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Original Article

Fasting Serum Lipid Profile and Its Association with Serum High Sensitivity C-Reactive Protein in Type II Diabetes Mellitus

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Abstract

Background: *Patients with type II diabetes mellitus frequently have altered lipid profiles. Detection of serum high sensitivity C-reactive protein is associated with cardiovascular events in type II DM as the presence of subclinical inflammation. The study was undertaken to observe the fasting serum lipid profile level and its association with serum hs-CRP in type II DM.*

Materials and methods: *A hospital-based observational study was carried out in the Outpatient Department of Endocrinology, Chittagong Medical College Hospital and Department of Biochemistry, Chittagong Medical College. By using non-probability consecutive sampling, a total of 176 participants were enrolled, with 126 type II DM and 50 in the control group. Plasma glucose and serum hs-CRP, fasting serum lipid profile was estimated.*

Results: *The mean serum hs-CRP level in patients with type II DM (9.1 ± 0.36 mg/L) was significantly (p 0.0001) elevated as compared to control (4.3 ± 0.09 mg/L). The result showed an increase in serum total cholesterol, serum triglycerides, serum HDL-C and serum LDL-C among the diabetic patients when compared with the healthy control group. Serum hs-CRP was significantly associated with serum TG and serum LDL-C in type II diabetics. Moreover, serum hs-CRP was found to have a significant positive correlation with serum LDL-C and serum TG. Only 77.78% of patients had increased LDL-C but altogether 85.71% of patients had increased serum hs-CRP levels.*

Conclusion: *According to the findings of this study,increased serum hs-CRP was well associated and positively correlated with components of the fasting lipid profile, indicating early identification of cardiovascular risk among type II diabetics.*

Key words: HDL-C; LDL-C; Serum hs-CRP; TC; TG; Type II DM.

INTRODUCTION

C-reactive protein is an acute phase protein which is generated shortly after an inflammatory stimulus from the liver cells.[1] Several cytokines like IL-1, IL-6 and TNF-α that are secreted locally in the area of the damaged tissue regulate the production of CRP.[1] Cardiovascular diseases, metabolic syndrome, Type II diabetes mellitus and obesity are associated with low grade of systemic inflammation and in these conditions, as inflammation is subclinical or low grade, hence CRP level does not increase at a greater amount as seen in severe systemic infections.[2] Rather its increment is small so that highly sensitive method is needed to estimate that small amount of CRP in blood, therefore hs-CRP estimation has been emerged in the field of medical sciences.[2] The possibility that CRP might have proatherogenic actions was first suggested in 1982 by the discovery of its specific binding to LDL-C and VLDL-C and was supported by its detection in atherosclerotic plaque.[3] In several recent clinical trials, measurement of hs-CRP as an inflammatory marker predicted risk of CVD independently of LDL-C.[4]

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Dyslipidemia in diabetes mellitus is often characterized by elevated fasting and postprandial levels of serum TG, TC, LDL-C and a significant decrease in the HDL cholesterol levels.[5]

Studies have shown levels of LDL-C, triglycerides and total cholesterol are associated with development and progression of atherosclerosis.[2]The transport vehicle of cholesterol and other lipids in body is Low Density Lipoprotein Cholesterol (LDL-C).[6] Once oxidized, LDL-C is called small dense LDL which can trigger a low grade local inflammation leading to cytokine release.[6] Phagocytosis of oxidized LDL by monocytes transforms them into foam cells with a lipid core which is the beginning of atherosclerotic plaque formation.[6] Moreover, the storage site of triglycerides is mainly adipose tissue which was earlier considered to be a passive organ is now known to express the pro-inflammatory cytokines like IL-6.[6] Excess loading of triglycerides in adipose tissue as seen in obesity can cause release of IL-6 by adipose tissue which can be involved in induction of low grade systemic inflammation as well as inflammation at blood vessels.[6] High serum level of High Density Lipoprotein Cholesterol (HDL-C) on the other hand is associated with reduced risk for development of atherosclerotic disease as it is involved in reverse cholesterol transport.[7] HDL-C particle are therefore believed to be anti-atherogenic and antagonize pathways of inflammation, thrombosis and oxidation of LDL-C.[7]

In light of the above considerations, measuring serum hs-CRP and fasting lipid profiles in type II diabetics may help in early diagnosis of cardiovascular disease. Therefore the aim of the study was to observe the fasting serum lipid profile level and its association with serum hs-CRP in patients with type II DM.

