

Original Article

Evaluation of C-Reactive Protein and other Inflammatory Markers in Acute Coronary Syndromes

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ABSTRACT

Objectives: The aim of the study is to evaluate the role of C-reactive protein (CRP), ESR, total WBC and fibrinogen in acute myocardial infarction (AMI) and in unstable angina (UA), the two very common manifestations of acute coronary syndromes (ACS).

Subjects and Methods: The present study included 100 ACS patients with age ranging from 42-60 years (mean 53 ± 6 years), of which 35 were presented with UA and 65 with AMI. The study also included 25 normal subjects, age and sex matched as controls.

Results: CRP levels were elevated in both AMI ($40.8 \pm 15.4\text{mg/l}$) as well as in UA ($32.9 \pm 17.7\text{mg/l}$) patients when compared to that of the normal controls ($12.6 \pm 2.8\text{mg/l}$). But the value of fibrinogen was found to be elevated significantly only in AMI patients ($381.9 \pm 32.1\text{mg\%}$). Other markers such as WBC and ESR were found to be elevated in both AMI and UA patients.

Conclusion : Elevation of CRP levels can be used as adjuncts in the diagnosis of ACS.

KEYWORDS: acute coronary syndromes, acute myocardial infarction, unstable angina, C-reactive protein, fibrinogen

INTRODUCTION

Acute coronary syndromes (ACS) are a diagnostic and pathophysiologic continuum ranging from unstable angina (UA) to Q wave myocardial infarction (MI). The myocardial ischemia of unstable angina and myocardial infarction results from excess demand or inadequate supply of oxygen. The acute reduction in coronary arterial perfusion resulting in ACS is primarily due to an atherosclerotic plaque disruption with superimposed thrombosis^[1]. It has been postulated that the propensity to develop an ACS does not depend on the number, distribution and severity of stenosis produced by the atheromatous lesions^[2]. A growing body of evidence supports the concept that local and systemic inflammatory response plays a role in the initiation and progression of atherosclerosis and its complications^[3]. C-reactive protein (CRP) is an acute phase reactant marker for underlying systemic inflammation. CRP has been reported to be elevated in patients with acute ischemia and MI^[4]. Furthermore, elevated CRP along with other acute phase reactants and cytokines with a focal predominance of inflammatory cells have been found in patients with unstable coronary syndromes^[4].

Fibrinogen, another acute phase protein and a clotting factor appears to be an independent risk

factor for cardiovascular diseases^[5]. As a key determinant of plasma and red cell viscosity, elevated levels of fibrinogen may decrease blood flow, particularly through stenotic vessels^[2]. Fibrinogen appears to directly enhance atherogenesis by its conversion to fibrin, which binds low density lipoprotein (LDL) and stimulates proliferation of vascular smooth muscle cells^[6]. A high white blood cell count and a high erythrocyte sedimentation rate have been thought to reflect the body's response to tissue injury in patients with AMI, and total leukocyte count correlates with the severity of coronary atherosclerosis^[7]. The present study was carried out to investigate the role of inflammatory markers in the diagnosis of ACS such as UA and AMI.

MATERIALS AND METHODS**Patient Selection**

Patients were admitted to the intensive coronary care unit (ICCU) of Amala Cancer Hospital with AMI and UA presenting within 24 hours of onset of chest pain were included in the study. Hundred patients were included in the present study (35 with UA and 65 with AMI). The age ranges from 42 to 60 years (mean age = $53 \pm$ six years), and the study included 95 males and five females. Twenty-five age and sex matched volunteers were also included in the study as

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Table 1
Serum lipid profiles in control and study groups with ACS

Groups	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Control	168.75 ± 14.64	88.17 ± 24.05	43.89 ± 11.55	107.25 ± 26.20
Patients with AMI	199.76 ± 18.82*	125.95 ± 66.36	37.53 ± 10.54	137.03 ± 37.26
Patients with UA	208.70 ± 22.04*	211.02 ± 17.63	40.30 ± 12.76	130.70 ± 16.45

Values are expressed as mean ± SD
*p<0.001

controls. They had no past history or evidence of cardiovascular disease, hypertension or diabetes mellitus. None of the control subjects gave history of neoplastic, hepatic, infectious or autoimmune diseases or any surgical procedure in the preceding six months. The study was approved by the institutional ethics committee.

