ABSTRACT

Aim: To evaluate the predictive role of inflammatory markers, serum hs-CRP and serum ceruloplasmin in patients of acute myocardial infarction.

Materials and methods: The study was conducted on 50 patients presented with clinical features of acute myocardial infarction of both sex and varying age groups, admitted to ICCU of J.L.N. Hospital, Ajmer (Rajasthan). They were compared with 50 healthy volunteers with identical demographic characteristics but without any disease. Serum hs-CRP and serum ceruloplasmin levels were measured in both the groups.

Results: A significant increase in serum hs-CRP and ceruloplasmin level were observed in all patients of acute myocardial infarction as compared to control group and these higher levels also correlate with higher CK-MB level.

Conclusion: In patients of acute myocardial infarction the serum hs-CRP and ceruloplasmin levels rise due to their property of acute phase protein.

Key words: Acute myocardial infarction, hs-CRP, Ceruloplasmin, Acute phase protein.

INTRODUCTION

Myocardial infarction is one of the most common problems encountered in casualty department. Myocardial infarction, commonly known as a heart attack is the interruption of blood supply to part of the heart due to occlusion of coronary artery following the rupture of a vulnerable atherosclerotic plaque. Myocardial infarction occurs when myocardial ischemia exceeds a critical threshold and overwhelms myocardial cellular repair mechanisms that are designed to maintain normal operating function and hemostasis. (1,2)

Symptoms of acute myocardial infarction (AMI) are chest pain, dyspnoea with rise in troponin or creatine kinase-MB (CK-MB) level greater than 99% compared to normal reference population. (3)

Many studies have shown that inflammation is an important factor in AMI. Inflammation contributes to different stages in the pathogenesis of coronary artery disease (CAD). Due to inflammation acute phase response occurs. This response is induced by pro-inflammatory cytokines, which are released from the inflamed tissue by inflammatory and parenchyma cells and stimulates the liver to synthesize a number of acute phase proteins. (4,5)

These acute phase reactants have been identified as valuable risk markers for the prediction of cardiovascular events. Among these, high sensitive C-reactive protein (hs-
CRP) and ceruloplasmin have been central to most studies in the field.

Several epidemiological studies have shown that plasma level of hs-CRP is a strong independent predictor of risk of future myocardial infarction, stroke, peripheral arterial disease, and vascular death among individuals without known cardiovascular disease.\(^6\) hs-CRP predicts future coronary events merely because it is associated with all of the major risk factors for atherosclerosis, namely dyslipidemia, smoking, hypertension, diabetes, abdominal obesity, depression, other psychosocial factors and many others.\(^7\) hs-CRP level was found to be a potent predictor of cardiovascular events than the LDL cholesterol level.\(^7\)

Ceruloplasmin is an important extracellular antioxidant. Ceruloplasmin, known as ferroxidase, is an enzyme synthesized in the liver containing six atoms of copper in its structure.\(^8\)

Ceruloplasmin is \(\alpha\)-2globulin protein. It carries 90% of the copper in our plasma. It is an acute phase protein which rises after any form of tissue injury.\(^9\)

Biochemical studies have shown that ceruloplasmin is a potent catalyst of LDL oxidation in vitro, but its role in lipoprotein oxidation and atherosclerotic lesion progression in vivo has not been directly assessed and is an important area for further studies.\(^10\)

Several prospective studies have indicated that the serum copper or ceruloplasmin level may be an independent risk factor for cardiovascular disease.\(^11\) The increased risk has been attributed to prooxidant function of ceruloplasmin, and recent experimental studies demonstrating the ability of ceruloplasmin to oxidatively modify low-density lipoprotein (LDL) seem to underline this concept.\(^12\)

The aim of the present study was to evaluate the serum level of hs-CRP and ceruloplasmin in patients of acute myocardial infarction whether it would be significantly increased in AMI patients.

**MATERIALS AND METHODS**

The study was conducted on 50 patients presented with clinical features of acute myocardial infarction of both sex and varying age groups, admitted to ICCU of J.L.N. Hospital, Ajmer (Raj.). In the control group, 50 healthy volunteers of identical age and sex without any disease were recruited. **Inclusion Criteria:** The diagnosis of AMI was established according to clinical criteria: chest pain, which lasted for up to hours, ECG changes (ST elevation of 2 mm or more in at least two leads) and elevation of serum cardiac marker serum creatinine phosphokinase (cpk-MB).

**Exclusion Criteria:** Patients with diabetes mellitus, renal insufficiency, hepatic disease, or patients taking lipid lowering drugs and any other major illness were excluded from the study.

**Sample Collection:** Blood samples from patients were collected for analysis at the time of admission to ICCU. About 10mls of venous blood were aspirated from antecubital vein of each individual, using plastic disposable syringes. Serum was obtained by centrifugation at 3000 rpm for 10 minutes; transferred immediately into another tube. Serum was analysed for estimations of ceruloplasmin, hs-CRP, CK-MB and lipid profile levels. Blood samples from the control subjects were also collected for similar testing.

Ceruloplasmin estimation was done by para-phenylenediamine oxidase (p-PPD) method.\(^13\) Serum hs-CRP was estimated by standard kits utilizing the immunoturbidimetric method.\(^14\) Routine investigations (Blood sugar, urea, creatinine, and SGOT, SGPT, CK-MB and lipid profile) were performed on Randox dytona autoanalyzer.

