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RESEARCH ARTICLE

High-sensitive C-reactive protein levels in diabetes associated with dyslipidemia

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ABSTRACT

Background: There is compelling evidence that inflammation is an important risk factor in cardiovascular disease (CVD) and diabetes mellitus. High-sensitive C-reactive protein (hs-CRP) is a predictive marker of inflammation as well as metabolic syndrome. **Aims and Objectives:** The purpose of this study was to correlate the significance of hs-CRP with cholesterol, triglyceride (TG), high density lipoprotein cholesterol (HDL-C), and low density lipoprotein (LDL) in patients with long-term hyperglycemia and healthy control group. **Materials and Methods:** This study involved 311 subjects (150 patients, 161 control group; between 40 and 65 years of age, mean age of patients and control group were 51.4 ± 9.6, 45.96 ± 3, respectively). Serum concentration of aforementioned analytes was measured among the patients and controls. **Results:** The concentration of parameters among case and control group were total cholesterol (227.84 ± 28.3, 167.45 ± 21.63 mg/dl), LDL cholesterol (158.43 ± 25.65, 117.30 ± 31.27 mg/dl), HDL-C (27.67 ± 11.11, 51.74 ± 12.61 mg/dl), TG (211.34 ± 36.42, 98.13 ± 67.40 mg/dl), and hs-CRP (29.49 ± 5.90, 2.18 ± 1.10 mg/L) were measured by Cobas 6000 autoanalyzer. A statistically significant ($P < 0.001$) difference was found in both groups. **Conclusion:** Diabetes mellitus has a profound effect on lipid metabolism and patient's lipid profile need to be monitored and managed frequently to prevent further complication such as CVD that may arise as a result of dyslipidemia.

KEY WORDS: High Density Lipoprotein Cholesterol; Total Cholesterol; Low Density Lipoprotein Cholesterol; High-sensitive C-reactive Protein

INTRODUCTION

Atherosclerosis is a multifactorial process but its most well-established risk factor is dyslipidemia. Important prognostic indicators of cardiovascular disease (CVD) are the ratio of total cholesterol to high density lipoprotein (HDL) cholesterol and the ratio of apolipoprotein B (Apo B) to Apo A-I. Inflammation predisposes to dyslipidemia characterized by low HDL, total cholesterol, and Apo A-I levels and increased levels of low density lipoprotein (LDL) cholesterol, triglycerides (TGs), and Apo B. Several investigators have reported that patients with inflammatory rheumatic diseases have an adverse lipid profile.[1-3] Numerous studies and experimental evidence indicate that atherosclerosis represents a chronic inflammatory process.[4] Thus, researchers have hypothesized that inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) may provide an adjunctive method for global assessment of cardiovascular risk that could result from dyslipidemia.[5-7] In support of this hypothesis, several large-scale prospective epidemiological studies have shown that plasma levels of hs-CRP are independent predictor of peripheral arterial disease and vascular death among

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individuals without known CVD.[8-14] In addition, among patients with acute coronary ischemia,[15-18] stable angina pectoris,[19] and a history of myocardial infarction,[20] levels of hs-CRP have been associated with increased vascular event rates.

The main existing hypothesis for the origin of atherosclerosis considered being an inflammatory process that occurs in different forms, leading to vascular endothelium injury. Chronic inflammatory processes favor clinical progression of atheroma plaques, which may suffer rupture and provoke thrombus formation and complications associated to atherosclerosis.

MATERIALS AND METHODS

Ethical clearance from the Institutional Ethical Committee was obtained to conduct this study. Diabetic patients with hyperlipidemia were selected on the basis of their serum total cholesterol and TG values. Serum total cholesterol values between 140 and 200 mg/dl were taken to be within normal limits. Age and sex matched non-diabetic controls with normal lipid profile were selected for comparison. The study was conducted on 311 subjects (150 patients, 161 control group; between 40 and 65 years of age, mean age 51.4 ± 9.6). The conducted study was a cross-sectional case control study. The inclusion criteria were age group between 30 and 70 years, both male and female patients. The study excluded smokers, alcoholics, pregnant females, patients diagnosed with carcinoma, liver dysfunction, and pediatric patients. The study variables included serum total cholesterol, TG, HDL, LDL, and hs-CRP, fasting blood glucose (FBG), liver enzymes and kidney function test.

Unhemolyzed serum samples were collected in 2 ml capped eppendorf tubes free of any metal contamination. All assays were performed within 48 h of serum separation. The collected samples were stored airtight at 2-8°C in the refrigerator.