Methods

10 ml of blood was withdrawn for laboratory analysis. Cholesterol was estimated by CHOD-PAP method^[8]. HDL-Cholesterol was estimated from the supernatant after precipitation by phosphotungstic acid and magnesium chloride (1.4 mmol/l phosphotungstic acid and 8.6 mmol/l magnesium chloride)^[9]. Triglycerides were determined by GPO-PAP method^[10] and LDL-cholesterol was calculated using the Friedewald's formula^[11].

WBC was counted using an automated hematology analyzer^[12]. ESR was determined by Westergren's method^[12]. Fibrinogen was determined by the rapid precipitation method using sulphosalicylic acid^[13] and C-reactive protein was determined by using Turbox/Turbox Plus analyser, based on immunoprecipitation assay, with nephelometric end-point detection^[14].

Statistical analysis was carried out using the Student's t test. Values were expressed as mean ± SD. Values having P < 0.001 on comparison were considered as significant.

RESULTS

Lipid parameters

The results of the present study showed elevated levels of total cholesterol in patients with AMI and with UA (Table 1) and the values were found to be statistically significant (p < 0.001), but the values of triglycerides, HDL and LDL, were not altered much when compared to that of the normal controls. Even though the LDL value was increased, it was not statistically significant.

Table 2
Inflammatory markers in control and study groups with ACS

Groups	WBC (Count/mm ³)	ESR (mmHg/hr)	Fibrinogen (mg%)	CRP (mg/l)
Control	8949 ± 1853	25 ± 10	315.2 ± 27.7	12.6 ± 2.8
Patients with AMI	11480 ± 4345*	55 ± 28*	381.9 ± 32.1*	40.8 ± 15.4*
Patients with UA	10359 ± 3212*	56 ± 16*	325.7 ± 29.4	32.9 ± 17.7*

Values are mean ± SD
*p<0.001

Inflammatory markers

Table 2 represents the values of inflammatory markers in ACS. The WBC values in both AMI and UA patients were increased. The ESR was also found to be increased in both groups of patients when compared to that of the normal controls. The value of fibrinogen was found to be elevated in patients with AMI (p < 0.001), but the increase was not significant in UA patients when compared to controls. C-reactive protein, the principle marker of inflammation was found to be significantly elevated in both AMI and UA patients (p < 0.001) when compared to normal controls.

DISCUSSION

Rupture of plaques with superimposed thrombosis is now considered to be the main cause of acute coronary syndromes that ranges from unstable angina to acute myocardial infarction. The main pathophysiological mechanism is plaque rupture or erosion that are followed by exposure of thrombogenic contents, such as collagen, to the circulation^[15].

Multiple lines of investigation have converged to suggest a prominent role of inflammation in atherosclerosis. Histologically atheromatous plaques obtained at autopsy have demonstrated the presence of inflammatory mononuclear cells with foci of monocytes, macrophages and T-lymphocytes in the arterial wall^[16]. Anatomically, the most common site of plaque rupture in acute coronary syndromes appears to occur in the shoulder region, where inflammatory cells are most prominent. As part of this inflammatory response, stimulation of the hepatic production of acute phase reactants has been shown to occur. These acute phase reactants have been proposed as potential indicator of underlying atherosclerotic disease and unstable atheromatous lesions^[4].

C-reactive protein is an acute phase reactant marker for underlying systemic inflammation. In our study we found an increased value of CRP in all

ACS patients. This finding confirms the already published data of increased levels of CRP seen in acute coronary syndrome^[4]. All our patients recovered except one with very high levels of CRP. From the clinicians point of view it will be useful to know whether CRP values predict a worse prognosis in acute coronary syndrome. However this will require a further study involving a large number of patients.

High concentrations of lipid parameters are the principle risk factors for atherosclerosis. The present study showed that there was no marked increased value of lipid parameters except cholesterol in patients with acute coronary syndromes. This finding cannot be considered as conclusive and may require a larger study for confirmation.

There is an increased total WBC count and erythrocyte sedimentation rate in patients with acute coronary syndromes compared with normal controls. The value of fibrinogen, which is also a risk factor for ACS, is found to be elevated only in AMI patients. It is slightly increased in UA patients but the value is not statistically significant. Fibrinogen has been extensively investigated in epidemiologic studies, and some pharmacological approaches, including aspirin, bezafibrate, pentoxifyline and ticlopidine administration, have been suggested to counteract some of the pathologic effects of elevated fibrinogen, including increased viscosity, platelet aggregation and red blood cell rigidity^[17]. These observations suggest that CRP levels can be used as a complementary test in the diagnosis of ACS.

CONCLUSION

This study indicates that elevation of CRP, an inflammatory marker is elevated in both UA and AMI patients.

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