

Comparison between Serum hsCRP and LDL Cholesterol as a Predictor for Ischemic Heart Disease

FARHEEN ASLAM, LUBNA SARFRAZ, SARA REZA

ABSTRACT

Background: Acute myocardial Infarction is major cause of morbidity & mortality in world and atherosclerosis is one of major causes of cardiovascular disease. Low-density lipoprotein-C (LDL-C) is independent risk factor of atherosclerosis and has been used to predict the risk of IHD. But high sensitivity C-reactive protein (hsCRP) is more powerful inflammatory marker and can be used to predict future cardiovascular event.

Aim: To investigate whether hsCRP or LDL-C is a better predictor of future ischemic heart disease (IHD).

Methods: Hundred and two patients of myocardial infarction and ninety eight controls were studied for hsCRP and LDL-C over a period of 2 years in pathology department at Quaid-e-Azam Medical collage Bahawalpur.

Results: The concentration of hsCRP in serum in cases of IHD is significantly higher (3.34 ± 0.73 than controls (0.67 ± 0.18) ($P < 0.0001$) but differences in concentration of serum LDL-cholesterol between IHD cases and controls are not significant ($P > 0.05$).

Conclusion: We conclude that the serum hsCRP is a better marker for risk of ischemic heart disease.

Keywords: Myocardial infarction, Atherosclerosis, hsCRP, LDL cholesterol

INTRODUCTION

Cardiovascular diseases are major causes of mortality. They are responsible for about 29.2% of total global deaths and 50% are due to ischemic heart disease (IHD)¹. The main cause of IHD is atherosclerosis. Low-density lipoprotein-C has been regarded as a causal and independent risk factor of atherosclerosis². But research has shown that half of all cardiovascular events occur in patients who have low or normal levels of LDL-C. So factors other than total cholesterol and LDL-C must be measured while evaluating coronary artery disease (CAD) risks³.

Inflammation plays a key role in the pathophysiology of atherosclerosis. The inflammatory cells, macrophages and lymphocytes are present in the atheroma⁴. They release various mediators like cytokines and chemokines that are responsible to increase the plasma concentration of C Reactive Protein (CRP) which further enhances inflammatory procoagulant response. Hence inflammation is important in all phases of heart disease, including the initiation of atherosclerotic plaques within the arteries, as well as the acute rupturing of these plaques that results in ischemic heart disease and even sudden death⁵. Although several acute-phase reactants and cytokines are predictive of cardiac diseases, high

sensitivity C Reactive Protein (hs CRP) is a better marker of inflammatory activity and might be useful to evaluate ischemic heart disease risk. It is a stable compound and commercially available assays of hsCRP have been standardized and show adequate precision. The test can be done at a low cost and has least pre-analytical variables such as age, sex, diet and diurnal variance^{6,7}. The present study aims to assess which one of the two, serum LDL-C or hsCRP is the better and useful marker of atherosclerosis.

MATERIALS AND METHODS

The case control study was conducted in the department of Patholgy at Quaid-e- Azam Medical College, Bahawalpur. The patients from the Department of Cardiology, Bahawal Victoria Hospital, Bahawalpur were taken as cases. The patients who were admitted to the cardiology department within six hours of onset of chest pain and initial diagnosis of myocardial infarction were included in the study. Patients with history of any concomitant infection, malignancy, trauma, cardiovascular or cerebrovascular events, such as MI, unstable angina, prior arterial revascularisation or stroke within 6 weeks preceding the enrolment were excluded from the study. Patients on therapy with steroids, immunosuppressive agents, statins or other lipid-lowering drugs and non steroidal anti-inflammatory drugs (excluding low doses of aspirin) were also not included in the study. The final study group included

Pathology Department, Quaid-i-Azam Medical College, Bahawalpur. Pakistan

Correspondence to Dr. Farheen Aslam, Demonstrator Pathology
Email: farheenaslam75@yahoo.com Cell: 92-300-9686232, House No: 8/D, Officers colony, Club road, Bahawalpur. Pakistan

39 females and 63 males, aged 63±12 years. Clinically healthy volunteers consisted of 44 women and 55 men, aged 64±10 years from the same region with no evidence of renal, metabolic or inflammatory disease, heart failure, and recent myocardial infarction served as control. The study protocol was approved by the ethical Committee of Bhawal Victoria hospital Bahawalpur and written informed consent was obtained from all patients and controls. Venous blood samples were collected from patients on hospital admission within 6 hours of onset of chest pain. Fasting venous blood samples from controls were collected in the morning. Serum was assayed on admission for cardiac troponin I (cTnI) (ARCHITECT ci8200, Abbott Diagnostics). Any increase of cTnI above 0.032ng/mL (the 99th percentile for the healthy population measured with a 10% coefficient of variation) was considered a positive result. LDL was measured directly on Mindray BS 400 using kits provided by Merck (Diagnostics). High-sensitivity CRP (hsCRP) was measured by immunoturbidimetric method using the Architect ci 8200 System, providing excellent precision with the coefficient of variation reported by the manufacturer of less than 6%. The value of hsCRP 3mg/l⁸ and for LDL cholesterol C 160mg/dl⁹ were considered as high risk for cardiovascular diseases. The data for biochemical analysis was subjected to standard statistical analysis such as Student's t test using the SPSS 15.

