

High Sensitive C - reactive protein – A Risk Marker For Coronary Artery Disease.

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Abstract : Background of the study - Coronary Artery Disease (CAD) remains the leading cause of morbidity and mortality in the present world. Clinical and laboratory studies have shown that inflammation plays a major role in the initiation, progression, and destabilization of atheromas. C-reactive protein (CRP), an acute phase reactant that reflects low-grade systemic inflammation, has been studied in a variety of cardiovascular diseases. Aim: To measure high sensitive c reactive protein (hs-CRP) value in patients with coronary artery disease and to compare it with controls. Outline of previous work – previous studies have demonstrated that elevated hs-CRP levels has strong correlation with coronary artery disease. Methodology – 50 subjects who were recently diagnosed as coronary artery disease (investigations already done during the period of hospitalization) were included in the study after a questionnaire analysis. Blood investigations include hs-CRP & serum lipid profile, were done during the period of hospitalization. The reports were collected and compared with the normal reference range. Results – in our study, hs-CRP, total cholesterol, and low density lipoprotein levels are significantly high in cases when compared to controls and high density lipoprotein levels are significantly low in cases when compared to controls. We observed a positive correlation between hs-CRP and lipid parameters. Conclusion – hs- CRP can be considered as a risk marker for coronary artery disease.

Keywords – Coronary Artery Disease, High Sensitive C Reactive protein, Total Cholesterol, Low Density Lipoprotein, High Density Lipoprotein.

I. Introduction

Inflammation plays a vital role in accentuating the formation of atherosclerotic plaque, and thus the measurement of inflammatory markers provide a method of assessing cardiovascular risk. Among the inflammatory markers, of late C- Reactive protein, is considered as inflammatory markers for coronary artery disease. CRP is an acute phase protein produced by liver, in response to any inflammation. It is used as a marker for low grade systemic inflammation. Conditions like Smoking, Blood Pressure and elevated cholesterol levels can also elicit inflammatory reactions that are detectable with C-reactive protein. However, CRP lack the sensitivity when inflammation are within normal range. More recently high sensitive CRP (hs-CRP) is used to detect the low level inflammation when it is within the normal range¹. This lack of sensitivity and specificity with measuring CRP, resulted in the estimation of CRP using laser nephelometry , which can detect the low level inflammation, even when it is within normal range.

Atherosclerosis in coronary arteries is not only due to lipid deposits, but, also due to systemic inflammation, both playing a major role in atherothrombotic inception and progression². Few studies have demonstrated that the possible association between CRP levels and coronary artery disease³. Thakur et al., estimated the levels of hs-CRP in coronary artery disease and found that there is a significant increase in hs-CRP levels in coronary artery disease⁴. In another study, Wolfgang et al., used hs-CRP to estimate the association of inflammation with the first incidence of coronary artery disease and concluded that hs-CRP is a sensitive systemic inflammatory marker for predicting the risk of CAD and also suggested that low grade inflammation is involved in the pathogenesis of atherosclerosis⁵. However, there are no studies that could emphasis on the cut-off value of hs-CRP in estimating the risks in coronary artery disease patients in south Indian population. This study was designed to estimate the hs-CRP levels in recently diagnosed coronary artery disease (CAD) and to see whether it can be used as a risk marker for CAD in South India urban population (Chennai).

II. Aim Of The Study

To measure hs-CRP value in patients with coronary artery disease and to compare it with controls.

III. Materials And Methods

Study population – 45 patients, who were recently diagnosed with coronary artery disease, were recruited for the study . They were selected after a questionnaire analysis. The diagnosis for cad was confirmed by clinical presentation and with any two positive investigations like ECG, Echocardiogram, Cardiac Enzymes

& Angiogram. 45 age and sex matched controls were selected. The study was approved by the institutional ethical committee. A well informed written consent was obtained from both the cases and controls after briefing them about the study.

Inclusion criteria: Age ranging between 35 to 80 years. Both the sex were included in this study.

Exclusion criteria: Recent infection, Inflammatory disease eg., arthritis., who were under NSAIDS

The study was done in Sree Balaji Medical College & Hospital (SBMC&H). 3ml of venous blood was collected from all the cases and control to assess the hs-CRP value. hs-CRP value is measured by using immunoturbidimetric test in the central laboratory in SBMCH. Lipid profile reports were collected from the patient's record.

