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Original Article

Assessment of C-reactive Protein in Cases of Acute Myocardial Infarction and Its Correlation with Risk Factors

Srilekha Sesani[1], M Vijayabhaskar[2], M I Madhulatha[3], Vijaya Lokary[1]

[1]Post-graduate Student, Department of Biochemistry, Mamata Medical College, Khammam, Telangana, India, [2]Professor and Head, Department of Biochemistry, Parul Institute of Medical Sciences & Research, Parul University, Vadodara, Gujarat, India, [3]Associate Professor, Department of Biochemistry, Mamata Medical College, Khammam, Telangana, India

Abstract

Introduction: Acute myocardial infarction (AMI) is a significant cause of morbidity and mortality worldwide, which results from occlusion of coronary artery. C-reactive protein (CRP) is an acute phase protein, synthesized by hepatocytes in response to cytokines released into circulation by activated leukocytes. It is a sensitive marker of coronary inflammation as well as the extent of myocardial necrosis. CRP measurement has many advantages in detection and monitoring the acute phase response.

Aim: To assess serum CRP level in newly diagnosed cases of AMI and to assess correlation with risk factors.

Materials and Methods: A total of 90 patients presenting with AMI admitted to ICCU in the Department of Cardiology, Mamata General & Super Specialty Hospital, Khammam, were included in the study. All the patients were diagnosed based on clinical examination electrocardiogram, troponin-I, and cardiac enzymes. Serum CRP levels were measured by enzyme-linked immunosorbent assay method. Patients were divided into two subgroups based on the presence of major risk factors hypertension: Diabetes mellitus and smoking. All values are expressed as mean ± standard deviation. The results obtained are analyzed statistically.

Results: This study showed that mean serum CRP levels were increased in the study group. Among two subgroups, mean CRP level increased significantly in the group with risk factors when compared with another group.

Conclusion: Patients with AMI cases shows the presence of major risk factors and higher CRP level who may require more stringent treatment and monitoring when compared with subjects without risk factors.

Key words: Acute myocardial infarction, C-reactive protein, Hypertension, Diabetes mellitus

INTRODUCTION

Acute myocardial infarction (AMI) is the significant cause of morbidity and mortality worldwide. In India, the majority of death occur due to MI.[1] MI results from the rupture of atherosclerotic plague with thrombus formation and occlusion of coronary artery resulting in reduction of blood supply to the portion of myocardium. Inflammation has also been studied extensively to play a major role in MI.[2] Since inflammation is believed to have a role in the pathogenesis of cardiovascular events, measurement of markers of inflammation has been proposed as a method to improve the prediction of the risk of these events.[4] Inflammation plays a crucial role in intermediary pathogenesis linking diabetes with a commonly existing conditions thought to originate through inflammatory mechanisms interleukin 6 a major proinflamatory cytokine is produced in a variety of tissues including activated leukocytes,adipocytes and endothelial cells. c-rp is the principle downmstream mediator of the acute phase response and is primarily derived via IL-6 hepatic biosynthesis.[5] Ford examined the relationship between C-reactive protein and BMI and diabetes andshowed elevated c-rp concentrations in patients with diabetes.[6] It has been theorized that acute myocardial

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Corresponding Author: Dr. Srilekha Sesani, Mamata Medical College, Khammam, Telangana, India. Phone: +91-8125915006. E-mail: srisesani@gmail.com

infarctions (AMIs) and other acute coronary events that are precipitated by atherosclerosis are due to arterial blockage from fat deposits. It is now known, however, that atherosclerosis involves more than just lipids. Inflammation has also been studied extensively to play a substantial role in myocardial infarction.[7] Kannel and McGee found that this diabetes report extended prior Framingham study findings with more-robust 20-year data for estimating the relative risk of specified atherosclerotic cardiovascular events from prior diabetes.[8]

Chae CU *et al* suggest that increased blood pressure may be a stimulus for inflammation and that this is a possible mechanism underlying the well-established role of hypertension as a risk factor for atherosclerotic disease.[10]

In 1999, Russel Ross was the first, who published that atherosclerosis is an inflammatory disease.[9] Inflammation is an important feature of atheroma and is associated with activation and proliferation of macrophages, endothelial cells, and smooth muscle cells. There have been studies in assessing C-reactive protein (CRP) values and biomarker of inflammation for prediction of cardiovascular events.[3] Several studies showed that CRP is not only inflammatory marker but is also involved in pathogenesis of MI. Recent observations suggest that the atherosclerotic process is characterized by a low-grade inflammation altering the endothelium of the coronary arteries and is associated with an increased level in markers of inflammation such as acute phase proteins and cytokines. Cumulative evidence indicates that inflammation, at both focal and systemic levels, plays a key role in destabilization and rupture of atherosclerotic plaques, leading to acute cardiovascular events.[11,12]