Serum HDL, total cholesterol, and TG were analyzed in autoanalyzer Cobas 6000. Serum LDL was calculated using Friedwald's formula. Kruskal–Wallis H-test was used to compare the median values in the two groups followed by Mann–Whitney *U*-test to compare the median values between each group. The $P < 0.05$ was considered statistically significant. Pearson correlation coefficient was measured to find out any linear correlation between the parameters.

RESULTS

The study included that a total of 311 subjects of which 150 were diabetic patients and 161 were healthy non-diabetic age-matched controls. The mean age of the patients were 51.4 and control group were 45.96 years. The mean serum total cholesterol level in diabetic patients (227.84 ± 28.3 mg/dl) and it was significantly elevated as compared to controls (167.45 ± 21.63 mg/dl) ($P < 0.001$).

The mean serum TG levels in diabetic patients (211.34 ± 36.42 mg/dl) was elevated significantly ($P < 0.001$) as compared to that of the control group (98.13 ± 67.40 mg/dl). The mean serum HDL as well as LDL level in diabetic patients were 27.67 ± 11.11 and 158.43 ± 25.65 mg/dl, respectively, and the difference was statistically significant ($P < 0.001$) as compared to controls 51.74 ± 12.61 mg/dl and 117.30 ± 31.27 mg/dl, respectively, and represented in Table 1. Serum HDL concentration showed a significant decrease in the patient group. The correlation coefficient between hs-CRP with lipid profile and liver enzyme as well as FBG is represented in Table 2. hs-CRP showed a significant positive correlation with TG ($r = 0.673$) and LDL (0.705) among the cases and negative correlation with HDL (−0.819). The correlation between hs-CRP with HDL among diabetic patient is represented in Figure 1. The significant increase in serum concentration of LDL was observed in the diabetic patient when it is compared with healthy control ($P < 0.001$).

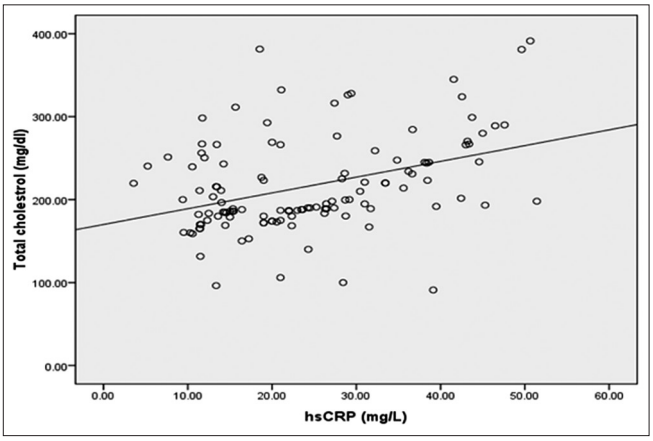

Figure 1: Correlation coefficient between high-sensitive C-reactive protein and total cholesterol in patients with diabetes mellitus

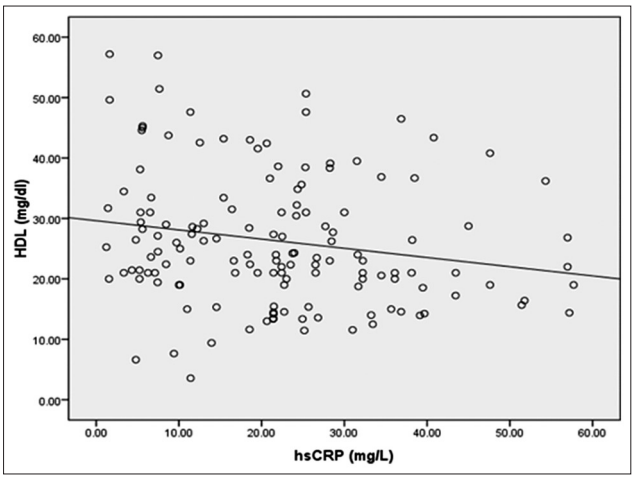

Figure 2: Correlation coefficient between high-sensitive C-reactive protein and high density lipoprotein in patients with diabetes mellitus

Table 1: Comparison of age, BMI and biochemical parameters of the diabetic patient and control group