Statistical Analysis: Results were tabulated and the values were expressed in Mean ± Standard Deviation. Significance was assessed by using Unpaired Student t-test. Pearson correlation analysis was also done.

IV. Results

Table 1: Physical Parameters of Both The Cases And Controls

Parameter	Controls	Cases	p – value
Age	60.44±9.44	60.53±9.62	0.96
Height	161.93±6.18	161.49±7.11	0.75
Weight	63.18±6.05	65.38±7.98	0.14
BMI	24.08±1.58	25.08±2.71	0.035*

P value < 0.05 – significant *

Figure 1: Physical Parameters Of Both The Cases And Controls

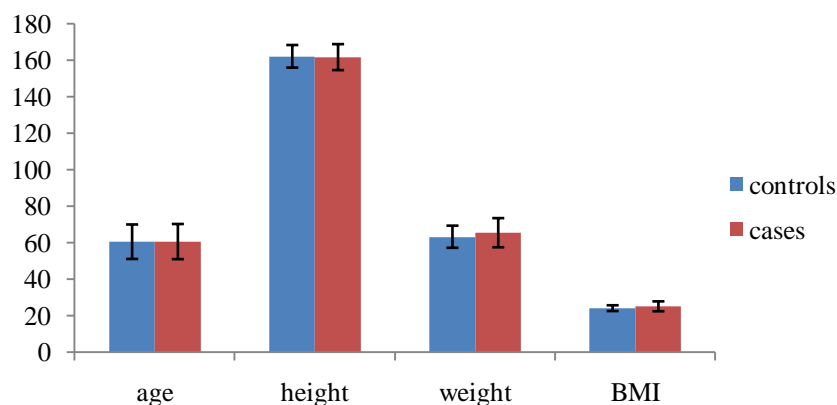


Table 1 and figure 1 : Represents the mean ± standard deviation and p value of age, height, weight and BMI. We can observe significance only in the BMI between cases and controls.

Table 2 : Study Parameters Of Both The Cases And Controls

	NORMAL RANGE	CONTROLS	CASES	P VALUE
hs-CRP	< 3 mg/L	1.5±0.56	5.1±1.13	< 0.001**
TC ^	< 200 mg/dL	179±10.54	215.1±19	< 0.001**
LDL ^^	< 100 mg/dL	86.7±9.4	139.2±14.9	< 0.001**
HDL ^^^	> 40 mg/dL	43.2±5.3	36.4±5.4	< 0.001**

P value < 0.005 – highly significant.

Figure 2& 3: Study Parameters Of Both The Cases And Controls

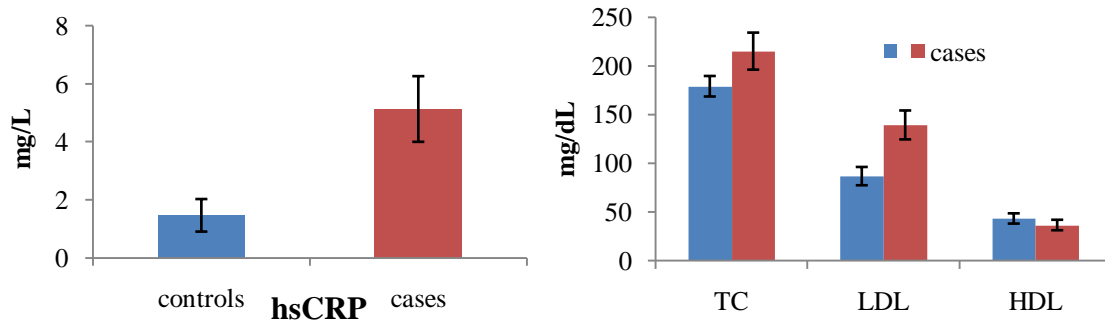


Table 2 and figure 2 & 3: represents the mean ± standard deviation and p value of TC, LDL, HDL and hs-CRP. We can observe significant increase in the values of TC, LDL, and hs-CRP and a significant decrease in the values of HDL between cases and controls.

