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Research Article

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Serum high sensitivity C-reactive protein, creatine kinase-MB, lipid profile and uric acid levels in acute myocardial infarction

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ABSTRACT

In recent years incidence of myocardial infarction has increased worldwide especially in developed and also in developing countries. Inflammation plays an important role in the initiation and progression of atherosclerosis and in the pathogenesis of acute cardiovascular events. The aim of the study was to assess serum high sensitivity C - reactive protein, Creatine Kinase -MB, lipid profile and uric acid levels in acute myocardial infarction patients. The present study was designed to ascertain the usefulness of these parameters in identification and prognosis of heart failure after myocardial infarction. Serum high sensitivity C - reactive protein, Creatine Kinase -MB, lipid profile and uric acid were estimated in 30 Acute MI cases diagnosed by physician by observing clinical signs and symptoms using standard methods on biochemistry analyzer. Serum high sensitivity C - reactive protein, Creatine Kinase -MB, total cholesterol, triglycerides and LDL-cholesterol levels were significantly (P<0.001) increased while HDL-cholesterol significantly decreased (P<0.001) and serum uric acid was not significantly altered in acute myocardial infarction cases as compared to controls. The estimation of Creatine Kinase -MB is useful for diagnosis of acute myocardial infarction is well documented in literature, but this study shows that the estimation of serum high sensitivity C - reactive protein level is also useful for diagnosis of acute myocardial infarction patients in daily clinical practice.

Keywords: Acute Myocardial Infarction (AMI), Creatine Kinase -MB (CK-MB), High Sensitivity C-reactive protein (Hs-CRP), Lipid Profile.

INTRODUCTION

The number of deaths that are caused by cardiovascular diseases is huge and predicted to rise even further. Every year approximately 17 million people throughout the world die of cardiovascular diseases (CVD) of one sort or the other [1]. It has been estimated that in the year 2020 as many as 31.5% of all deaths will be due to CVD.

Inflammation plays a role in the development of atherosclerosis and coronary heart disease [2]. The most common cause of coronary heart disease is atherosclerosis with erosion or rupture of a plaque causing transient, partial or complete arterial occlusion. Several risk factors are evaluated for atherosclerosis which is main cause of myocardial infarction (MI) such as obesity, diabetes, stress, smoking, hypertension, hyperlipidemia, and chronic inflammation due to different causes such as infection [3, 4].

High sensitive CRP has been shown to have prognostic value in patients with acute coronary syndromes; however, the most promising use of hs-CRP has been in the primary prevention setting. hs-CRP not only may be a marker of low grade chronic systemic inflammation but also may be directly involved in atherosclerosis [5].

More than 20 large prospective trials have shown that the inflammatory biomarker high-sensitivity CRP is an independent predictor of future cardiovascular events it predicts risk of incident hypertension and diabetes [6]. hs-

CRP is a marker of inflammation and a potential independent predictor of cardiovascular disease as it may play role in the development of atherosclerosis; additionally, it also adversely affects mortality [7].

Measurement of CK and CK-MB levels has long been used for the diagnosis of AMI. Following myocardial injury, the initial CK-MB rise occurs 4 to 9 hours after the onset of chest pain, peaks at 24 hours and returns to baseline at 48 to 72 hours [8].

The pathogenesis of AMI is multifactorial; however several studies have implicated impaired lipid metabolism as one of the crucial factors in the development of this disease. High levels of total cholesterol (TC), LDL and triglycerides (TG) and low levels of HDL cause deposition of lipid in arteries leading atherosclerosis; hence lipid profiles are routinely measured for risk assessment in preventing CAD [9]. But the biomarker value of lipid profile is not clear due to conflicting findings in various studies.

Beside hs-CRP as an inflammatory factor, several studies indicated that serum level of uric acid has been brought up as a predictable factor for patients with Coronary Artery Disease (CAD) and Congestive Heart Failure (CHF). It has been shown that there is a relation between the serum level of uric acid with Left Ventricular Ejection Fraction (LVEF), systolic pulmonary arterial pressure (PAP), and mortality among patients with heart failure [10-12].

Large cohort studies have shown that uric acid is an important independent risk factor for cardiovascular mortality [13,14] The role of uric acid in coronary heart disease is less clear. Some studies reported an independent association between uric acid and coronary heart disease [15], but others only found an association in women [16].
As early as the 19th century, it was known that high uric acid levels are associated with hypertension. Despite the lack of experimental studies, increased uric acid levels were commonly considered a consequence rather than a cause of cardiovascular disease. However, both animal and human studies have recently shown that high uric acid levels may impair kidney function by causing glomerular damage and preglomerular arteriolosclerosis, two effects that ultimately result in arterial hypertension [17]. Recently, a population-based study in elderly persons also found an association between uric acid and stroke [18].