CRP is an acute phase protein synthesized by hepatocytes in response to cytokines released into circulation by activated leukocytes. CRP inhibits endothelial cell nitric oxide synthase production via destabilizing endothelial nitric oxide synthase.[18] Decreased no release causes CRP-mediated inhibition of angiogenesis-stimulating endothelial cell apoptosis. CRP activates complement system which mediates monocyte and neutrophil recruitment in an injured myocardium, and therefore, leads to increase in infarct size.[18] CRP measurement has many advantages in detection and monitoring the acute phase response.

MATERIALS AND METHODS

The total of 90 cases presenting with AMI admitted to ICCU in the Department of Cardiology Mamata General & Super Speciality Hospital, Khammam, were included in the study. All the patients were diagnosed based on clinical examination, electrocardiogram, troponin-I, and cardiac enzymes. 90 patients are selected as controls. Serum CRP levels were measured by immunoturbidimetry (ERBA kit) method.

Cases were divided into two subgroups based on the presence of major risk factors hypertension: Diabetes mellitus and smoking. Among them, 54 cases with risk.

Study Design

Cross-sectional comparative study.

Exclusive Criteria

1. Patients below 30 and above 50 aties,
2. Patients on statin treatment.

Inclusive Criteria

Patients in the range of 30-50 years.

Statistical Analysis

Mean and standard deviation values of all biochemical parameters were calculated in study and control groups, and the mean difference was compared using *t*-test.

RESULTS

This study showed that mean serum CRP level was significantly increased in the study group when compared with controls. Among two subgroups, mean serum CRP level was increased significantly in the group with risk factors when compared with another group without risk factors (Tables 1 and 2; Figures 1 and 2).

DISCUSSION

CRP, an acute phase protein, is a marker of systemic inflammation that has been associated with increased risk of incident MI. Tissue necrosis is a potent acute phase stimulus following MI; there is a major CRP response, the magnitude of which reflects the extent of myocardial necrosis.[15] In the early phase of MI, proinflammatory cytokines directly interfere with the myocardial contractility, the vascular endothelial function and recruitment of other inflammatory cells.[14] Patients of AMI showed increased CRP level.

An association between sustained high values of CRP following AMI and its adverse outcomes was first reported in 1982.[13] Recent observation suggests that the atherosclerotic process is characterized by a low-grade inflammation altering the endothelium of coronary arteries and is associated with an increase in the level of markers of inflammation. In an attempt, to improve global cardiovascular risk prediction considerable interest has focused on CRP. CRP is not only an excellent biomarker of inflammation but it is also a direct participant in

Table 1: Mean±SD, *P* value among cases and controls

Parameter	Cases (mean±SD) *n*=90	Controls (mean±SD) *n*=90	*P*
CRP	9.72±2.74	1.97±0.86	<0.01

SD: Standard deviation, CRP: C-reactive protein

Table 2: Mean±SD, *P* value among subgroups (cases with risk factors and without risk factors)

Parameter	Subgroup-1 (*n*=54)	Subgroup-2 (*n*=36)	*P*
	Cases with risk factors	Cases without risk factors	
CRP	13.71±3.01	6.72±1.54	<0.02