Table 3 & Figure 4 : Grading Of Risk According To Hs-CRP Values.

hs- CRP mg/L	Controls	Cases
< 1	11	
1--3	34	2
>3		43

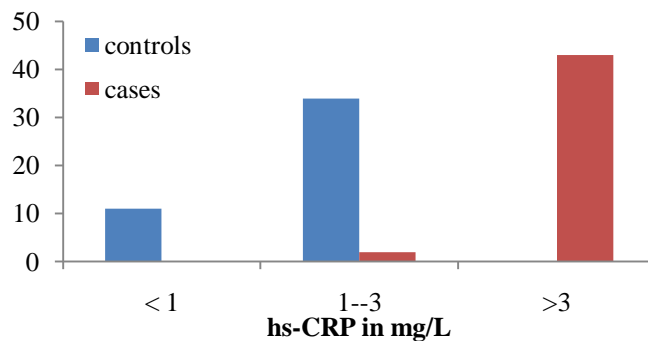
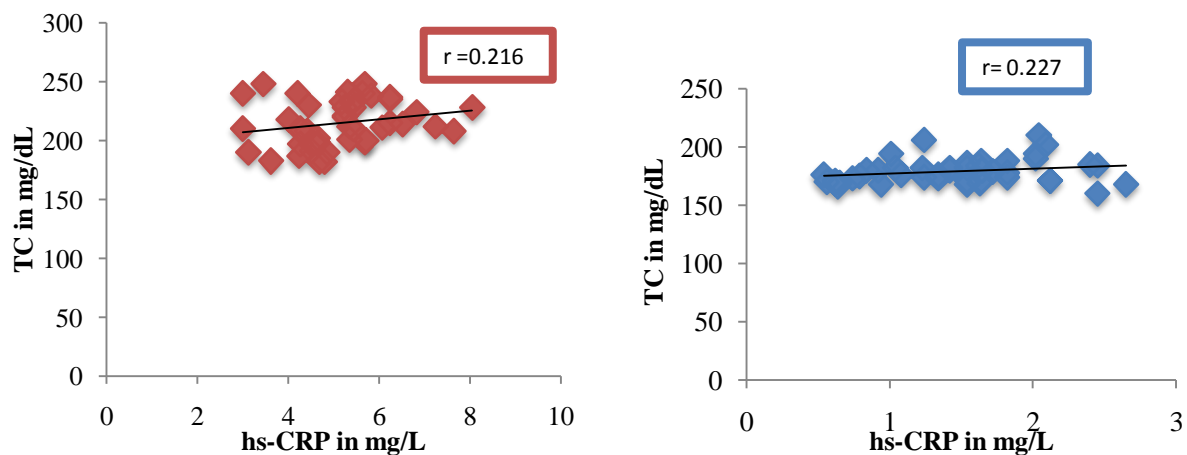


Table 3 and figure 4: represents the number of cases and controls, classified according to the hs-CRP risk group. We can note that most of the cases were in the severe risk group with hs-CRP values more than 3 mg/L

Figure 5 & 6: correlation between total cholesterol and hs-CRP cases and controls



Figures 5 & 6: represents the correlation between hs-CRP and TC in controls and cases respectively. In both the groups there is a positive correlation between the two parameters, however, the values of TC are much higher in cases..

Figure 7 & 8: correlation between low-density lipoprotein and hs-CRP cases and controls

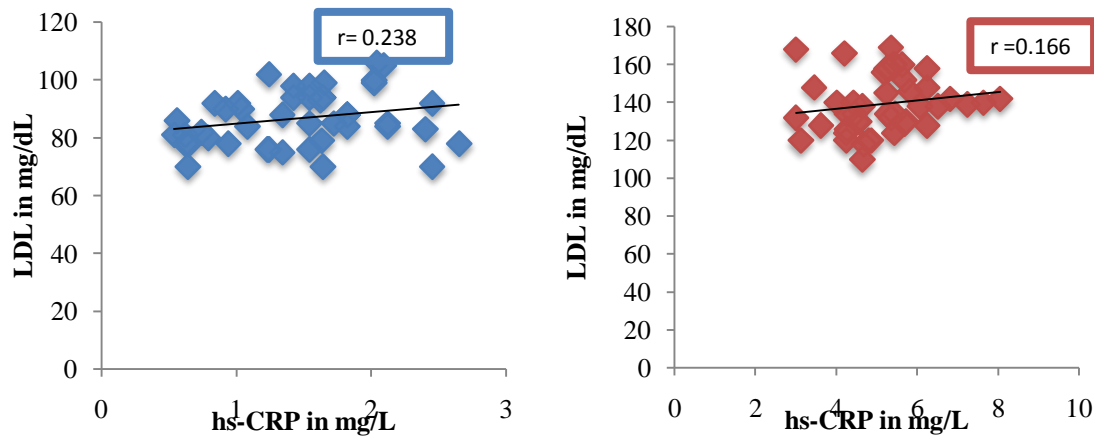


Figure 7 & 8: represents the correlation between hs-CRP and LDL in controls and cases respectively. In both the groups there is a positive correlation between the two parameters. However, the values of LDL are much higher in cases.