It is a matter of controversy as to whether uric acid is an independent predictor of mortality in patients with coronary artery disease (CAD) or whether it represents only an indirect marker of adverse outcome by reflecting the association between uric acid and other cardiovascular risk factors. Hence the present study was undertaken to compare the levels of serum hs-CRP, CK-MB, lipid profile and uric acid of AMI with respect to normal subjects.

EXPERIMENTAL SECTION

The study comprises of 30 AMI cases (24 male and 6 female) admitted to BLDEU's Shri B. M. Patil Medical College Hospital and Research Centre, Vijaypur, North Karnataka and 30 normal healthy age and sex matched control (22 male and 8 female) subjects. The age of the subjects ranged between 18-55 years in both groups. Acute MI cases were diagnosed by physician by observing clinical signs and symptoms and taking detailed history from family members and patient. The present study was carried out in the Department of Biochemistry. The entire experimental and investigative protocol was approved by institutional ethical committee.

The name of the patient, age, sex, pulse rate, blood pressure of the patient, duration of hospital stay, ventricular dysfunction and cardiac manifestations at the time of admission to the hospital were recorded. The patients suffering from other diseases such as active inflammatory diseases, pulmonary tuberculosis, renal failure, Diabetes Mellitus and physiological condition such as pregnancy were excluded from study.

Immediately after admission to the hospital, 5 ml venous blood samples were collected in plain bulb from the subjects under aseptic conditions, before starting the appropriate treatment. Serum was separated by centrifugation at 3,000 rpm for 10 minutes, at room temperature. Then all samples were immediately placed at 4^0 C until they were processed, to get accurate and reproducible results.

Estimation of Serum hs-CRP was done by Nephelometry at Thyrocare Laboratory, Mumbai. Serum uric acid estimation was carried out by enzymatic colorimetric test. Serum CK-MB was assessed by immunoinhibition method using Agappe Kit. Serum total cholesterol, TG and HDL-cholesterol were estimated by Agappe Kit using enzymatic methods. LDL-cholesterol and VLDL- cholesterol were calculated by Friedewald equation.

The biochemical parameters obtained from study groups were statistically compared with those obtained from controls. All the data collected has been analyzed on the basis of mean values, standard deviation and unpaired t–

test. The values were compared for corresponding degree of freedom at 99.95% level of significance for hs-CRP, CK-MB, lipid profile.

RESULTS AND DISCUSSION

Atherosclerosis is the major cause of MI and inflammation is considered as the main cause of atherosclerosis. Distribution of the subjects depending upon the sex is shown in Table-1.

Table -1: Distribution of Subjects Depending on Sex

Subjects	Male		Female	
Controls	22	(73.3%)	8	(26.7%)
Acute MI Cases	24	(80%)	6	(20%)

Fig. 1: Displays Distribution of AMI Cases Depending on Sex

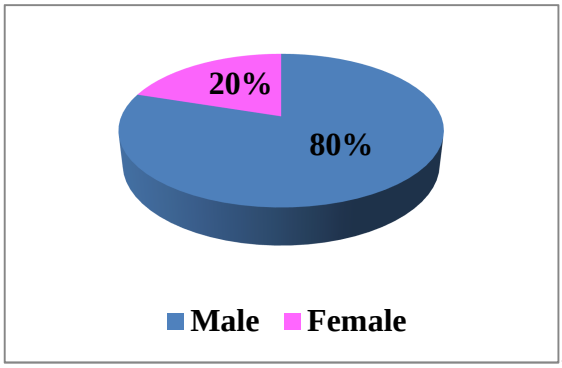


Table 2: Mean ± SD Values of Serum Hs-Crp, CK-Mb and Uric Acid Levels in Controls and Acute MI Cases

Parameters	Controls (N=30)	Acute MI cases (N= 30)
hs-CRP (mg/dl)	0.06 ± 0.03	0.94 ± 0.25***
CKMB (mg/dl)	6.53 ± 2.47	104.08 ± 41.39***
Uric acid (mg/dl)	4.3 ± 0.87	4.9 ± 2.2^{NS}

****P<0.001, NS- Non significant as compared to control*

Table 3: Mean ± SD Values of Serum Lipid Profile in Controls and Acute MI Cases

Lipid Profile Parameters	Controls (N=30)	Acute MI cases (N=30)
Total Cholesterol (mg/dl)	159.63 ± 22.76	225.64 ± 41.37***
Triglycerides (mg/dl)	86.9 ± 13.23	150.35 ± 25.88***
HDL- Cholesterol (mg/dl)	46.23 ± 14.26	24.43 ± 6.52***
LDL-Cholesterol (mg/dl)	103.56 ± 15.53	147.88 ± 32.33***
VLDL-Cholesterol (mg/dl)	29.83 ± 7.63	35.68 ± 12.75^{NS}