MATERIALS AND METHODS

This hospital-based observational study was carried out in the Outpatient Department of Endocrinology, Chittagong Medical College Hospital in collaboration with the Department of Biochemistry, Chittagong Medical College. The study was conducted from January 2016 to December 2016. The study was undertaken after approval by the Ethical Review Committee of Chittagong Medical College and the concerned departments.

Patients with acute infection/systemic diseases with known serum C-reactive protein levels ≥6 mg/L were excluded from the study. A total of 50 non-diabetic controls, aged in between 40-55 years with normal lipid profiles were selected for comparison. Based on OGTT, 126 patients with type DM aged between 40 to 64 years were selected by non-probability consecutive sampling. A questionnaire regarding the variables of interest was also noted.

Before the screening procedures, all the participants approved informed written consent. Upon arrival in the morning, a 5 ml of fasting venous blood sample was obtained from each participant under all aseptic precautions. Subjects were then allowed to drink 75 gm of oral glucose in 300 ml of water within 3 – 4 minutes. They were asked not to eat before taking the second sample. After 2 hours of oral glucose consumption, another 3 ml venous blood sample was taken. For the measurement of plasma glucose, venous blood samples were collected into the sodium flouride containing test tube. Serum was separated by centrifugation for 10 minutes at 3000 rpm.

Plasma glucose was determined by the glucose oxidase method using the multichannel autoanalyzer. Serum hs-CRP was measured by nephelometry in Siemens BN proSpec system. The concentration of fasting serum lipid profile was determined by an enzymatic kinetic method using an auto-analyzer.

All the data were processed and analyzed using Microsoft excel and IBM-SPSS v 22.0 for Windows. Statistical inference was based on a 95% confidence interval and a p-value ≤0.05 was considered statistically significant. Quantitative data were expressed as mean ± SEM. The student's t-test for the quantitative variable was used to measure the significance. Qualitative data were expressed in frequency and percentage. Chi-squared (χ^2) test is used to measure the significance of association between categorical variables. The Pearson correlation coefficient observed a correlation analysis between variables. In the relevant presentations, tables and diagrams were produced where necessary.

RESULTS

A total of 176 people took part in the study, with 126 of them having type II diabetes mellitus and 50 being healthy non-diabetic controls. Males and females were equally represented among the cases.

Table I Comparison of age and biochemical parameters of cases and control group

Variables	Case (n = 126) (Mean ± SEM)	Control (n = 50) (Mean ± SEM)	p Value*
Age (Years)	48.75 ± 0.56	45 ± 0.52	0.0001
FPG (mmol/L)	12.1 ± 0.33	5.25 ± 0.04	0.0001
2 HPG (mmol/L)	18.55 ± 0.41	6.51 ± 0.06	0.001
Serum hs-CRP (mg/L)	9.1 ± 0.36	4.3 ± 0.09	0.0001

p value* = ≤ 0.05 (Significant) ≥ 0.05 (Not Significant).

Table I shows that the mean age of the patients was 48.75 and of control group was 45 years. The mean serum hs-CRP level was 9.1 ± 0.36 mg/L in diabetic patients and it was significantly elevated as compared to controls (4.3 ± 0.09 mg/L).

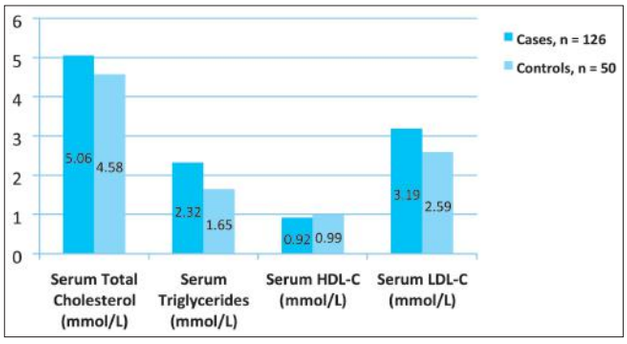

Figure 1 Comparison of fasting serum lipid profile among the cases (n = 126) and controls (n = 50)

