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Biochemistry

CORRELATION OF SERUM C-REACTIVE PROTEIN WITH GLYCEMIC STATUS AND LIPID PROFILE IN TYPE 2 DIABETIC SUBJECTS

Shivarajashankara YM Department of Biochemistry, KVG Medical College, Sullia, DK District, Karnataka, India.

Anil S Baipadithaya Department of Obstetrics and Gynecology, KVG Medical College, Sullia, DK District, Karnataka, India.

Shivashankara A R* Department of Biochemistry, Father Muller Medical College, Mangalore, Karnataka, India. *Corresponding Author

ABSTRACT Growing evidence suggests that inflammation plays the key role in the pathogenesis of type 2 diabetes including obesity-related insulin resistance, impaired insulin secretion, and diabetes-related vascular complications. Previous studies have shown that C-reactive protein (CRP), the acute phase reactant and the marker of inflammation is elevated in patients with impaired glucose tolerance and diabetes mellitus. The present study has made an attempt to assess the correlation of serum CRP level with multiple biochemical parameters viz., plasma glucose, glycated hemoglobin, triglycerides, LDL-cholesterol and HDL-cholesterol in type 2 diabetic subjects. Type 2 diabetic subjects (n=102) and healthy controls (n-=114) were the subjects of the study. Levels of fasting plasma glucose (FPG), post-prandial plasma glucose (PPPG), glycated hemoglobin (HbA1c), serum CRP and serum lipids were estimated. Type 2 diabetic patients showed significantly higher levels of FPG, PPPG, HbA1c, total cholesterol, triglycerides, LDL-cholesterol and lower levels of HDL- cholesterol when compared to controls. Serum CRP level had significant positive correlation with FPG, PPPG and HbA1c%. There was no significant correlation of CRP level with serum lipid parameters. The present study demonstrated significant correlation of serum CRP with glycemic status, indicating role of inflammatory marker in diagnosis and management of inflammatory complications in type 2 diabetes mellitus.

KEYWORDS : C-Reactive Protein, Diabetes Mellitus, Glycemic Status, Plasma Glucose.

INTRODUCTION

Diabetes mellitus is a chronic, progressive disease and leads to complications in many parts of the body and can increase the overall risk of dying prematurely. The number of people suffering from type 2 diabetes is constantly increasing up to the worldwide epidemic scale [1]. As per the Global Report on Diabetes by the World Health Organization, globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population [1].

Growing evidence suggests that inflammation plays the key role in the pathogenesis of type 2 diabetes including obesity-related insulin resistance, impaired insulin secretion, and diabetes-related vascular complications [2]. Previous studies have shown that C-reactive protein (CRP), the acute phase reactant and the marker of inflammation is elevated in patients with impaired glucose tolerance and diabetes mellitus [3,4]. Few studies have shown that increased CRP levels are an independent risk factor for future diabetes [5,6]. There are reports of positive correlation of serum CRP level with dyslipidemia in type 2 diabetes mellitus [7]. Serum hs-CRP level has been reported to show significant positive correlation with serum triglyceride level and in type 1 diabetic patients [8].

There is paucity of studies especially with the Indian population, on correlation of serum CRP level with glycemic status and serum lipids. The present study has made an attempt to assess the correlation of serum CRP level with multiple biochemical parameters viz., plasma glucose, glycated hemoglobin, triglycerides, LDL-cholesterol and HDL-cholesterol in type 2 diabetic subjects.

MATERIALS AND METHODS

Study Design and Duration :

The present cross sectional study was carried out in the Medical College Hospital from July 2017 to June 2018. The protocol was approved by the Institutional Ethics Committee.

Source of Data :

The study subjects were the type 2 diabetic patients visiting the outpatient department of the hospital (Group-1) and age- and sex-matched healthy controls (Group-2). The age group of the subjects was 30-60 years. Subjects with liver diseases, renal disorders, infections, inflammation, and subjects taking anti-inflammatory and lipid-lowering drugs, smokers and alcoholics were excluded from the study. The diabetic subjects (group-1) were without any complications.

The sample size was calculated to be 102 for group-1 and 114 for group-2.

Voluntary informed consent was obtained from all the study subjects.

Sample Collection:

Fasting blood samples were collected from diabetic patients and controls taking aseptic precautions.

