



EVALUATION OF ASSOCIATION BETWEEN SERUM HS-CRP AND LIPID PROFILE IN TYPE 2 DIABETES MELLITUS

Biochemistry

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ABSTRACT

High sensitive C-reactive protein (hs-CRP) is an established marker of low grade systemic inflammation. A chronic low-grade inflammatory condition has been proposed to underline increased risk for atherosclerotic disease, including renal dysfunction and cardiovascular disease suggesting a possible link between the high incidence of macrovascular complications and diabetes. Insulin resistance results in high concentrations of serum lipids in diabetics due to increased mobilization of free fatty acids from fat depots. Because serum hs-CRP and serum lipid profile reflect closely related component of the same disease process, a strong relationship between these variables may be anticipated. We selected 50 patients of Type-2 diabetes mellitus and 50 normal healthy individuals to evaluate this association. Serum estimations showed a significant increase ($p < 0.001$) in hs-CRP, Total cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein (LDL) and Very Low Density Lipoprotein (VLDL) in diabetics when compared to controls. In contrast there was significant decrease ($p < 0.001$) in HDL-C in diabetics. The statistical analysis depicted a non significant correlation between serum hs-CRP and total cholesterol ($p = 0.909$, $r = -0.017$), serum triglyceride ($p = 0.294$, $r = 0.151$) and serum HDL ($p = 0.724$, $r = -0.051$) in type 2 diabetic patients. This finding may therefore, suggest that hs-CRP act as an independent marker for cardiovascular risk factor.

KEYWORDS

INTRODUCTION:

Type 2 diabetes mellitus is now recognized as an inflammatory condition associated with insulin resistance and abnormal endothelial vascular reactivity.^[1] Circulating C-reactive protein (CRP) is a very sensitive marker of low grade systemic inflammation and it has been suggested that this acute-phase protein impairs vascular endothelial function.^[2] It is reported that high serum levels of C-reactive protein is a novel cardiovascular risk factor that impairs endothelial function.^[3] The contribution of inflammation to morbidity in the closely related conditions of cardiovascular disease, obesity, the metabolic syndrome, and type 2 diabetes has been the focus of extensive research and intense speculation over the past decade.^[4] The abnormal high concentrations of serum lipids in diabetics is due, mainly to increase in the mobilization of free fatty acids from fat depots, since insulin inhibits the hormone sensitive lipase.^[5]

Because serum hs-CRP and lipid profile seem to be closely related component of the same disease process, a strong relationship between these variables may be anticipated.

MATERIALS AND METHODS:

The present study was a case control prospective study undertaken in the Department of Biochemistry in collaboration with Department of Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. A total of 100 subjects willing to participate in the study with informed consent were included in the study. 50 patients of poorly controlled Type 2 Non Insulin Dependent Diabetes Mellitus (NIDDM) between 40-65 yrs of age, of either sex whose HbA1c was $> 7\%$ and 50 healthy, age and sex matched controls from the same population but without any disease and without family history of DM.

Exclusion criteria:

Patients suffering from type-1 DM, patients with acute complications of DM like Diabetic ketoacidosis, history of acute infections, other ailments like gross congestive heart failure, tuberculosis, gout, rheumatoid arthritis and skeletal muscle injury, serum creatinine $> 1.5\text{mg/dl}$, renal failure and those giving positive dip stick test for proteinuria were not included in the study.

The patients and controls were screened for fasting blood sugar (FBS), lipid profile and hs-CRP and the values were compared with that of normal healthy subjects. Hs-CRP was estimated by Quantia –CRP (M A Mendall et al 1996)^[6], a turbidimetric immunoassay. Complete Lipid profile included the following estimations-a. Total Serum Cholesterol was estimated by CHOD-PAP Method (Allain C.C. et al 1974)^[7] b. Serum Triglyceride was estimated by GPO-Trinder Method. (McGowan MW et al 1983)^[8] c. Serum High Density Cholesterol (HDL-C) was estimated by Phosphotungstic Acid Method (Gordon T. Et al 1977)^[9] d. Low Density Lipoprotein-Cholesterol (LDL-C) and Very Low Density Lipoprotein-Cholesterol (VLDL-C) by Freidwald equation (Freidwald equation W.T.1974) Serum creatinine was estimated by jaffes kinetic method (Watchel et al 1995)^[10] and its calibrator has been standardized to ID-MS.

RESULT:

There was no significant effect of age ($p > 0.05$) and sex distribution ($p > 0.05$) in the study. Table 1 shows that FBS, HbA1c, total cholesterol, triglyceride and hs-CRP levels were significantly high while HDL-C were significantly low in cases as compared to the controls. Whereas no significant difference was found in the values of creatinine and eGFR in cases when compared to controls.

