Original article:

**Raised uric acid level– A risk factor in myocardial infarction**

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**Abstract**

**Background:** Myocardial infarction (MI) continues to be the major cause of morbidity and mortality worldwide despite growing public awareness of the disease and major advances in its treatment. It remains the leading cause of death in India and represents an enormous cost to health care system. Atherosclerosis is the hallmark of MI, which contains cholesterol, lipid and lipophages along with uric acid crystals. Elevated uric acid levels have been found to be associated with increased platelet aggregability and its activation thereby increasing the risk of coronary thrombosis. Hence, the present study was planned to explore the role of uric acid in MI.

**Aims and objectives:** To assess the role of serum uric acid as a risk factor as well as prognostic factor for MI. To estimate serum uric acid level in MI. To estimate level of serum CPK-MB in MI.

**Material and methods:** This study is a cross sectional study. The study population contained 60 subjects divided in two groups, 30 controls - age and sex matched healthy individuals and 30 cases - patients with AMI.

**Result:** Mean serum uric acid level in controls was 5.1 ± 1.3mg/dl. Mean serum uric acid level in cases 8.4 ± 0.9mg/dl. In cases, Coefficient of correlation between serum CPK-MB and serum uric acid was 0.87 (P value < 0.0001). Hence serum CPK-MB and serum uric acid were positively correlated in MI. **Conclusion:** Uric acid level was seen significantly high in MI patients as compared to normal individuals. Also a strong positive correlation in CPK-MB and serum uric acid was found. So uric acid can be considered as one of the risk factors for coronary artery disease.

**Keywords:** AMI, Uric acid, CPK-MB

**Introduction**

Myocardial infarction (MI) is the end result of occlusion of coronary arteries due to atheromatous plaques that supply the myocardium with oxygen and nutrients\(^1\). The process begins as disruption of endothelial function. The fatty streak (earliest visualized lesion of atherosclerosis) is transformed into the fibrous plaque secreted by smooth muscle cells. Acute Myocardial Infarction (AMI or MI), more commonly known as a heart attack, is a medical emergency. Through ages it has astonished all with its sudden yet catastrophic outcome and has always been a challenge to every Physician. CK - MB is an 86,000 Dalton isoenzyme that is predominantly located in myocardial cells and is released into the circulation in the setting of CAD\(^2\). It is the gold standard parameter for the diagnosis of cardiovascular mishappenings. CK - MB becomes elevated in the circulation 3 – 6 hours after symptom onset in MI, and remains elevated for 24–36 hours\(^3\).

Uric acid is the final oxidation product of purine catabolism in humans and in higher primates. The last metabolic step, the
conversion of hypoxanthine to uric acid is regulated by the enzyme xanthine oxidase (XO). As a part of this process reactive oxygen species (ROS) are produced. The major sources of XO are the liver and the small intestine, but there are evidences for local production of XO by the endothelium and myocardium. XO is associated with enhanced oxidative stress. XO activity is up-regulated in many cardiovascular diseases. Recent evidence suggests that uric acid is an important independent risk factor for cardiovascular mortality. Xanthine oxidase activity and uric acid synthesis are increased in vivo under ischaemic conditions, and therefore elevated serum uric acid may act as a marker of underlying tissue.

**Material and methods**

This study was a cross sectional study. The present study was carried out at B J Medical college, Sassoon hospital. The study protocol was approved by the Research and Ethical committee of BJMC, Pune. Oral informed consent was obtained from the patients’ relatives and normal subjects, prior to study. The study is conducted in a group of 60 individuals consisting of 30 normal healthy subjects as control (Group I) who were the staff and 30 diagnosed cases of Myocardial Infarction taken randomly from the admitted patients (IPD) of MICU (Group II).

The study period was of 1 year and all the patients were in the age group of 35-60 years of both sexes.

**Inclusion criteria**: Cases of AMI based on a history of Heavy, Squeezing or Crushing central chest pain, characteristic electrocardiogram (ECG) changes and elevated creatine kinase isoenzyme MB (CK-MB) and patients who give the consent.

**Exclusion criteria**: Valvular heart disease, pericarditis, chest pain due to respiratory or gastrointestinal or musculoskeletal cause, liver or renal disease, diabetes mellitus, psoriasis, leukemia and Patients who refuse to give consent.

CPK-MB is measured with immunoinhibition method. Uric acid is estimated by Trivedi and Kabasakalian with a modified Trinder peroxidase method using TBHB.

Data was analyzed using Graph Pad Prism software version 5.0 (Graph Pad software, CA, USA). Statistical treatment of data included calculation of mean, standard deviation, t-value and coefficient of correlation.

**Results**

The average age of the subjects in controls (Group I) was 55.17 years and that of cases (Group II) was 56.30 years, which shows that age was nearly equal in both groups. Sex ratio was also nearly equal. The mean serum CPK-MB in group II is significantly increased (101.0 ± 5.8) as compared to mean serum CPK-MB in group I (10.04 ± 5.8) (P < 0.0001) **Graph 1.** The mean serum uric acid in group II (8.4 ± 0.9) was significantly increased as compared to mean serum uric acid in group I (5.1 ± 1.3) (P < 0.0001) **Graph 2.** In cases, Coefficient of correlation between serum CPK – MB and serum uric acid was 0.87 (two tailed P value < 0.0001). Hence serum CPK – MB and serum uric acid were positively correlated in coronary artery disease patients **Graph 3.** In controls, Coefficient of correlation between serum
CPK – MB and serum uric acid is 0.19 (two tailed P value = 0.3). Hence serum CPK – MB and serum uric acid were not correlated in controls.