The columns show that the mean serum total cholesterol level in diabetic patients was 5.06 ± 0.11 mmol/L and it was elevated in comparison to controls (4.58 ± 0.08 mmol/L). The mean serum TG concentration showed an increase in the patient group (2.32 ± 0.09 mmol/L) than controls (1.65 ± 0.02 mmol/L). The mean serum HDL-C as well as serum LDL-C level in diabetic patients were 0.92 ± 0.01 mmol/L and 3.19 ± 0.08 mmol/L, respectively when compared to controls 0.99 ± 0.01 mmol/L and 2.59 ± 0.02, respectively.

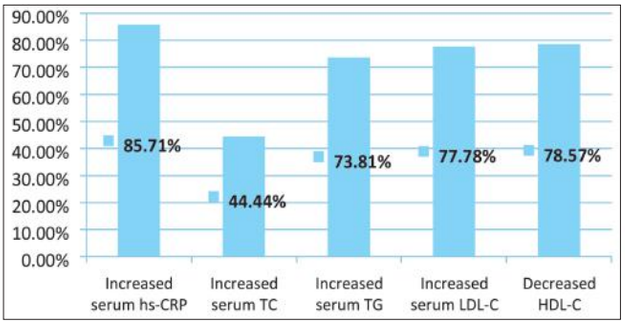

Figure 2 Prevalence of Biochemical parameters among the cases (n = 126)

The diagram shows that in type II DM, 85.71% of patients had increased serum hs-CRP levels. Hypercholestrolemia, hypertriglyceridemia and increased serum LDL-C were seen in 44.44%, 73.81% and 77.78% of cases respectively. Level of serum HDL-C was low in 78.57% of type II diabetics.

Table II Association of serum hs-CRP with fasting serum lipid profile in the cases (n =126)

Variables (mmol/L)	Increased Serum hs-CRP ≥ 6 mg/L	Normal Serum hs-CRP < 6 mg/L	Total Cases	χ^2 Value	p value*
Serum TC 5.17	58	12	70	1.05	NS
Serum TC 5.17	50	6	56		
Serum TG 1.69	21	12	33	17.8	< 0.00001
Serum TG 1.69	87	6	93		
Serum LDL-C 2.58	15	13	28	27.63	< 0.00001
Serum LDL- C 2.58	92	6	98		

p value* = ≤ 0.05 (Significant) ≥ 0.05 (Not Significant).

Table II shows that serum TG and LDL-C were significantly associated with increased serum hsCRP but serum TC was not associated with serum hs-CRP level in study subjects.

Table III Pearson's correlation coefficient among serum hs-CRP with fasting serum lipid profile in cases (n = 126)

Correlations between variables	Pearson's Correlation coefficient (r)	p value*
Serum hs-CRP with serum TC	+ 0.11	NS
Serum hs-CRP with serum TG	+ 0.62	< 0.00001
Serum hs-CRP with serum LDL-C	+ 0.69	< 0.00001
Serum hs-CRP with serum HDL-C	+ 0.1	NS

p value* = ≤ 0.05 (Significant) ≥ 0.05 (Not Significant).

Table III shows a strong and significant positive correlation between the serum hs-CRP with serum TG and serum LDL-C. A statistically non-significant and negligible positive correlation was seen between serum hs-CRP and serum TC and serum HDL-C.

DISCUSSION

Dyslipidemia is a well-known risk factor for cardiovascular diseases in type II diabetes mellitus. Typical dyslipidemia in a diabetic patient consists of high serum total cholesterol, triglycerides, LDL-C, and low HDL-C. Consistent with earlier observations, we found that patients with type II DM had elevated levels of serum hs-CRP (9.1 ± 0.36 mg/L) compared with healthy control (4.3 ± 0.09 mg/L).[8] In Table I, we demonstrated that the increase of hs-CRP was significantly (p 0.0001) higher in type II diabetes mellitus as compared to healthy non-diabetic individuals. Li Jin Pu and colleagues reported that increased levels of hsCRP < 10 mg/L was associated with a 2.593 fold increased risk for coronary artery disease in patients of type II DM and also found increased hs-CRP levels were associated with other indicators of DM related cardiovascular risk parameters.[9] The high serum hs-CRP concentration in diabetes reported in this study and by other authors could be due to an increase in adipose tissue mass that enhances cytokines production by adipocytes, cytokines production is known to stimulate the hepatic synthesis of CRP.[10]

