

A Study of Clinical Profile with High Sensitivity C-Reactive Protein and Lipid Profile in Coronary Artery Disease

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Abstract- BACKGROUND: Coronary artery disease (CAD) is the leading cause of death in India and worldwide. CAD is most commonly due to atherosclerosis of the coronary arteries. Empirical evidence suggests that inflammation plays a critical role in all stages of atherosclerosis. Of the potential risk factors, high sensitivity C - reactive protein (Hs -CRP), is one of the downstream vascular inflammatory marker and most promising. It is considered to be the most robust tool with test characteristics desirable and subservient for clinical use.

AIMS AND OBJECTIVES: To evaluate the significance of Hs -CRP as one of the most reliable marker in CAD. To study the role of lipid abnormalities as a risk factor in CAD. To evaluate the lipid profile in comparison with the Hs -CRP value in CAD.

MATERIALS AND METHODS: The study was conducted on 100 subjects attending medicine OPD divided into two groups, 50 subjects having CAD manifested as acute coronary syndrome and the other 50 subjects are healthy control.

RESULTS AND CONCLUSION: In the present study Serum Total Cholesterol, Serum Triglycerides, Serum Hs-CRP and the mean values of BMI were significantly higher among the cases and there exists a significant positive correlation between them.

I. INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death and disability in India and the leading cause of death worldwide. Although CAD mortality rates worldwide have declined over the past four decades, CAD remains responsible for about one-third or more of all deaths in individuals over age 35¹⁻³. CAD accounts for 20% of all deaths in the South Asian region (SAR).

CAD is most commonly due to atherosclerotic occlusion of the coronary arteries. Earlier, atherosclerosis was considered to be a bland condition associated lipid storage that reduces the arterial lumen. It is now believed to be a chronic inflammatory condition that starts at a very young age.

Evidence of inflammation in atherosclerotic lesions has been noted from the earliest histologic observations and inflammation is central to understanding the pathogenesis of atherosclerosis⁴⁻⁷. Macrophages that have taken up oxidized LDL release a variety of inflammatory substances, cytokines, and

growth factors^{8,9}. Among the many molecules that have been implicated are: monocyte chemotactic protein (MCP)-1^{10,11}; intercellular adhesion molecule (ICAM)-1; macrophage and granulocyte-macrophage colony stimulating factors^{12,13}; CD40 ligand; interleukin (IL)-1, IL-3, IL-6, IL-8, and IL-18^{14,15,16}; and tumor necrosis factor alpha¹⁷⁻¹⁹.

Lipid abnormalities play a critical role in the development of atherosclerosis^{9,20-26}. Several epidemiologic studies conducted in countries around the world showed an increasing incidence of atherosclerosis when serum cholesterol concentrations were above 150 mg/dL (3.9 mmol/L). High levels of LDL cholesterol²⁰⁻²⁶ are particularly important risk factors for atherosclerosis²¹. HDL, in contrast to LDL, has putative antiatherogenic properties that include reverse cholesterol transport, maintenance of endothelial function, and protection against thrombosis. There is an inverse relationship between plasma HDL-cholesterol levels and cardiovascular risk.

Of the potential risk factors presently available, high sensitivity C - reactive protein (Hs -CRP), is one of the downstream vascular inflammatory marker and is among the most promising. It consistently associates with the increased risk of atherosclerotic cardiovascular disease independent of cholesterol level^{28,29}, although genetic data do not support its function as a causal risk factor. It has been considered as a useful marker to identify individuals with increased vascular inflammation^{27,30}. Thus, Hs-CRP is considered to be the most robust tool with test characteristics desirable and subservient for clinical use.

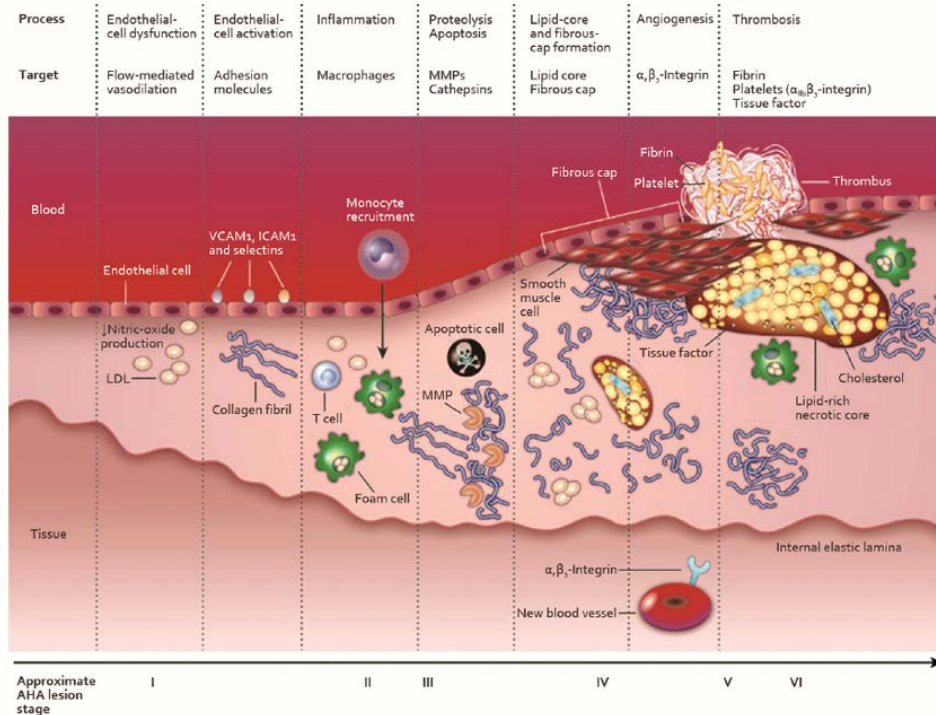
Serum levels of lipids have proven among the most potent and best substantiated risk factors for atherosclerosis in general and CAD in particular. The uptake of oxidized LDL -derived cholesterol by subintimal macrophages characterizes the formation of the atherosclerotic plaque, initiating a local inflammatory reaction. Dyslipoproteinemias constitute a major risk factor for atherosclerosis and CAD, and their proper recognition and management can reduce cardiovascular and total mortality rates.

