

## EVALUATION OF BIOCHEMICAL PARAMETERS IN PATIENTS OF MYOCARDIAL INFARCTION

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### ABSTRACT

**Objective:** To estimate routine biochemical parameters Liver Function Tests, Kidney Function Tests, Serum Electrolytes, Calcium, phosphorus, total protein, albumin and Fasting Plasma Glucose in patients of Myocardial Infarction and compare with controls to evaluate if any of them can be used as a supportive marker of CAD risk assessment.

**Material Methods:** Study group had 50 patients of documented Myocardial Infarction and 50 age and sex matched controls. Investigations were carried out on venous blood samples collected from subjects after overnight fasting which included LFT (S. Bilirubin, ALT ,AST,ALP), KFT (B.Urea, S.Creatinine, S.Uric acid) , S .Electrolytes (S. Sodium, S.Potassium) S.Calcium and S. Phosphate and Fasting Plasma Glucose .These chemistries were carried out in fully automated clinical chemistry analyzer, Beckman (SYNCHRON CX9) using standard reagents/kits.

**Results:** Fasting plasma glucose ( $p<0.01$ ) , Uric Acid( $p<0.01$ ) and Calcium ( $p<0.05$ )was found to be significantly higher in study group compared to control group

**Conclusion:** In the rural areas with dearth of good laboratory and healthcare services, these can be evaluated to be used as simple and cost effective biochemical markers of CAD risk although they are to be used in conjunction with other markers. However, more longitudinal and prospective studies are required to find a causal relationship between these routine biochemical markers (uric acid, Fasting plasma glucose, calcium) and myocardial infarction in Indian Population

**KEY WORDS:** Myocardial Infarction, Uric Acid, S. Calcium, CAD

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### INTRODUCTION

There has been considerable progress in the diagnosis and treatment of Coronary Artery Disease (stable angina, unstable angina and myocardial infarction)however it still remains a major public health problem in developed countries, and it has become a major problem in developing

countries. Following myocardial infarction (MI) some proteins and enzymes labelled as cardiac markers (CPK, MB/ Troponin T & I) are released in to the circulation in large quantity from necrotic heart muscle. These markers like CPK-MB, Troponin-T, Troponin-I and myoglobin, have specific temporal profile in relation to MI the estimation of these

markers require costly reagents and equipments for their estimation. Assessment of CAD as well involves invasive procedure like angiography.

In the rural areas with dearth of good laboratory and healthcare services, it becomes difficult to measure these markers. Numerous epidemiological studies have investigated role of uric acid as a risk factor for cardiovascular diseases and a negative prognostic marker for mortality in subjects with pre-existing heart failure<sup>1,2,3,4,5</sup>. Elevated fasting plasma glucose<sup>6,7,8</sup> and elevated serum calcium<sup>9,10</sup> have also emerged as CAD risk indicators in many studies. So, we estimated routine biochemical parameters Liver Function Tests, Kidney Function Tests, Serum Electrolytes, Calcium, phosphorus, total protein, albumin and Fasting Plasma Glucose in patients of Myocardial Infarction and compare with controls to evaluate if any of them can be used as simple and cost effective marker of CAD risk assessment although they cannot be used in isolation as well as not for definitive diagnosis of acute presentation like MI.

## MATERIAL AND METHODS

The study was carried out in the Department of Biochemistry in collaboration with the Department of Medicine, Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital, New Delhi. The study was approved by Scientific Review Board and Ethics Committee of Lady Hardinge Medical College. It was an observational case control study in which a total of 100 subjects were included in the study with informed consent. They were selected from the wards and emergency of medicine department, LHMC & SSK Hospital. Study group had 50 patients of

documented Myocardial Infarction who presented to emergency department, of either sex and above 40 years of age. Subjects with either of the Clinical features of MI and/or typical ECG changes suggestive of ST elevation MI (STEMI) / Q wave MI or clinical and biomarker features (Troponin T, CK-MB) suggestive of Non ST elevation MI (NSTEMI). Control group had 50 age and sex matched subjects with no present or past history or clinical evidence suggestive of Coronary Artery Disease.

