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Research Article

**RELATION OF HIGHLY SENSITIVE C – REACTIVE PROTEIN
LEVELS WITH CORONARY ARTERY DISEASE SEVERITY**¹Dr Muhammad Asadullah, ²Dr Muhammad Adil, ³Dr Ahmad Qadri¹Allama Iqbal Medical College, Lahore²Allama Iqbal Medical College, Lahore³Allama Iqbal Medical College, Lahore**Article Received:** August 2020**Accepted:** September 2020**Published:** October 2020**Abstract:**

Coronary artery disease is a major component of cardiovascular disease and the leading cause of death in developing countries. The disease is characterized by a long asymptomatic period of atherogenesis resulting in an increase in plaque and a symptomatic period of angina or a clinical coronary event. In the present study, levels of the highly sensitive C-reactive protein (Hs-CRP) were determined in patients with coronary artery disease with one-, two- and three-vessel disease and compared with the severity of the disease. A moderate correlation was found with a p value below 0.001. It is suggested that the Hs-CRP should be performed in all patients with significant thrombotic atherosclerosis. These tests are relatively inexpensive and detect a predisposition to future events such as acute MI (myocardial infarction) in patients with coronary artery disease.

Key words: coronary artery disease (CAD), very sensitive levels of C-reactive protein (Hs-CRP)

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INTRODUCTION:

Coronary artery disease is a major component of cardiovascular disease and is the leading cause of death in developing countries. The disease is characterized by a long asymptomatic period of atherogenesis resulting in plaque build-up and a symptomatic period of angina, or a clinical coronary event that usually results in serious complications if left untreated.

Hs-CRP, a marker of vasculitis, is associated with plaque formation, progression, and rupture. Similarly, elevated Hs-CRP levels were associated with poorer clinical outcomes. Coronary calcifications are calcified plaques, which make up about one fifth of the total volume of coronary plaques.

There is strong evidence that cardiovascular conditions are linked with inflammation. Likewise, there is role of inflammation in the pathogenesis of atherosclerosis. This ultimately leads to the occurrence of acute cardiovascular events. The chronic inflammatory process in atherosclerosis usually results in an acute clinical event by plaque rupture and therefore causes acute coronary syndromes. Many large prospective trials have shown that the inflammatory biomarker high-sensitivity C-reactive protein (hsCRP) is an independent predictor of future cardiovascular events.⁴ Several studies from Europe and United States indicate that elevated levels of hsCRP among apparently healthy men and women are a strong predictor of future cardiovascular events. Addition of hsCRP to conventional risk factors acts as an independent significant predictor of cardiometabolic risk. hsCRP has been reported to be an independent significant predictor and a risk factor of cardiometabolic risk, with an additive value to metabolic syndrome components. It has a long-term predictive value in patients with diagnosed coronary artery disease (CAD) and angina pectoris. It is also useful as predictor in individuals with multiple risk factors. hsCRP not only is an important predictor of first myocardial infarction but also for recurrent coronary events. In most of the studies reported, the association of hsCRP with cardiovascular risk has been found to be highly significant in global risk-assessment programs. Little data is available regarding association of hsCRP with the presence and severity of CAD.

CRP is a biochemical by-product that rises sharply following an inflammatory stimulus (eg, Acute MI). Hepatocytes produce CRP in response to elevated levels of IL-6. C-reactive protein (CRP), named for its ability to precipitate the somatic C polysaccharide *Streptococcus pneumoniae*, was the first acute phase protein described. CRP is an extremely sensitive systemic marker of inflammation and tissue damage. It is a member of the pentraxin family of plasma proteins, which are part of the superfamily of folded calcium-dependent lectins that bind ligands and lectins (bind carbohydrates).

MATERIALS AND METHODS:

This study was conducted at the Department of Medicine Jinnah Hospital Lahore for six months duration from January 2020 to June 2020 and patients were randomly selected. The sample size was calculated from data from preliminary studies of 12 patients with single, double and triple vessel disease compared to normal healthy controls. All subjects underwent standard interviews.

Participants were asked about their medical history, including specific questions related to physician-diagnosed hypertension, diabetes, and gastric and duodenal disease. 3 ml of blood was collected for evaluation of the principle of the Hs-CRP test.