****P<0.001, NS- Non significant as compared to control*

We observed significant increase (P< 0.001, 1466%) in hs-CRP level in acute MI subjects as compared to controls. CRP is produced non-specifically as a result of various infectious and inflammatory triggers. There is a significant and rapid increase in the level of CRP in plasma during the inflammatory process in the body [19, 20]. Normally CRP is present in the blood in very low concentration (< 1 mg/L). In acute infections, especially the level of CRP in blood elevates. Hs-CRP is an acute-phase reactant produced by the liver under the control of interleukin-6. Serum concentrations measure acute inflammatory events such as infection, as well as the chronic inflammatory response elicited by atherosclerotic plaque formation. Hs-CRP has been shown to have prognostic value in patients with acute coronary syndromes; however, the most promising use of hs-CRP has been in the primary prevention setting [21]. Thus hs-CRP had a stronger relation with heart failure.

There was a significant increase (P<0.001, 1493%) in serum CK-MB levels in acute MI cases as compared to controls. Following MI, the initial CK-MB rise occurs 4-9 hours after the onset of chest pain, peaks at 24 hours and returns to baseline at 48-72 hours [8]. It is easier to detect reinfarction using serial CK-MB measurement which is the advantage of measurement of CK-MB in MI. In past serial measurement of CK-MB level was the standard approach for detection of perioperative MI. Measurement of CK-MB is currently the test choice to confirm the diagnosis of an AMI.

Fig. 2: Percentage Change Graph of Serum Lipid Profile and Uric Acid Levels in Acute MI Cases With Respect To Control Group

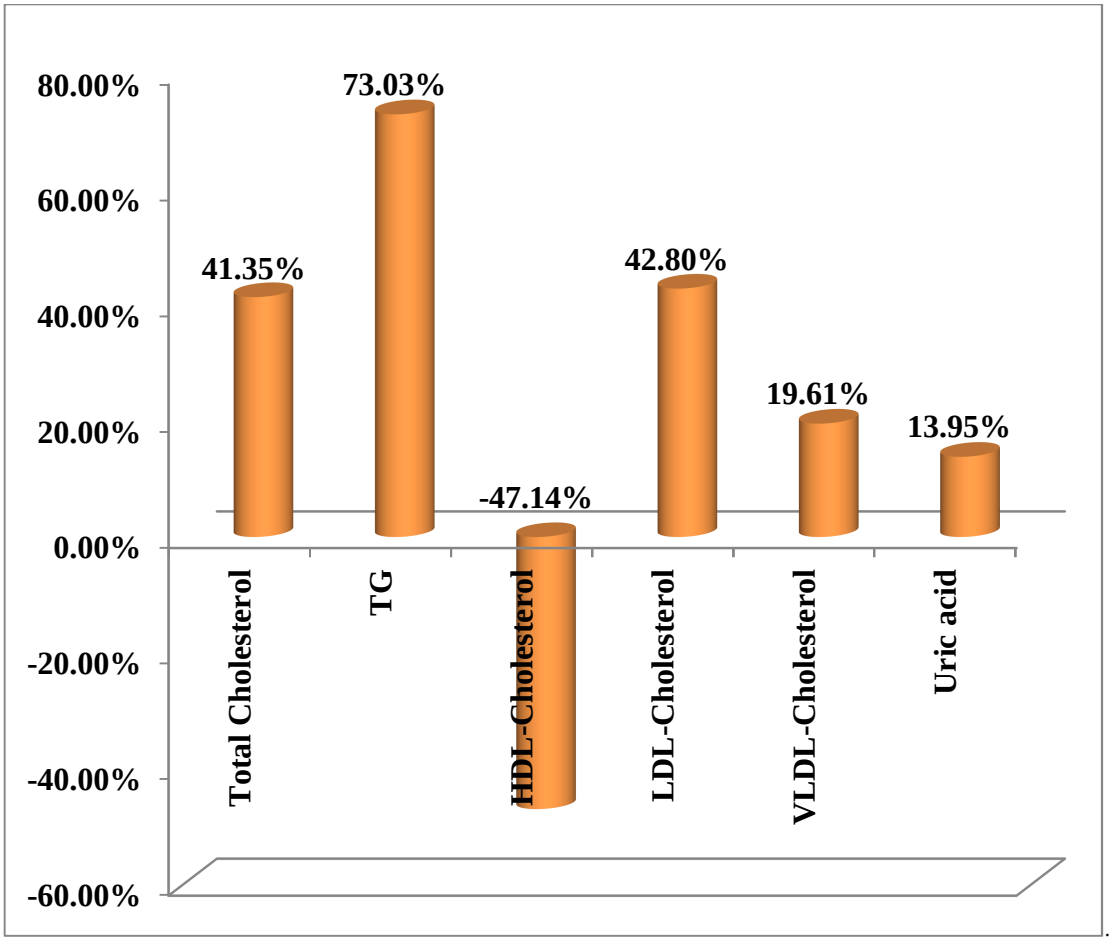
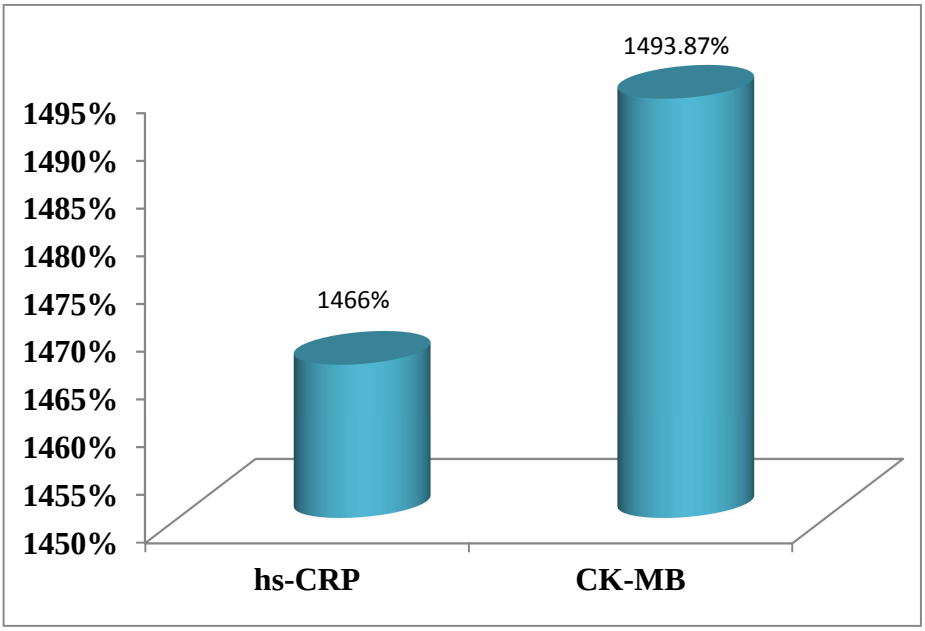