Informed consent was obtained from all subjects. All cases and controls were subjected to detailed clinical history and examination with special reference to cardiovascular disease risk factors followed by investigations from venous blood samples collected after overnight fasting which included LFT (S. Bilirubin, ALT, AST, ALP), KFT (B.Urea, S.Creatinine, S.Uric acid), S. Electrolytes (S. Sodium, S.Potassium) S.Calcium and S. Phosphate and Fasting Plasma Glucose. The blood sample in plain vial was allowed to clot at room temperature. It was then centrifuged at 3500rpm for 5 min. Investigations were carried out in fully automated clinical chemistry analyzer, Beckman (SYNCHRON CX9) using standard reagents/kits (Randox). All the chemicals used in this study were of analytical grade. Na<sup>+</sup> and K<sup>+</sup> were measured by Ion Selective Electrolyte Analysis. Fasting Plasma Glucose was measured by Glucose Oxidase - Peroxidase method. Serum Calcium was measured by Arsenazo III dye Method. S Phosphorus was measured by phosphomolybdate method. Total protein by biuret and albumin by Bromocresol Green method. Urea measured by Urease Kinetic Method, creatinine by Alkaline Picrate Method and Uric Acid by Uricase Kinetic Method. S.bilirubin measured by

Diazo End Point Method. SGPT (ALAT) and SGOT (ASAT) by Kinetic Assay (IFCC version without Pyridoxal Phosphate activator) and ALP by Kinetic Assay.

## STATISTICAL ANALYSIS

Statistical analysis was done by using GraphPad Prism (Version 5.02) software programme ([www.graphpad.com](http://www.graphpad.com)). Mean and standard deviation of all parameters was calculated. Unpaired Student's t test was used to analyze clinical and laboratory data and chi square test was used wherever required.  $p \leq 0.05$  was considered statistically significant and  $p \leq 0.01$  was considered highly significant.

## DISCUSSION

The mean age of the subjects in the study group was  $47.18 \pm 4.83$  years and in control group was  $47.36 \pm 4.81$ . Both the groups were matched for age. The statistical difference between the two was not significant ( $p = 0.852$ ) and thereby the comparability of the two groups was established. The occurrence of myocardial infarction is more common in elderly population; however the incidence is increasing at an earlier age<sup>11,12</sup> in India compared to the west. So we took study group with subjects 40 -59 years of age. The study population consisted of 54% females and 46% males compared to 60% females and 40% males in the control group. Females were more than males in the two groups but this was incidental. The difference between the two groups was not significant ( $p = 0.687$ ) thereby the two groups were comparable.

As per the conventional risk factors, the distribution of family history of hypertension, diabetes and CAD in the

two groups shows that family history of hypertension was present in 62% of cases, family history of diabetes mellitus in 54% and family history of CAD in 30 % of cases compared to 22%, 22% and 6% in controls respectively, which was significant for all ( $p < 0.05$  for all the three). It correlates with the earlier findings that family history of hypertension and diabetes and CAD are associated with marked increase in the risk of CAD<sup>13,14</sup>. Susceptibility to many common diseases is influenced by genetic factors. This is often recognized by an increased incidence of the disease in first-degree relatives of affected individuals but not in a pattern typical of classical single gene disorders. Asthma, hypertension, diabetes and ischemic heart disease show this pattern<sup>15</sup>.

Among the personal history of smoking, diabetes and alcohol intake, only smoking was found to be significantly higher in the study group (30%) compared to controls (12%) with  $p$  value 0.048. However personal history of DM (10% versus 6%) and alcohol intake (18% versus 14%) were not found to be significantly different in the two groups. These have been observed as major risk factors in some studies<sup>13,16</sup>. It can be due to small sample size or fewer diabetic patients enrolled in our study.