Table 1 : Comparison of various parameters estimated in patients and controls

	Cases (Mean±SD)	Controls (Mean±SD)	p value
Fasting blood sugar (mg/dl)	194.38 ± 53.60	100.30 ± 12.46	< 0.001*
HbA1c (%)	8.758 ± 1.83	5.148 ± 0.51	< 0.001*
Total cholesterol (mg/dl)	223.20 ± 45.41	174.46 ± 33.90	< 0.001*
Triglycerides(mg/dl)	224.70 ± 76.77	161.14 ± 32.42	< 0.001*
HDL-C(mg/dl)	40.48 ± 8.18	55.00 ± 12.04	< 0.001*
Albumin in urine (mg/L)	35.36 ± 15.36	18.28 ± 1.47	< 0.001*
Serum creatinine (mg/dl)	1.09 ± 0.257	1.05 ± 0.318	0.502***
eGFR (ml/mim/1.73 m2)	68.28 ± 24.83	68.54 ± 31.87	0.201***
hs-CRP (mg/dl)	1.29 ± 1.79	0.57 ± 0.09	< 0.005**

* $P < 0.001$ = highly significant

** $p < 0.05$ -significant

*** $p > 0.05$ - non significant

Table 2 shows that FBS and HbA1c had a highly significant correlation with hs-CRP in type 2 diabetics. Total cholesterol, triglyceride and HDL-C had a non-significant correlation with hs-CRP in type 2 diabetic patients.

Table 2: Correlation of hs-CRP in type 2 Diabetes Mellitus with FBS, HbA1c and lipid profile

	hs -CRP (mg/dl)	
	r	P
Fasting blood sugar (mg/dl)	0.404	0.404**
HbA1c (%)	0.432	0.432**
Total cholesterol (mg/dl)	0.017	0.017***
Triglycerides(mg/dl)	0.151	0.151***
HDL-C(mg/dl)	-0.051	-0.051***

*P<.001 =highly significant

**p<0.05-significant

***p>0.05- non significant

DISCUSSION:

Type 2 DM is now recognized as an inflammatory condition associated with insulin resistance and abnormal endothelial vascular reactivity. It is an increasingly prevalent risk for atherosclerotic micro and macro vascular diseases. There is a strong and independent association between even slightly elevated concentrations of CRP and cardiovascular events in initially healthy subjects and in patients with manifest atherosclerosis.^[11] In our study the difference between the mean \pm SD values for serum CRP in normal individuals (0.57 ± 0.09 mg/dl) and patients (1.29 ± 1.79 mg/dl) was highly significant ($t = 2.88$, $p < 0.005$) with patient group having significantly higher levels than the normal individuals. (Table 1) It has recently been postulated that Type-2 diabetes mellitus may represent a disease of innate immune system. Thus, the positive association between CRP and type 2 diabetes may simply reflect underlying endothelial dysfunction and subclinical atherosclerosis.^[12] C- reactive protein (CRP) is one of the most sensitive acute-phase reactants in humans, its elevated serum levels are a precise index of inflammatory activity and have been related with coronary heart disease, dyslipidemia and obesity supporting the hypothesis that inflammation plays a role in the development of metabolic syndrome and diabetes.^[13,14] It is reported that high serum levels of C- reactive protein is a novel cardiovascular risk factor that impairs endothelial function.^[15] Measurement of this acute-phase reactant is being routinely used to detect and monitor inflammatory changes and interventions that reduce CRP levels have been found to decrease the occurrence of coronary event.^[16]

In our study Plasma Lipid profile showed significant increase ($p < 0.001$) in Total cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein (LDL) and Very Low Density Lipoprotein (VLDL) in diabetics when compared to controls. In contrast there was significant decrease ($p < 0.001$) in HDL-C in diabetics. (Tables 1) It is known that cholesterol, triglycerides, LDL and VLDL are elevated in diabetic patients. The abnormal high concentrations of serum lipids in diabetics is due, mainly to increase in the mobilization of free fatty acids from fat depots, since insulin inhibits the hormone sensitive lipase. Excess fatty acids in serum of diabetics are converted into phospholipids and cholesterol in liver. These two substances along with excess triglycerides formed at the same time in liver may be discharged into blood in the form of lipoproteins.^[15] These results were supported by studies of M. M. Yassin et al (2010)^[17] and Dayanand C D et al (2010)^[18]. In our study (TABLE 2) we found a non- significant positive correlation of serum hs-CRP with total cholesterol and triglyceride while a non-significant negative correlation with HDL which was supported by the study of Martin B et al (1998)^[19] which also showed the similar results. It can be argued that hs-CRP may be an independent risk factor for resistance in the prediction of cardiovascular events. Chen Chung Fu et al (2008)^[21] also had same results as our study. D A Muttur et al (2010)^[20] showed non significant positive correlation between hs-CRP and TC, and non significant negative correlation with HDL but highly significant positive correlation between hs-CRP and triglyceride was seen. It has recently been postulated that Type-2 diabetes mellitus may represent a disease of innate immune system. Thus, the positive association between CRP and type 2 diabetes may simply reflect underlying endothelial dysfunction and subclinical atherosclerosis.^[12] In our study no significant correlation was observed between hs-CRP and lipids profile which may therefore suggest that hs-CRP act as an independent marker for cardiovascular risk factor. This can be further justified by CRP being a very sensitive and an early marker of inflammation.

CONCLUSION:

In type 2 diabetic patients, hs-CRP is non-significantly associated with elevated serum total cholesterol, triglyceride and decreased levels of HDL. Thus it can be argued that hs-CRP may be an independent risk factor for resistance in the prediction of cardiovascular events. This study may also highlight the importance of proper glycemic control in arresting the progression of inflammation.

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