RESULTS

The personal profiles and clinical parameters of all the subjects under study are shown in Table 1. Low-density lipoprotein-C concentration in control group has mean value 94.0 mg/dl whereas in IHD cases, it was 98.30 mg/dl. High sensitivity C-reactive protein concentration in control showed the mean value 0.67 mg/l whereas in IHD cases it was 3.34 mg/l. Thus the concentration of hsCRP in serum in cases of IHD is significantly higher than controls (P<0.0001) but differences in concentration of serum LDL-cholesterol between IHD cases and controls are not significant (P =0.09) (Table 2). Table 3 shows the distribution of patients in different risk groups as predicted by hs-CRP concentration. 77% of cases are having hsCRP concentration of more than 3mg/L.

Table 1: Personal profile of control and cases suffering from ischemic heart disease

	Control	Cases
Number of cases	98	102
Age	63±12	64±10
Gender		
Male	55	63
Female	43	39

Table 11: Concentration of serum LDL-cholesterol and hsCRP in cases and controls

	Concentration of serum LDL(mg/dl)	Concentration of serum CRP (µg/L)
IHD cases	98.3± 15.92	3.34± 0.73
Controls	94 ± 14.45	0.67±0.18
P value	p> 0.5	P < 0.001

Table 3: Distribution of cases according to their serum concentration of hsCRP in serum

Concentration of serum CRP (mg/L)	Distribution of cases in each group
< 1	7
1-3	17
>3	76

DISCUSSION

The elevated concentration of low-density lipoprotein cholesterol (LDL-C) is one of the best known risk factors of ischemic heart disease but focusing on LDL-C is not an optimal diagnostic and therapeutic strategy¹⁰. Recent studies have shown that the size of LDL particle is more important as compared to LDL-C concentration in atherogenesis^{11,12}. In routine clinical practice estimation of LDL particle size is not applicable due to complicated methodology.¹³ Triglyceride-rich lipoproteins, very low-density lipoproteins (VLDL) and intermediate-density lipoproteins (IDL) also have atherogenic properties. Patients, who achieved a reduction in LDL-C even below 70mg/dL, still are at risk of atherothrombotic events¹⁴.

Atherosclerosis is a chronic inflammatory response of the arterial wall¹⁵. All stages i.e., initiation, growth, and complication of the atherosclerotic plaque¹⁶ might be considered to be an inflammatory response to injury of endothelium. CRP is primarily synthesized by liver in response to interleukin-6 (IL-6) and interleukin-1. It is one of several cytokines released by activated leukocytes and smooth muscle cells in atherosclerotic plaques¹⁷. It inhibits nitric oxide production from endothelial cells which promote vasoconstriction, leukocyte adhesion, platelet activation, oxidation and thrombosis¹⁸. So CRP is an independent predictor of endothelium dependent vascular function among patient with coronary heart disease (CHD).

Many physicians have begun to measure hsCRP to improve the identification of patients at risk of cardiovascular events. The level for predicting atherosclerotic event has been recommended as low risk at 1 mg/l, average at 1–3mg/l and high risk at 3 mg/l⁹.

In present study it is observed that the rise of hsCRP was highly significant as compared to control group (P\0.0001). It was considerably comparable to

Krintus et al study¹⁹. Ray et al. concluded that the addition of hsCRP to lipid-based measurements significantly improved risk prediction²⁰. Framingham Study had also shown that hsCRP has sufficient risk prediction value for atherosclerosis.²¹ Another study conducted by Kilic et al suggested the prognostic efficacy of hsCRP in Acute Coronary Syndrome patients presenting within 6 hours from the onset of chest pain. The optimal cut-off value to identify the long-term prognosis was also considered in this cohort study²².

In present study it has been shown that a very high percentage of myocardial infarction cases (76%) have serum hsCRP level more than 3 mg/l, hence falling in high risk group whereas only 24% percent were having lower concentration.

There are several potential mechanisms that may account for the observed relationship between IHD and CRP levels. It may upregulate angiotensin receptors and enhance expression of plasminogen activator inhibitor-1 by endothelial cells²³. Both these changes promote atherogenesis. Williams et al. demonstrated that CRP increases the activity of matrix metalloproteinase 1 and collagenases that contribute to the destabilization of atherosclerotic plaque²⁴. To increase the robustness of our findings we enrolled patients diagnosed with IHD within first 6 hours from the onset of chest pain. We established this time frame restriction in the inclusion criteria to minimize a potential impact of necrosis-related inflammatory reaction on CRP concentration. Moreover we improve the diagnostic accuracy of LDL by measuring it directly rather calculating it by Friedwield equation. Our case and control population were only slightly different in terms of age and gender distribution. CRP concentration above 3mg/L is currently recommended by the Centers for Disease Control and Prevention (CDC) and the American Heart Association (AHA) as an independent predictor of cardiovascular events⁹. There are certain limitations to our study. First, findings of our study have potential for confounders because of its case-control design, so the results are not definitive. Second, we enrolled a broad spectrum of IHD patients and relationship between CRP concentration and IHD patients may vary among different types of IHD.

CONCLUSION

We can therefore conclude that measurement of hsCRP can be considered as a better predictor for cardiovascular disease than the serum LDL-cholesterol. However, more prospective studies are required to designate serum hsCRP level as an independent risk factor of IHD.

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