II. PATHOPHYSIOLOGY

Atherosclerosis is responsible for almost all cases of coronary artery disease (CAD). This insidious process begins with fatty streaks that are first seen in adolescence; these lesions

progress into plaques in early adulthood, and culminate in thrombotic occlusions and coronary events in middle age and later life. Risk factors include Age, Family history of premature CAD, Hypertension, Lipid abnormalities, Diabetes mellitus, Chronic Kidney Disease, Metabolic Syndrome, Cigarette Smoking, Diet, Obesity, Excess alcohol intake, Sedentary lifestyle, Psychosocial factors, inflammatory markers,

hyperhomocysteinemia. These risk factors disturb the normal function of endothelium. These functions include local control of vascular tone, control of inflammatory cell adhesion and diapedesis. The loss of these defences accelerates or modify a complex and chronic inflammatory vascular process that ultimately manifests as fibrous atherosclerotic plaque.



Multiple factors contribute to the pathogenesis of atherosclerosis, including endothelial dysfunction, dyslipidemia, inflammatory, and immunologic factors, plaque rupture, and smoking. The endothelium forms an active biologic interface between the blood and all other tissues. The single layer of continuous endothelium lining arteries forms a unique thromboresistant layer between blood and potentially thrombogenic subendothelial tissues. The endothelium also modulates tone, growth, hemostasis, and inflammation throughout the circulatory system. Endothelial vasodilator dysfunction is an initial step in atherosclerosis and is felt to be caused principally by loss of endothelium-derived nitric oxide³¹. Most widely accepted theory of atherosclerosis states that the process represents the body's attempt to heal in response to an endothelial injury.

The hsCRP has been noted to have opsonizing properties, increasing the recruitment of monocytes into atheromatous plaque and also inducing endothelial dysfunction by suppressing basal and induced nitric oxide release. The hsCRP *per se* has also been found to increase the expression of vascular endothelial plasminogen activator inhibitor-1 (PAI-1) and other adhesion molecules and alter LDL uptake by macrophages³². However, interventions that directly inhibit hsCRP would have to be evaluated before conclusively establishing hsCRP as a direct contributor to the atherosclerotic process.

III. DIAGNOSIS

The initial evaluation for CAD includes a detailed patient history including a comprehensive list of CAD risk factors, a thorough physical examination and an electrocardiogram. Once this initial evaluation is performed, laboratory blood tests should include measurement of lipids, glucose, creatinine, haematocrit. Urine test for evidence of diabetes and renal disease should be done. stress testing, and a cardiac imaging may be necessary to obtain further diagnostic insight.

IV. DIAGNOSTIC CRITERIA

ELECTROCARDIOGRAPHIC MANIFESTATIONS OF ACUTE MYOCARDIAL ISCHEMIA

ST-Elevation:

New ST elevation at the J point in two adjacent leads with the following cut points:

- ≥ 0.1 mV in all leads (except V2 -V3).
- In leads V2-V3 the following cut points apply:
 ≥ 0.2 mV in men ≥ 40 years
 ≥ 0.25 mV in men < 40 years
 ≥ 0.15 mV in women.

ST Depression and T Wave Changes

- New horizontal or down sloping ST depression ≥ 0.05 mV in two contiguous leads

•T-wave inversion ≥ 0.1 mV in two contiguous leads with a prominent R wave or R/S ratio > 1

clinical presentation and investigations like
 •Characteristic electrocardiogram (ECG) changes
 •Positive treadmill test
 •Positive Echocardiographic findings
 •Positive Trop T

V. CORONARY ARTERIOGRAPHY

Coronary arteriography remains the gold standard for determining the presence of obstructive CAD. It is used to detect or exclude serious coronary obstruction. It is indicated in patients with chronic stable angina despite medical therapy, patients with symptoms to rule out or confirm CAD, patients with high risk of sustaining coronary events.