**Statistical analysis:** All statistical analysis was performed using statistical package for the social sciences (spss). Data were expressed as mean ± S.D .Results were evaluated using the student t-test for paired data. A p-value less than 0.05 is considered significant and more than 0.05 is non-significant.
RESULTS

Table I shows the demographic characteristics of study population in control and AMI patients in which body mass index was found significantly high in AMI patients as compared with control. Systolic and diastolic blood pressures were also significantly high in the patients group as compared with controls.

The present study showed a significantly higher serum total cholesterol levels in AMI patients (p<0.001) than that in the controls. Also a significantly higher serum triglyceride and LDL-cholesterol levels (p<0.001) in those patients as compared to control subjects (Table II).

Table III illustrates the level of inflammatory markers in control and AMI patients. There was a significant increase in serum hs-CRP level in AMI patients as compared to control subjects. Serum ceruloplasmin level was also found significantly high in AMI patients as compared to control subjects (p<0.001).

DISCUSSION

Acute myocardial infarction (AMI) is defined as death or necrosis of myocardial cells. It is a diagnosis at the end of the spectrum of myocardial ischemia or acute coronary syndromes.

Acute myocardial infarction (AMI) occurs when localized myocardial ischemia causes the development of a defined region of necrosis. MI is most often caused by rupture of an atherosclerotic lesion in a coronary artery. This causes the formation of a thrombus that plugs the artery, stopping it from supplying blood to the region of the heart.

Spontaneous thrombosis of a coronary artery produces regional myocardial ischemia and ultimately myocardial infarction.

The root cause of AMI is mainly atherosclerosis. It seems to be a chronic inflammatory condition, which later develops into an acute clinical event by the induction of plaque rupture, causing thrombosis. Hence Inflammation occupies a very important central position in all phases of atherosclerosis. Cholesterol has been singled out as the primary factor in the development of atherosclerosis.

In the present study, we found that the serum level of hs-CRP was significantly higher in patients with AMI of onset < 6 h than controls. These findings of our study are similar to Tomoda H et al. study in which they found higher CRP levels within 6 h after the onset of AMI and suggested that these levels reflect the vulnerability of culprit coronary lesions.(15)
The results of our study highlight the important role of this novel inflammatory marker in the clinical setting of AMI. Chowdhury N et al. also found positive correlation between serum Ischemia modified albumin (IMA) and positive acute phase reactants hs-CRP and ceruloplasmin in patients of AMI. (16)

In both children and adults, higher CRP levels directly correlate with various cardiovascular risk factors, including body mass index, systolic blood pressure (BP), levels of triglycerides and total cholesterol, heart rate and history of CAD or stroke, and it inversely correlate with HDL cholesterol and diastolic blood pressure. (17)

The higher level of hs-CRP is due to plaque rupture and thrombus formation. This may imply that patients with high hs-CRP have had more severe atherosclerotic coronary disease with a poorer clinical outcome of MI than those with lower CRP levels.

There are many possible mechanisms by which hs-CRP enhances atherosclerosis. Hs-CRP activates the complement pathway (18) and induces adhesion molecule expression by human endothelial cells. (19) hs-CRP also has been found to play a role in monocyte recruitment into the arterial wall. (20) hs-CRP enhances the entry of LDL particles into macrophages, (21) and it has been found to induce plasminogen activator inhibitor-1 expression. (22) Elevated CRP is also associated with endothelial dysfunction. (23)

Serum ceruloplasmin level was found significantly high as compare to control subjects. These findings are similar to Bhagwat K study in which they observed high concentration of serum ceruloplasmin in patients with acute myocardial infarction and with other forms of coronary heart disease and further showed that ceruloplasmin level decreases slowly and reaches the baseline within a month. (24)

Ceruloplasmin is an important intravascular antioxidant and it protects tunica intima against free radical injury. Ceruloplasmin functions as ferroxidase by catalyzing the oxidation of (Fe+2 to Fe+3) and correlates well with its level and antioxidant activity. (25)

Ceruloplasmin exhibits a cardioprotective effect and prevents oxygen free radical induced release of noradrenalin, a powerful vasoconstrictor. (26)

Increased serum ceruloplasmin concentrations are presented by patients with various cardiovascular conditions like atherosclerosis, abdominal aorta aneurysm, unstable angina and peripheral arterial disease.

An increase of ceruloplasmin can be mediated many unspecific factors causing tissue injury or inflammation. Endothelial injury and inflammatory processes are thought to be involved in the pathogenesis of atherosclerosis.

Studies have shown that ceruloplasmin can be considered an important risk factor predicting AMI and cardiovascular diseases. (11) Evidence suggests that LDL can be oxidized to an atherogenic form (oxidized LDL) within arterial wall by macrophages and other cells. This oxidation may be mediated by copper ions released from ceruloplasmin in atherosclerotic lesions. (27)

**CONCLUSION**

From this study it is concluded that serum hs-CRP and serum ceruloplasmin levels in patients of AMI were found to be abnormally high.

The raised hs-CRP and ceruloplasmin levels in patients of AMI suggest involvement of inflammation in the etiopathogenesis of MI and have prognostic utility in AMI. Serum hs-CRP and ceruloplasmin levels are potent predictors of prognosis in patients with AMI and elevated levels of these inflammatory markers at the time of admission indicate a poor prognosis in patients with AMI. Hence the present study concluded that, higher serum hs-CRP and ceruloplasmin levels on admission in patients of AMI are due to their property of acute phase protein.
Limitations: We had only one baseline hs-CRP and ceruloplasmin values and no follow-up values. However, further study on serum hs-CRP and ceruloplasmin levels and serial estimation of these levels in AMI can throw some light on this aspect.

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