Table 2 illustrates values of different routine parameters among the study and control groups. It was interesting to note that though both the groups had fasting plasma glucose in the normal range with the mean level in the study and control groups being  $91.62 \pm 18.82$  mg/dl and  $81.90 \pm 14.90$  mg/dl respectively, still there was significant difference between the two ( $p < 0.05$ ). Available data provide circumstantial evidence that impaired glucose tolerance contributes significantly to the overall cardiovascular risk and may

be even more frequent in patients referred with myocardial infarction than (non-diagnosed) diabetes mellitus<sup>6</sup>. Uncertainty still remains about the exact shape of the glucose–coronary artery disease relationship and the level at which a patient is more prone to CAD. It has been suggested that slightly elevated glucose levels, even in the non-diabetic range, might be associated with increased macrovascular disease<sup>8</sup>. Hyperglycaemia has also been suggested to be a direct cause of some of the changes associated with atherosclerosis like glycation of LDL, but several other factors could act as casual links in this association such as impaired fibrinolysis and high fibrinogen levels and high levels of leptin<sup>6</sup>. Other pathways include oxidative stress and formation of advanced glycation end products that accelerate atherosclerosis when blood glucose is only slightly raised<sup>17</sup>. Also, a raised glucose level at baseline may indicate emerging insulin resistance and a downward trajectory in glycemia control, with increased risk of glucose intolerance, diabetes, and CHD in subsequent years<sup>18,19</sup>.

So, from above discussion it appears that the disease process may start much earlier than the presentation for the diagnosis of diabetes mellitus suggesting that metabolic and vascular disease may run in parallel or may be derived from one underlying pathophysiological mechanism. In our study, kidney function test assessment showed there was no significant difference between mean blood urea ( $p=0.737$ ) and serum creatinine ( $p=0.303$ ) in study and control group respectively. However Serum uric acid in study group was higher ( $4.99 \pm 0.95$  mg/dl) compared to control group where the mean was  $4.46 \pm 0.85$  mg/dl. This difference was significant as  $p$  value came out to be 0.004. This is in consensus with

the study by Nadkar M Y et al who observed serum uric acid levels were higher in patients of acute myocardial infarction<sup>1</sup>. He also correlated prediction of mortality (using Killip class) and serum uric acid level after acute myocardial infarction and found it to be a good predictor in Indian population<sup>1</sup>. On the contrary Culleton et al suggested that uric acid did not play a causative role in development of CAD by analysing data from Framingham Heart Study. In men, after adjustment for age, elevated serum uric acid level was not associated with increased risk for an adverse outcome of CAD. Although in women, after adjustment for age, uric acid level was predictive of coronary artery disease<sup>20</sup>. Mechanism by which uric acid may be associated with atherosclerotic disease remains uncertain. A large body of evidence links uric acid with the metabolic syndrome of insulin resistance, obesity, hypertension, and dyslipidemia. Uric acid may also be an indicator for increased oxidative stress. Xanthine oxidase, a critical enzyme in the degradation of purines to uric acid, has been shown to be an important source of superoxide free radicals<sup>21</sup>. The activity of xanthine oxidase increases during ischemia and intensifies during reperfusion in coronary endothelial cells<sup>22</sup>. Adenosine synthesized locally by vascular smooth muscle in cardiac tissue is rapidly degraded by the endothelium to uric acid, which undergoes rapid efflux to the vascular lumen due to low intracellular pH and negative membrane potential<sup>23</sup>. Xanthine oxidase activity<sup>24</sup> and uric acid synthesis<sup>25</sup> are increased in vivo under ischaemic conditions, and therefore elevated serum uric acid may act as a marker of underlying tissue ischaemia. Although the mechanisms by which uric acid may play a pathogenetic role in

cardiovascular disease is unclear, hyperuricaemia is associated with deleterious effects on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, and aggregation<sup>22</sup>. Serum calcium level in the study group was higher ( $9.31 \pm 0.47$  mg/dl) compared to the control group ( $9.14 \pm 0.31$  mg/dl), p value came out to be 0.031 which was significant. This finding was consistent with the study by Lind et al. in which serum calcium was found to be an independent, prospective risk factor for MI in middle-aged males suggesting a role for extracellular calcium levels in the atherosclerotic process. It was a follow up study for 18 years in which serum calcium levels were significantly elevated at the baseline in the subjects who developed a MI when compared with the rest of the cohort<sup>21</sup>. Although our study was a study with small sample size and consisted of both males and females, we still found significant difference between the two groups. In Tromso study by Rolf et al. it was shown in all age groups, serum calcium levels were higher in men with a history of myocardial infarction than in those without, and the difference was significant<sup>9</sup>. Rubin et al found serum calcium levels in multiethnic population were positively associated with carotid plaque thickness, a powerful early predictor of clinical coronary and cerebrovascular disease<sup>10</sup>. Because of these findings it has been suggested that extracellular calcium plays a role in atherosclerotic process by causing plaque calcification.