Figure 9 & 10: correlation between low-density lipoprotein and hs-CRP cases and controls.

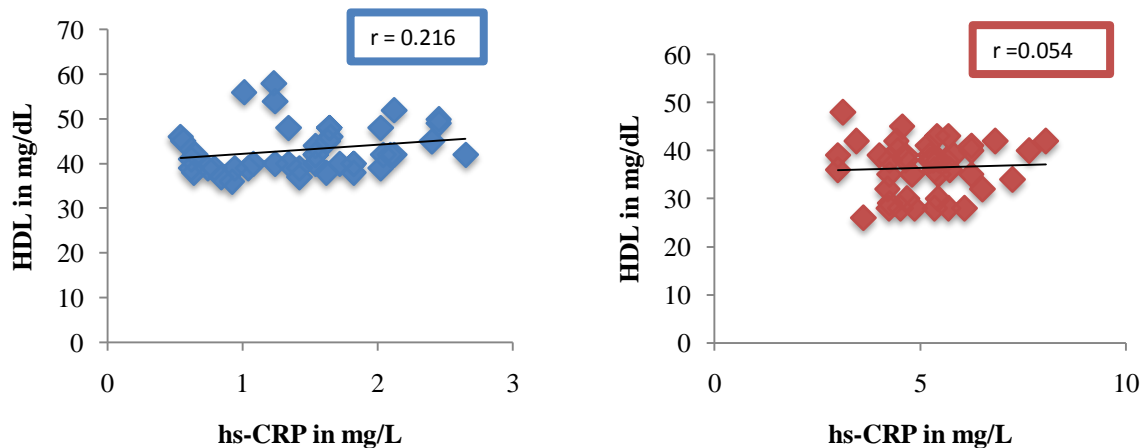


Figure 9 & 10: represents the correlation between hs-CRP and HDL in controls and cases respectively. In controls there exists a positive correlation between the two parameters, but in cases only a weak positive correlation exists between the two parameters.

V. Discussion

hs-CRP is divided into three risk groups according to the American Heart Association.

- Low Risk - <1 mg/L
- Moderate Risk - 1 To 3 mg/L
- High Risk - > 3 mg/L

In our study, out of 45 cases 43 have hs-CRP values more than 3 mg/l, this clearly proves that our patients belong to high risk category in consistent with previous studies⁶. Out of 45 controls, 34 are in moderate risk group and 11 are in low risk group (table 3 and figure 4). More number of subjects falling under the moderate risk group might be either due to underlying systemic illness like Diabetes Mellitus and Hypertension or these controls might have impending thrombogenesis which is reflected in there hs-CRP values.

In our study we observed there is an increased concentration of total cholesterol and low density lipoprotein but decrease in high density lipoprotein in cases when compared to controls (table 2). The concentration of TC, LDL and HDL correlates positively with hs-CRP values in both cases and controls

(Figures 5, 6, 7 and 8). However, there is only a weak positive correlation between HDL and hs-CRP in cases (Figures 9 and 10).

The cause of elevated levels of hs-CRP seems to be due to persistent inflammation in CAD. hs-CRP enhances atherosclerosis by activating complement pathway and induces adhesion molecule expression by human endothelial cells, monocyte recruitment into the arterial wall. It enhances the entry of LDL particles into macrophages. It induce the plasminogen activator inhibitor-1 expression and it also cause endothelial dysfunction. Recent studies states that hs-CRP can be produced within the vascular smooth muscle of diseased coronary arteries and this may directly lead to expression of several mediators of atherothrombotic process⁷.

VI. Conclusion

With this study we conclude that hs-CRP can be used as a risk-marker for coronary artery disease. In clinical scenario, hs-CRP estimation can be employed as a screening tool in the prediction of future coronary artery events. hs-CRP can also be used for primary prevention of CAD.

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