Fig. 3: Percentage Change Graph of Serum Hs-Crp, & Ck-Mb in Acute Mi Cases with Respect to Control Group



Lipid abnormality is one of the important risk factor for ischemic heart disease. There are several assessments on variations of serum lipid profiles following MI. We observed significant increase (P<00 41.35%) in serum TC, TG (73.03%), LDL-cholesterol (42.80%) levels and significant decrease in HDL-cholesterol (-47.14%) levels as compared to controls. Our results are inconsistent with Ahmad Shirafkhan et al [22]. There are number of risk

factors which influence the formation of plaques due to excess cholesterol. The changes in lipid parameters following AMI are due to acute phase response. The acute phase response induces marked changes in lipid metabolism like increased plasma triglyceride levels and decreased HDL levels [23]. The increase in serum cholesterol and TG levels may depend on genetic basis [24]. Increase in cholesterol leads to increase in LDL-cholesterol as LDL carries most of cholesterol in plasma. The risk of AMI was associated with increase in LDL-cholesterol and decrease in HDL-cholesterol in both Asians and non-Asians [25]. However few workers have reported a reduction in total cholesterol, HDL-cholesterol and LDL-cholesterol while others have reported no change in serum total cholesterol and HDL-cholesterol after acute MI [26, 27].

In our study most of the patients had normal serum uric acid level. Many studies found that uric acid plays a clear and independent role in cardiovascular disease [13-15, 18]. There is relatively little information on the role of uric acid as a risk factor for stroke. In the general population, an association was found between uric acid and fatal stroke [28]. Elevated serum uric acid concentration has been shown to be the strong predictor of cardiovascular mortality in several recently published studies. Bickel C et al [29] studied the influence of uric acid levels on mortality in patients with CAD. He supported the use of serum uric acid levels as a predictor of in-hospital death in patients hospitalized for decompensate heart failure. Lazzari et al [30] found that 21.5% of patients with AMI had a rise in uric acid level and the risk of mortality among these patients during hospitalization was 3.9 times more than patients with normal level of uric acid. It has been shown that there is a positive correlation between the occurrence of heart failure and uric acid & hs-CRP levels.

CONCLUSION

The levels of serum hs-CRP were significantly increased in acute MI cases; therefore we encourage the use of hs-CRP as a diagnostic tool for MI patients in daily clinical practice.

It has therefore been proposed that increased use of the monitoring of inflammatory and other diagnostic markers could be of use in the screening and prediction of the risk of infarction.

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