Assays:

Level of glucose was estimated in the plasma by glucose oxidase-peroxidase method [9]. Level of glycated hemoglobin (HbA1c) was measured in the whole blood by latex-enhanced immunotur bidometric method [10]. Serum CRP level was estimated by nephelometric method using the Mispa-1 nephelometer from Agappe diagnostics. The method was a latex-enhanced immunoassay in which CRP binds to specific antibody which has been absorbed to latex particles, resulting in agglutination. The agglutination is directly proportional to the concentration of CRP in the serum [11].

Total cholesterol level in the serum was estimated by the enzymatic cholesterol oxidase-peroxidase method[12]. Level of LDL-cholesterol was assayed by selective solubilization of LDL followed enzymatic determination of cholesterol[13]. Serum HDL-cholesterol was estimated by selective inhibition of other cholesterol sources by polyanions; and then determination of cholesterol content of HDL by enzymatic method[14]. Serum triglyceride level was assayed by the enzymatic method using glycerokinase, glycerol 3-phosphate oxidase and peroxidase[15].

Statistical analysis:

The data were expressed as mean ± SE. The statistical analysis was done using IBM SPSS version-16. The significance of difference between the Controls and Diabetics was assessed by the Student's 't' test. The correlation of serum CRP with other biochemical parameters was evaluated by the Karl-Pearson's Correlation Analysis.

RESULTS

The results of our study are presented in tables 1 and 2, and figures 1 to 3. The mean age of controls was 49.5 ± 11.6 years, and the mean age of

diabetic subjects was 51 ± 7 years.

The levels of fasting and post-prandial plasma glucose, whole blood glycated hemoglobin (HbA1c), triglycerides, total cholesterol, LDL-cholesterol were significantly higher and HDL-cholesterol level was significantly lower in diabetic patients, in comparison to healthy controls. The level of CRP in the serum was significantly higher in diabetic patients when compared to healthy controls. All the results were highly significant (P value = 0.000). (Table1).

As presented in Table 2 and figures 1 to 3, the Karl Pearson correlation analysis observed significant positive correlation of serum CRP with Fasting plasma glucose (r= 0.828; P =0.000), post-prandial plasma glucose (r= 0.426; P =0.000)and HbA1c (r= 0.923; P =0.000). There was no significant correlation with CRP with serum levels of triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol (Table 2). ‘

Table1. Biochemical Parameters in the Blood Samples of Normal Controls and Type 2 Diabetic Patients (Values are Mean ± SE)

	Diabetic (Group-1; n= 102)	Controls (Group-2; n= 114)	P Value and Significance (2-tailed)
Plasma Glucose, Fasting (mg/dl)	179. 7 ± 4.3	90.3 ± 0.56	0.000; Highly Significant
Plasma Glucose, Post-Prandial (mg/dl)	274.9 ± 4.4	114.9 ± 0.99	0.000; Highly Significant
Glycated Hemoglobin, HbA1c (%)	9.1 ± 0.14	4.8 ±0.05	0.000; Highly Significant
Serum Triglycerides (mg/dl)	185.5 ± 6.2	77.2 ± 1.6	0.000; Highly Significant
Serum Total Cholesterol (mg/dl)	250.6 ± 3.6	172.2 ± 2.1	0.000; Highly Significant
Serum LDL Cholesterol (mg/dl)	183.5 ± 3.6	110.4 ± 2.1	0.000; Highly Significant
Serum HDL Cholesterol (mg/dl)	29.9. ± 0.5	43.3 ± 0.6	0.000; Highly Significant
Serum CRP (mg/L)	18.8 ± 0.6	3.2 ± 0.1	0.000; Highly Significant

Table 2.Correlation of Serum CRP with Other Biochemical Parameters in Diabetic Patients.

Correlation	r Value	P value	Significance
CRP – Fasting Plasma Glucose	0.828	0.000	Highly Significant
CRP- Post-Prandial Plasma Glucose	0.426	0.000	Highly Significant
CRP- HbA1c	0.923	0.000	Highly Significant
CRP- Serum Triglycerides	0.094	0.348	Not Significant
CRP- Serum Total Cholesterol	0.143	0.152	Not Significant
CRP- Serum LDL Cholesterol	0.185	0.063	Not Significant
CRP- Serum HDL Cholesterol	0.004	0.969	Not Significant

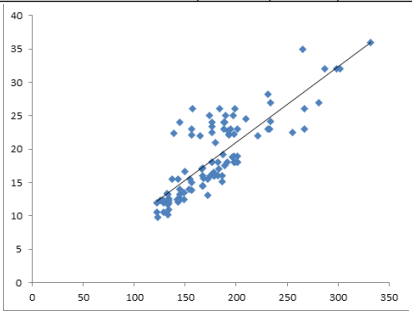

Figure1. Correlation between Fasting Plasma Glucose and Serum CRP in type 2 Diabetic Patients (X axis: Fasting Plasma Glucose in mg/dl; Y axis: CRP in mg/L).