GRAPH 1: Bar diagram showing comparison of mean serum CPK – MB levels in group I (control) and group II (MI Patients)

GRAPH 2: Bar diagram showing comparison of mean serum Uric acid levels in group I (control) and group II (MI Patients)

GRAPH 3: Scattered diagram showing the correlation between CPK – MB and Uric acid in group II (MI Patients).
In cases, Coefficient of correlation between serum CPK – MB and serum uric acid was 0.87 (two tailed P value < 0.0001). Serum CPK – MB and serum uric acid show significant positive correlation in myocardial infarction patients. In controls, Coefficient of correlation between serum CPK – MB and serum uric acid was not significant. Hence serum CPK – MB and serum uric acid were not correlated in controls.

**Discussion**

Myocardial infarction is the single largest killer of both men and women. MI is a condition in which the blood supply to the heart muscle is partially or completely blocked. It is a complex degenerative disease that causes reduced or absent blood flow in one or more of the arteries that encircle and supply the heart. The disease may be focal or diffuse. Myocardial ischemia is a condition that exists when the fractional uptake of oxygen in the heart is not sufficient to maintain the rate of cellular oxidation, which results in structural and functional abnormalities of the heart as a consequence of an inadequate supply of blood to its tissue. This oxidative stress may damage to cellular proteins and cause myocardial adipocyte apoptosis and necrosis.

The more cardio specific enzymes CK - MB reaches a peak in 1 - 1 ½ day and is down to baseline in 4 days. Joseph H Keffer indicated that CPK – MB has been and remains the central biochemical reflection of myocardial injury. Kumar A found that the immunoinhibition method is suitable due to low cost of reagents, applicable to automated throughput chemistry analysers, making CPK – MB determination quick and convenient. Serum CPK – MB levels were significantly raised [101.0 ± 58.7] in group II (MI patients) as compared to the group I (controls) [10.04 ± 5.8] (Graph 1).

Uric acid is the breakdown product of purines from DNA, RNA, ATP and cAMP. In this process hypoxanthine is converted by the enzyme xanthine oxidase to xanthine and further to uric acid. Both steps induce the release of free radicals. Uric acid may accumulate in the body due to increased production (cell death, intake of alcohol or purine rich diet) or decreased elimination (impaired renal function, use of diuretics). In present study level of serum uric acid is seen high in CAD patients as compared to controls (Graph 2). In the atherosclerotic proinflammatory environmental milieu the original antioxidant properties of uric acid paradoxically become pro - oxidant thus contributing to the oxidation of lipoproteins within the atherosclerotic plaques. Various mechanisms have been suggested through which uric acid may be implicated in atherosclerotic process and its clinical complication. Uric
acid values are increased during the episodes of pain in patients of angina. It can act as a pro-oxidant particularly at increased concentrations, and may thus be marker of oxidative stress\textsuperscript{12}. J Hum Hypertens\textsuperscript{13}, suggested the rise in the levels of uric acid in CAD as a risk factor for CHD. There is an association between serum uric acid level and many CAD risk factors. The association between increased uric acid levels and CAD is independent of hypertension and nephropathy. Several mechanisms could cause the uric acid metabolic pathway to be a CV risk factor. Uric acid may stimulate vascular smooth cell proliferation, and reduce vascular nitric oxide production. The action of xanthine oxidase leads to generation of superoxide anions\textsuperscript{14}. This could mean that xantine oxidase activity is the key risk factor, with uric acid just an epiphenomenon. Uric acid per se has been described as a scavenger with antioxidant effects\textsuperscript{14-17}. It is noteworthy that some preliminary intervention studies have shown that the xanthine oxidase inhibitor Allopurinol lowered blood pressure in hypertensive adolescents\textsuperscript{18}, and had anti-ischemic effects in patients with angina pectoris\textsuperscript{19}. Allopurinol also reduced cardiovascular and hospitalization risk in a small study of patients with renal failure\textsuperscript{20}. A recent study found that hyperuricemia was significantly associated with poor outcomes in heart failure patients without chronic kidney disease, but not in hyperuricemic persons with renal failure\textsuperscript{21}. The latter could suggest that hyperuricemia may predict poor outcomes primarily as a marker of xanthine oxidase activity, and not due to impaired renal excretion of uric acid. Blake GJ\textsuperscript{22}, in his study found that serum levels of myocardial enzymes and inflammatory indices (CPK – MB and Uric acid) correlate with CAD severity in Greek patients. Corry DB et al\textsuperscript{23}, had shown the serum uric acid level as an independent predictor of mortality in populations at high risk of CAD. Measurement of serum uric acid levels contributes to the risk stratification beyond the CAD scores that are currently used. Routine measurement of serum uric acid levels may therefore be useful in patients at high risk of CAD. Lind L\textsuperscript{24}, in his study observed significantly increase in the levels of CPK - MB, CRP and uric acid in CAD patients when compared to control subjects.

Correlation between CPK – MB and uric acid was found highly significant (P value < 0.0001) in coronary artery disease patients (Graph 3). A relationship between hyperuricemia and CV disease has been established since the 1900's. Present study is supporting the same. Increased uric acid serum levels are a common finding in patients with high blood pressure, insulin resistance,
obesity and CV disease. Furthermore, uric acid as a CV risk factor has been addressed in numerous prospective and cohort studies.\(^25\)

**Conclusion**

Our observations show that serum uric acid is significantly raised in CAD patients as compared to normal individuals. Also serum CPK-MB and serum uric acid show statistically significant positive correlation. So serum uric acid can considered as a risk factor as well as prognostic indicator of CAD.

**Bibliography**