## CONCLUSION

Fasting plasma glucose was significantly higher in study group compared to control group. Several studies have indicated that slightly elevated fasting plasma

glucose levels; even in the non-diabetic range is associated with increased macro vascular disease and thereby increased risk of CAD. Serum calcium has been found to be significantly higher in study group compared to controls. This can be due to extracellular calcium playing a role in atherosclerosis. Serum uric acid was elevated in study group compared to controls. It has been suggested to be a biochemical marker for MI because of its role in free radical injury.

So, elevated fasting plasma glucose, serum calcium and uric acid can be used to assess the risk of CAD. However, we suggest that a causal concept needs special attention because a risk factor must be dealt with long before the manifestation of the disease. Therefore, more longitudinal and prospective studies are required to find a causal relationship between these routine biochemical markers (uric acid, Fasting plasma glucose, calcium) and myocardial infarction in Indian Population. If established these can help in preventive and diagnostic strategies for CAD along with clinical evaluation especially in rural areas of developing countries like India.

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## RESULTS

**Table I:** CHARACTERISTICS OF STUDY AND CONTROL GROUP

	<b>Study Group (N=50)</b>	<b>Control Group (N=50)</b>	<b>P Value</b>
<b>Age</b>	47.18 ± 4.83 (Mean ±S.D.)	47.36 ± 4.81 (Mean ±S.D.)	0.852
<b>Sex</b>	Male - 23(46%) Female- 27(54%)	Male – 20 (40%) Female – 30 (60%)	<b>0.687</b>
<b>Family History of Hypertension [ Number(% )]</b>	31 (62%)	11(22%)	<b>&lt;0.001**</b>
<b>Family History of Diabetes [Number(%)]</b>	27 (54%)	11(22%)	<b>&lt;0.001**</b>
<b>Family History of CAD [Number(%)]</b>	15 (30%)	3 (6%)	<b>0.002**</b>
<b>Personal History of Diabetes [Number(%)]</b>	5 (10%)	3 (6%)	0.461
<b>Personal History of Smoking [Number(%)]</b>	15 (30%)	6(12%)	<b>0.048*</b>
<b>Personal History of Alcohol Intake [Number(%)]</b>	9 (18%)	7 (14%)	0.585

\*p<0.05; significant ,\*\* p<0.01;highly significant

**Table II:** ROUTINE BIOCHEMICAL PARAMETERS IN STUDY AND CONTROL

PARAMETER	STUDY GROUP (MEAN±S.D)	CONTROL GROUP (MEAN±S.D)	P VALUE
Plasma Glucose (Fasting) (mg/dl)	91.62 ± 18.82	81.90 ± 14.90	<b>0.005**</b>
Serum Sodium (mmol/L)	143.90 ± 5.77	142.00 ± 5.69	0.100
Serum Potassium (mmol/L)	3.83 ± 0.51	3.95 ± 0.52	0.259
Serum Calcium (mg/dl)	9.31 ± 0.47	9.14 ± 0.31	<b>0.031*</b>
Serum Phosphorous(mg/dl)	3.46 ± 0.70	3.39 ± 0.63	0.479
Blood Urea (mg/dl)	23.86 ± 4.37	23.52 ± 5.66	0.737
Serum Creatinine (mg/dl)	0.82 ± 0.20	0.79 ± 0.16	0.303
Serum Uric Acid (mg/dl)	4.99 ± 0.95	4.46 ± 0.85	<b>0.004**</b>
Serum Bilirubin (mg/dl)	0.72 ± 0.17	0.66 ± 0.14	0.068
ALT(IU/L)	21.20 ± 4.40	19.80 ± 6.64	0.210
AST(IU/L)	22.72 ± 8.09	21.44 ± 5.61	0.360
ALP (IU/L)	79.10 ± 22.28	75.04 ± 17.05	0.309
Serum Total Protein (g/dl)	7.12 ± 0.63	7.27 ± 0.53	0.196
Serum Albumin (g/dl)	3.35 ± 0.39	3.46 ± 0.34	0.139

\*p<0.05; significant ,\*\* p<0.01;highly significant