	Case (*n*=150)	Control (*n*=161)	*P* value
Age (year)	51.4±9.6	45.96±4.3	<0.051
BMI	23.90±2.79	22.56±2.12	<0.021
Total cholesterol (mg/dl)	227.84±28.3	167.45±21.63	<0.001
TG (mg/dl)	211.34±36.42	98.13±67.40	<0.001
HDL (mg/dl)	27.67±11.11	51.74±12.61	<0.001
LDL (mg/dl)	158.43±25.65	117.30±31.27	<0.001
hs-CRP (mg/L)	29.49±5.90	2.18±1.10	<0.001
FBG (mg/dl)	176.64±61.08	89.24±18.29	<0.001
Creatinine (mg/dl)	0.75±0.58	0.65±0.79	<0.241
Urea (mg/dl) (10-40)	25.60±15.1	27.65±10.34	<0.038
Total protein (6-8 g/dl)	6.65±0.84	6.78±0.76	<0.58
Albumin (3.5-5.0 g/dl)	4.40±0.45	4.25±0.32	<0.51
Globulin (2.0-3.5 g/dl)	2.80±0.21	3.10±0.45	<0.061
AST (20-60 IU/L)	44.42±21.71	55.32±11.54	<0.02
ALT (11-45 IU/L)	74.43±9.45	34.20±21.08	<0.022
ALP (50-390 U/L)	109.34±34.76	268.54±55.28	<0.001

HDL: High density lipoprotein, LDL: Low density lipoprotein, hs-CRP: High sensitive C-reactive protein, FBG: Fasting blood glucose, BMI: Body mass index, ALP: Alkaline phosphatase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 2: The correlation coefficient between hs-CRP with lipid profile and FBG in diabetic patients and controls

Group	TG	HDL	LDL	FBG	ALP	AST	ALT
Case							
hs-CRP							
r	0.673	−0.819	0.705	0.207	0.167	0.120	0.208
p	0.0001	0.0001	0.0001	0.023	0.031	0.21	0.022
n	150	150	150	150	150	150	150
Control							
hs-CRP							
r	0.178	−0.718	0.154	0.074	0.051	0.182	0.341
p	0.071	0.0001	0.069	0.549	0.631	0.031	0.026
n	161	161	161	161	161	161	161

r: Correlation coefficient, p: Significance, n: Number of participant, hs-CRP: High sensitive C-reactive protein, FBG: Fasting blood glucose, HDL: High density lipoprotein, LDL: Low density lipoprotein, ALP: Alkaline phosphatase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

DISCUSSION

Our investigation provides evidence of a positive association between hs-CRP levels and triglycride, LDL, FBG, alkaline phosphatase (ALP), alanine aminotransferase, and aspartate aminotransferase among the patients with long-term diabetes. This association was independent of age, sex, body mass index (BMI) suggesting that elevated risk for future CVD might not be limited to increase lipid profile alone in this population. Similar observations have been made in previous studies.[21]

Consistent with earlier observations,[22] we found that diabetic patients had higher levels of hs-CRP compared with healthy control. Elevated hs-CRP levels frequently cluster with well-established risk factors of Type 2 diabetes such as obesity and insulin resistance.[23] Therefore, we extensively evaluated the effect of markers of these conditions on hs-CRP levels. In other studies, BMI was observed to be the dominant contributors of hs-CRP levels, but in our study, there was no significant difference in BMI between the patient and control group. These observations emphasis the involvement of inflammation as a result of dyslipidemia and hyperglycemia is a determinant factor in alteration of hs-CRP levels in this population hence monitoring of hs-CRP may provide a prognostic significance. Similar observations have been previously made in other studies.[24] The accumulating evidence suggests that hs-CRP may be associated with an increasing risk of future cardiovascular events in otherwise healthy individuals.[25] The magnitude of this association, however, seems to be strongly affected by the presence or absence of Type 2 diabetes. Here, we demonstrate that the increase of hs-CRP is significantly higher in Type 2 diabetes as compare to healthy non-diabetic individuals.

The advantages of this study include the systematic recruitment of subjects and controls and rigorous assessment of 14 biochemical parameters. Given the marked difference in the levels of biochemical parameters between case and control group, samples have been obtained from a well-defined population, representing a single ethnic group inhabiting urban locales. Nevertheless, our study is limited since it was a single-center study, which precludes conclusions regarding the geographical relationships between hs-CRP with dyslipidemia and diabetes. This study strongly warrants future investigations that probe the role of genetic variants and other environmental factors that influence the elevation of hs-CRP levels in this high-risk group.

CONCLUSION

Diabetes is known to influence lipid metabolism and are common in dyslipidemic patients. This study was conducted to find out how the alteration in lipid profile in diabetic patients could have an effect on extend of an inflammation in patients attending the Kasturba Hospital. Serum total cholesterol level in diabetic group was found to be elevated compared to non-diabetic group, and this elevation was statistically significant. Serum TG levels were elevated in diabetic group as compared to healthy control and elevation was statistically significant. Serum HDL levels were lower in diabetic group when it is compared with control group.

Serum LDL levels in patients was elevated when compared to control group. Among the liver, panel ALP showed lower concentration in diabetes group but it was in normal range. Diabetes mellitus has a profound effect on lipid metabolism and patient's lipid profile need to be monitored and managed frequently to prevent further complication such as CVD that may arise as a result of dyslipidemia.

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