction. 16 subjects in the study population had ejection fraction <30%, all of whom had serum uric acid> 9mg/dl. 66.67% of the subjects that expired during the study period were included in this subgroup. This is further proof that serum uric acid can be used to predict mortality and severity of left ventricular dysfunction and heart failure. This is supported by the study done by Li Chen[23] et al.

Conclusion

Serum uric acid levels are elevated in patients with ST Elevated myocardial infarction. There is a strong correlation between serum uric acid levels at the time of admission and in-hospital and short-term mortality in patients with ST elevated myocardial infarction. Patients with elevated SUA levels had higher mortality rates and Major adverse cardiovascular outcomes. Patients with elevated Troponin I had higher mortality. Elevated serum uric acid had positive correlation with systemic hypertension and smoking. Higher serum uric acid levels were seen in cases of anterior wall and anteroseptal wall STEMI. Patients with elevated serum uric acid had lower ejection fraction during echocardiographic study.

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