Low-grade inflammation plays an important role not only in the pathogenesis of diabetes mellitus but also has an association with dyslipidemia in diabetics.[1] Elevated mean serum total cholesterol, triglycerides, LDL-C, and lower HDL-C levels have been described in type II diabetes when compared with healthy non-diabetics.[11] This conclusion is consistent with our findings, which indicated that individuals with type II DM had higher mean levels of serum total cholesterol, triglycerides, LDL-C as well as lower HDL-C (Figure 1). The abnormal high concentrations of serum lipids in DM are mainly due to an increase in the mobilization of free fatty acids from fat depots since insulin inhibits the hormone-sensitive lipase.[12] Excess fatty acids in the serum of diabetics are converted into phospholipids and cholesterol in the liver.[12] The possible mechanism responsible for hypertriglyceridemia may be due to increased hepatic secretion of very-low-density lipoprotein and delayed clearance of triglyceride-rich lipoproteins, which is predominantly due to increased levels of substrate for triglycerides production, glucose and free fatty acids.[13]

Our investigation provides evidence of a statistically positive association between serum hs-CRP with serum triglycerides and serum LDL-C among the patients with type II diabetes mellitus (Table II). This finding is in accordance with a study done by Graziella et al, involving 3249 patients with type II DM.[14] They found out that with respect to people with CRP

values in the lowest tertile (< 1.6 mg/L), those with CRP values in the highest tertile (> 4.4 mg/L) had significantly higher values of TC, LDL, TG and significantly lower values of HDL.[14] In addition, this study showed a strong and significant positive correlation between serum hs-CRP Levels with serum TG ($p < 0.00001$, $r = +0.62$) and serum LDL-C (p 0.00001, $r = +0.69$) in Table III. A statistically non-significant and weak correlation were seen between serum hs-CRP levels and serum HDL-C ($r = +0.1$) and serum TC ($r = +0.11$). These findings are exactly in agreement with findings of a comparative study done by Palvasha et al where they have found similar correlations of hs-CRP with parameters of lipid profile.[15] Similar findings are shown by studies done by Sung et al. and Rhee et al.[16,17]

High CRP, dyslipidemia, and LDL-C are reported to be the main risk factors for the chronic complications of T2DM.[10] C-reactive protein mRNA and protein have been found to be abundantly present in atherosclerotic lesions.[18] There is convincing experimental evidence linking C-reactive protein to plaque disruption and the onset of cardiovascular events.[18] It was illustrated in Figure II that only 77.78% of patients were categorized as having increased cardiovascular risk according to high LDL-C levels but altogether 85.71% of patients had increased cardiovascular risk according to serum hs-CRP levels. CRP has been found to be a stronger predictor of heart attack and stroke than LDL-C and also persons having high CRP and Low LDL have a higher CVS risk than those having low CRP and high LDL.[19] These observations emphasize the involvement of inflammation as a result of dyslipidemia and hyperglycemia is a determinant factor in the alteration of hs-CRP levels in this population, hence monitoring of serum hs-CRP may provide a prognostic significance.[20] With all this understanding in mind, if we assess serum hs-CRP regularly in type II DM, we will be able to anticipate and postpone CVS complications especially in those patients who have a normal level of LDL-C and are believed to have low CVS risk.

CONCLUSION

Diabetes mellitus has a significant impact on lipid metabolism, and patients' lipid profiles must be closely monitored and controlled to avoid future micro and macrovascular complications. The goal of this study was to observe the fasting serum lipid profile level and its relationship with serum hs-CRP in individuals with type II diabetes mellitus. Despite the fact that serum hs-CRP is not regularly measured in type II DM patients, past research and the findings of our study suggest that it may be helpful to do so together with lipid profiles for early prediction of cardiovascular complications, and intervene accordingly to prevent them.

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DISCLOSURE

All the authors declared no competing interest.

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