SD: Standard deviation, CRP: C-reactive protein

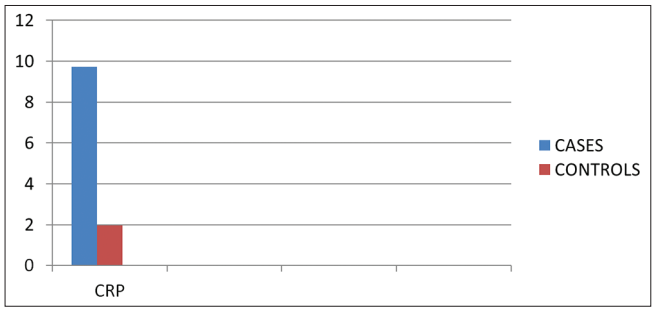

Figure 1: Mean±standard deviation, *P* value among cases and controls

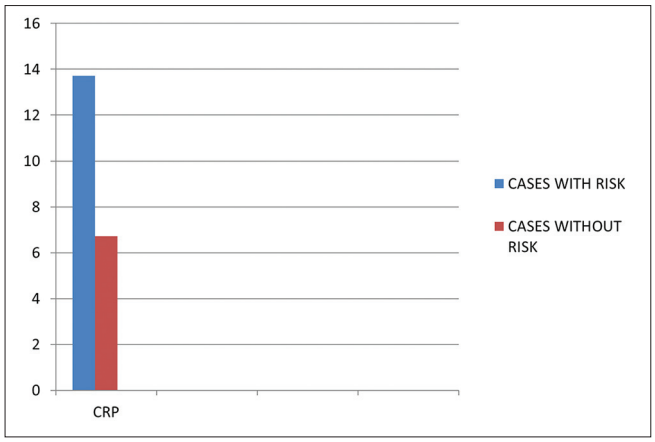

Figure 2: Mean±standard deviation, *P* value among subgroups (cases with risk factors and without risk factors)

atherogenesis. The mechanism of CRP pathogenicity is binding of abundant CRP to the ligands exposed in dead and damaged cells, triggering substantial complement activation with release of chemotactic factor and opsonization of cells in and around the lesion leading to enhanced infiltration by inflammatory cells and consequent damage.[14] Elevated CRP has been associated with many diseases such as CHD, insulin resistance, hypertension, and metabolic syndrome. In addition to its role as a biomarker, some studies found that CRP has a role in the development of endothelial dysfunction and elevated blood pressure.

Subclinical inflammation as indicated by elevated CRP levels may be one of the causal mechanisms contributing to the development of hypertension. There is evidence to indicate that systolic BP could promote oscillatory shear stress to stimulate the release of proinflammatory cytokines.[20] Inflammatory cytokines from obesity, insulin resistance could promote arterial inflammation.[21] The inflammatory state itself may promote the release of free radicals and could increase NO degradation rate and lower its availability. CRP downregulates NO synthase and reduces NO release and bioactivity.[22] Possible effect of systemic inflammation on BP may be mediated through alteration in the synthesis and degradation of vasodilating and vasoconstricting factors. Previous cross-sectional studies have been shown that CRP levels are positively associated with systolic blood pressure,[23,24] pulse pressure,[25] and hypertension.[26]

Insulin resistance (IR), a reduced physiological response of peripheral tissues to the action of insulin, is one of the major causes of Type 2 diabetes and plays a critical role in the pathogenesis of cardiovascular diseases (CVDs). Recent studies have shown that the worldwide prevalence of IR and its associated risk factors have increased markedly. IR is believed to be associated with chronic inflammatory response which is characterized by abnormal cytokine production and the activations of proinflammatory signaling pathways.[27-29]

The systemic inflammatory biomarker CRP when measured in the blood with high sensitivity assay has been reported to be a strong and independent predictor of MI, ischemic stroke, Type 2 diabetes, and hypertension. Several studies have provided strong evidence of association between CRP and CVD risk independent of traditional risk factors, such as cholesterol, blood pressure, alcohol consumption, and smoking habit.[30-32] This is in accordance with the study of Gelaye *et al.*

Components of the metabolic syndrome (i.e., central obesity, increased plasma triglyceride concentrations, low plasma concentrations of high-density lipoprotein-cholesterol, hypertension, and increased concentrations of blood glucose) correlate with increased plasma CRP concentrations, and CRP measurement contributes to risk prediction in individuals with the metabolic syndrome.[19]

Elevated CRP levels are a strong independent predictor of Type 2 diabetes and may mediate associations of TNF-αR2 and IL-6 with Type 2 diabetes.

This is in accordance with the study conducted by Sano *et al.*[16] and Auer *et al.*[17]

Sanchis *et al.* found that CRP levels increase in patients with AMI with hypertension and diabetes mellitus.

Dibra *et al.* found that diabetes was positively related to CRP concentration.

In our study, the increased CRP level was more pronounced in the presence of major risk factors. As hypertension, diabetes mellitus and smoking are well-known independent risk factors for atherosclerosis. The patients with these risk factors may require more stringent treatment and should be monitored for future complications.

CONCLUSION

CRP levels are increased in AMI, and the increase was more pronounced in patients associated with risk factors. The patients with these risk factors may require more stringent treatment and should be monitored for future complications.

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