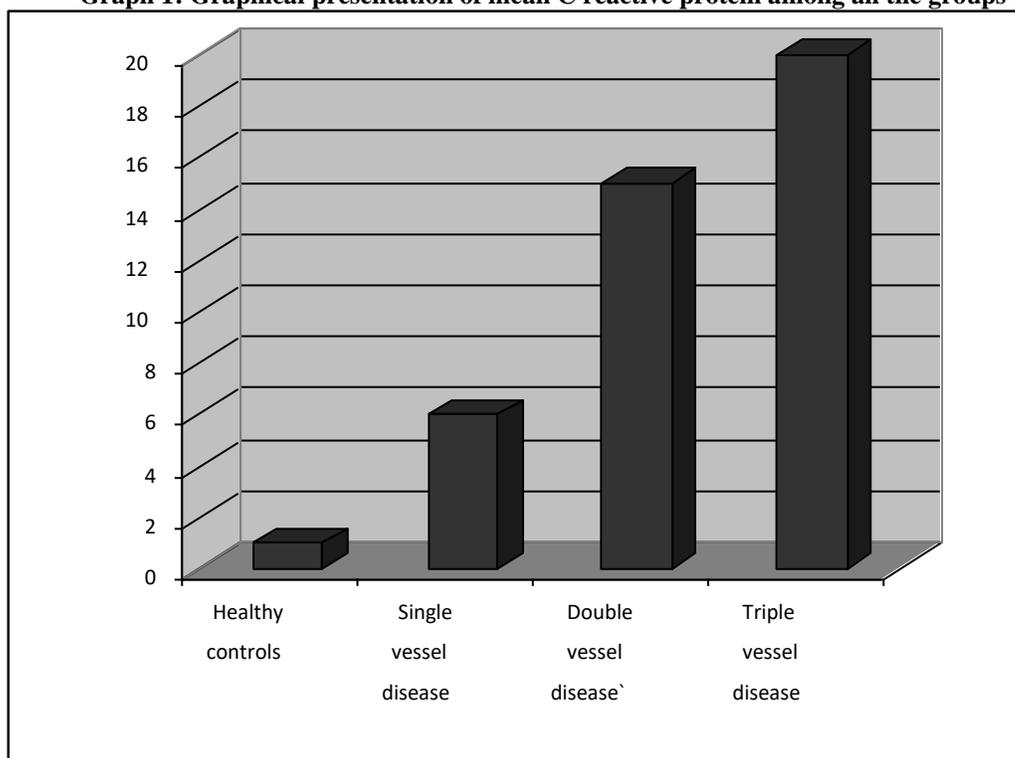
Anti-CRP antibodies linked to the latex microparticles react with an antigen in the sample to form an antigen / antibody complex. After agglutination, it is measured turbidimetrically on Roche automated clinical chemistry analyzers. Statistical analysis: Collected data was entered and analyzed using SPSS version 15.0. Quantitative C-reactive protein variables are described using means \pm 6 standard deviations and percentages.

RESULTS:

This study included a total of 60 cases of coronary heart disease and 20 healthy subjects. Table 1 shows CRP in all four groups, the mean CRP level in healthy controls was 1.03 with a standard deviation of 0.60. In case of single vessel disease, it was 5.99 \pm 0.30, double vessel disease 14.74 \pm 6.42, and triple vessel disease 20.56 \pm 10.

Table 1: Highly sensitive C - reactive protein (Hs-CRP) of patients with reference to the disease status group

	CRP mg/l			
	Mean	Standard Deviation	Min.	Max.
Healthy controls	1.03	0.60	0.50	2.50
Single vessel disease	5.99	3.31	0.30	14.00
Double vessel Disease	14.74	6.42	3.00	24.00
Triple vessel disease	20.56	10.50	3.00	43.00

Graph 1: Graphical presentation of mean C reactive protein among all the groups**DISCUSSION:**

Coronary artery disease is one of the leading causes of death worldwide. For decades, risk factors for coronary artery disease have been identified and shown to be related to the severity of the disease, e.g. hypertension, smoking, diabetes, etc.

This study is based on a collection of eighty cases, of which sixty are known cases of coronary artery disease. The diagnosis and severity of the disease was established on the basis of angiographic evaluation. Sixty have been grouped into single, double, and triple vessel disease to establish disease severity scores. Twenty cases of healthy blood donors were also selected and marked as controls to compare the results.

A similar study was performed in Indian population to determine the concentration of hsCRP and its association with coronary atherosclerosis assessed by coronary angiography. In line with our results they reported that the serum concentration of hsCRP was associated with presence of CAD, but regarding severity the correlation was non-significant. It is recently reported that there is state-level geographic variation in inflammatory biomarkers among otherwise healthy women which cannot be completely attributed to traditional clinical risk factors and lifestyle. It is suggested that future research approaches should aim to identify additional factors that may explain geographic variation in biomarkers

of inflammation among healthy women. In a recent study by Hrirra et al reported that ApoB and hs-CRP levels were markedly associated with the severity of CAD in Tunisian patients and their findings are similar to our results. The possible limitations of our study are limited number of subjects and cross-sectional design. Prospective studies on large scale are needed to explore the true pathogenic role of hsCRP in assessing cardiovascular risk.

Several authors have described the relationship between C-reactive proteins and the severity of coronary artery disease. Their results support the concept of the contribution of endothelial thrombogenesis to atherosclerosis; Hs-CRP level significantly correlates with the angiographic features of thrombotic and eccentric changes. Patients with completely closed lesions without visible thrombus had low levels of CRP, suggesting its role as a marker of acute inflammation.

The study was conducted in Karachi by Ghazala et al., who investigated the role of Hs-CRP concentration and angiographic characteristics of coronary lesions, and assessed the relationship between preoperative Hs-CRP levels and coronary angiographic changes. The results confirmed elevated Hs-CRP levels with specific injuries of high-risk coronary arteries. This was also seen in our study and thus confirmed the role of Hs-CRP in coronary artery disease.

In another study conducted in Chandigarh, India by Malhotra AS et al who attempted to investigate the determination and correlation of anti-cardiolipin antibodies with high-sensitivity C-reactive proteins and their role in predicting short-term treatment outcomes in patients with acute coronary syndrome.

In conclusion, they concluded that anticardiolipin (aCL) antibodies may be involved in the pathogenesis of acute coronary syndrome, but are not significantly associated with recurrences of short-term events in patients with ACS. Moreover, aCL does not appear to have a significant correlation with Hs-CRP in determining short-term outcomes in patients with acute coronary syndrome.

CONCLUSION:

Ultimately, we concluded that CAD patients had higher levels of Hs-CRP. These tests are relatively cheap and will detect a predisposition to future events

such as acute MI (myocardial infarction). Currently, Hs-CRP costs Rs. 500 / - per test, if the patient has associated hyperlipidemia, administration of some statins also leads to a reduction in CRP levels through anti-inflammatory action by blocking the mevalonate pathway and isoprenoid synthesis. Therefore, Hs-CRP should be performed in all patients with significant thrombotic atherosclerosis.

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