Exclusion criteria:

Confounding factors which could interfere in the biochemical analyses of study subjects and alter the results like
 •Smoking
 •Diabetes mellitus
 •Active inflammatory diseases
 •Nutritional deficiencies

VI. MATERIALS AND METHODS

The study was conducted on 100 subjects attending medicine OPD and divided into two groups, 50 subjects having coronary artery disease manifested as acute coronary syndrome and the other 50 subjects are age and sex matched healthy control.

Statistical Methods:

For each parameter mean and standard deviation was calculated. The value of $p < 0.05$ was taken as significant. The qualitative variables were compared using χ^2 test. The statistical software system SPSS version 22 for windows was used for analysis. Univariate and bivariate correlation was made using Kendall's tau method to confirm the significance of variables with Hs-CRP and lipid profile.

Study design: Observational Case control study.

Inclusion Criteria: Patients presenting with chest pain in whom the diagnosis of coronary artery disease was confirmed by

VII. RESULTS AND ANALYSIS

Table 1: Age distribution of cases and controls

Age in years	No of cases	No of controls
30-40	5	4
41-50	19	19
> 50	26	27

In the present study mean age of cases was 51.24 ± 7.89 , mean age of control was 52.18 ± 7.36 . The minimum age was 33 for cases and 37 for control. The maximum age of cases and controls were 69 and 68 respectively. Majority of cases were > 40 years of age.

Table 2: Gender distribution of cases and controls

SEX	CASES	CONTROLS
MALE	16	16
FEMALE	34	34

The number of males included in the study was 16 (32%) and the number of females was 34 (68%). The female preponderance was due to application of the exclusion criteria (cigarette smoking)

Table 3: Distribution of cases & controls based on S.Total cholesterol

S.Total cholesterol (Mg/dl)	CASES	CONTROLS
< 180	14	28
180 – 199	7	13
200 – 239	19	7
> 240	10	2

Total cholesterol was estimated for all study subjects, 36 cases as compared to 22 controls had S.TC > 180 Mg/dl, of which 10 cases were > 240 Mg/dl.

Table 4: Distribution of cases & controls based on TGL

TGL (Mg/dl)	CASES	CONTROLS
< 150	28	35
150 – 199	12	6
200 - 500	10	9
> 500	NIL	NIL

In this study, 22 cases as compared to 15 controls had TGL > 150Mg

Table 5: Distribution of cases & controls based on Hs-CRP

Hs-CRP (mg/L)	CASES	CONTROLS
< 1	7	36
1 – 3	37	14
> 3	6	NIL

In this study, 37 cases had Hs-CRP in the range of 1 – 3mg/L and 6 cases were > 3mg/L as compared to the control group which had 36 subjects with values < 1mg/L and 14 in the range of 1 – 3mg/L.

Table 6: Correlation between risk factors, lipid profile and Hs-CRP.

PARAMETER	Hs-CRP	SIGNIFICANCE
T.CHOLESTEROL	< 0.001	HS**
TGL	< 0.005	S*
HDLc	> 0.05	NS
LDLc	< 0.005	S*
VLDLc	> 0.05	NS
BMI	< 0.001	HS**

** Correlation is significant at the 0.01 level (2 tailed)

* Correlation is significant at the 0.05 level (2 tailed)

VIII. DISCUSSION

In this study 50 patients diagnosed as coronary artery disease by ECG, Echocardiogram, and cardiac enzymes who satisfied the inclusion and exclusion criteria were taken as cases and 50 age and sex matched controls satisfying the exclusion criteria were taken as controls, cardiac and clinical profile was assessed in both groups and a correlation was made between clinical profile, Lipid profile and Hs-CRP.

Lipid Profile in CAD

The mean value of T.cholesterol was high in cases as compared to controls, and was statistically significant, $p < 0.001$. Comparing HDLc, LDLc, VLDLc and TGL between cases and controls, there was no significant correlation except for LDLc which was statistically significant $p < 0.002$.

Hs-CRP in CAD

In this present study 43 cases had Hs-CRP > 1mg/L as compared to 14 controls. Among the 43 cases, 6 had Hs-CRP values > 3mg/L. The mean Hs-CRP levels was higher among cases compared to control, and it was statistically significant ($p < 0.001$). This data suggests a strong correlation between high Hs-CRP and CAD.

Lipid profile and Hs-CRP in CAD

In the present study, there was a significant correlation between Hs-CRP and T.Cholesterol ($p < 0.001$), TGL ($p < 0.005$), LDLc ($p < 0.004$) and VLDLc ($p < 0.007$). There was no statistically significant correlation of Hs-CRP with HDLc.

IX. CONCLUSION

1. In the present study Serum Total Cholesterol, Serum Triglycerides, Serum Hs-CRP and the mean values of BMI were significantly higher among the cases.
2. There exists a significant positive correlation between Serum Hs-CRP and parameters of lipid profile namely, Serum Total Cholesterol, LDLc, VLDLc, and Triglycerides.

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