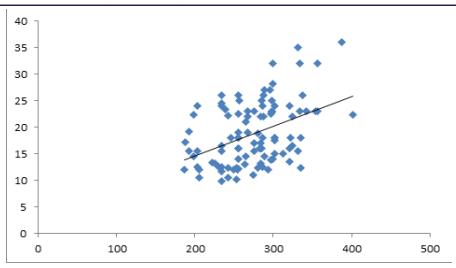

Figure2. Correlation Between Post-Prandial Plasma Glucose and Serum CRP in type 2 Diabetic Patients (X axis: Post-Prandial Plasma Glucose in mg/dl; Y axis: CRP in mg/L).

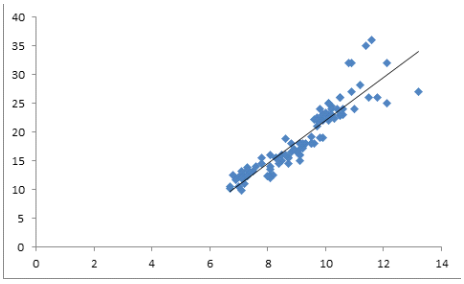

Figure3. Correlation Between Blood HbA1c% and Serum CRP in type 2 Diabetic Patients (X axis: Blood HbA1c% ; Y axis: CRP in mg/L).

DISCUSSION

In the present study, we made an attempt to assess the level of CRP in type 2 diabetes, and its correlation with glycemic status and lipid profile. We observed significantly higher serum CRP in diabetic subjects in comparison to healthy controls, and significant positive correlation of CRP level with fasting plasma glucose, post-prandial plasma glucose and glycated hemoglobin. Though the lipid profile of diabetic patients was significantly different from that of controls, CRP did not show any significant correlation with lipid profile parameters.

C-reactive protein is a marker of systemic inflammation, has been reported to be increased in type 2 diabetic patients. Higher CRP levels have been linked to later development of diabetes mellitus. In the present study, CRP levels showed significant positive correlation with fasting plasma glucose, post-prandial plasma glucose and glycated hemoglobin levels in type 2 diabetic patients. Previously, Abdrabo reported significant positive correlation of serum high-sensitive CRP (hs-CRP) with fasting glucose and HbA1c [16]. Chronic hyperglycemia has been shown to promote inflammation by release of pro inflammatory cytokines from adipocytes, and acute phase reactants from liver [17]. In a study by King and co - workers, type 2 diabetic patients who had elevated HbA1c (>/= 9.0%) had a significantly higher percent of elevated CRP than people with low HbA1c (</= 7.0%) [18]. Another study reported bi-directional correlation among CRP level and HbA1c% in type 2 diabetic adults, and reduction of CRP level with reduction in HbA1c% [19]. Roopakala et al. observed significant positive correlation of serum hs-CRP level with HbA1c% in patients with diabetic nephropathy [20]. In type 2 diabetic patients with or without CHD, serumhs-CRP level showed significant positive correlation with fasting plasma glucose, HbA1c% and serum insulin levels [21]. These studies along with the findings of our study suggest significant role for CRP in pathogenesis of type 2 diabetes and its complications.

The present study observed significant alterations in serum lipids. Serum levels of triglycerides, total cholesterol and LDL cholesterol were significantly higher, and serum HDL-cholesterol level was significantly lower in diabetic subjects than controls. However, there was no significant correlation of plasma glucose, HbA1c% or CRP with lipid profile parameters. A cross sectional study with Sudanese diabetic population, observed significant positive correlation of CRP level with LDL-cholesterol [7]. Serum hs-CRP level has been reported to show significant positive correlation with serum triglyceride level and in type 1 diabetic patients [8]. Our study did not observe such a correlation.

CONCLUSIONS

The present study demonstrated significant correlation of serum CRP with glycemic status, indicating role of inflammatory marker in

diagnosis and management of inflammatory complications in type 2 diabetes mellitus. Future studies with larger sample size are required to assess utility of serum CRP as a biomarker of diabetic complications.

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