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Original Research Article

A Hospital-Based Study Determining the Relation between Various Biochemical Parameters in Individuals with Type 2 Diabetes Mellitus

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to determine the relation between HbA1C, Lipid profile and CRP in individuals with type 2 diabetes mellitus.

Material & Methods: This was a hospital-based prospective study comprised of 100 patients with type 2 diabetes mellitus reporting to department of General Medicine for the duration of 12 months.

Results: In this study of 100 patients, 70 patients were males, and 20 were females with mean CRP levels of 1.18±1.22 and 1.14±0.98, respectively. There was no significant difference between male and female patients ($p>0.05$). There was no significance between different age groups in this study ($p>0.05$). There was no significant correlation between CRP and BMI in this study. FBS and HbA1C were directly correlated. PPBS showed a direct correlation with both HbA1C and CRP in this study. There was a significant positive correlation between CRP and total cholesterol ($p<0.05$). There was no significant correlation between CRP and LDL cholesterol ($p>0.05$). There was a negative correlation between HDL cholesterol and CRP. There was significant positive correlation between CRP and triglyceride levels ($p<0.05$).

Conclusion: In this study of 100 patients with T2DM, it was found that CRP is significantly correlated with HbA1C level. A positive correlation was found between serum CRP and HbA1C in the initial group and in the follow-up patients, showing that CRP levels lowers with better glycemic control and correlates with dyslipidaemia profile

Keywords: C-reactive protein, Glycemic control, Hemoglobin A1c, Type 2 diabetes mellitus.

Introduction

Diabetes mellitus is a metabolic disorder characterised by the defects in insulin secretion or action; chronic hyperglycaemia can lead to microvascular and macrovascular complications if the blood sugars are not under optimal control. The glycaemic control is assessed by the measurement of glycated haemoglobin (HbA1c) which has its own advantages and disadvantages. [1] till date HbA1c is the widely used tool to assess the glycaemic status. Endothelial dysfunction, subclinical inflammation, and impaired fibrinolysis might contribute to the progression of macrovascular as well as microvascular complications.

Factors associated with an increase in mortality rates among those with diabetes mellitus include male gender, longer duration of diabetes, insulin use. [2] It is perceived that chronic low grade inflammation might potentially be a cause underlying the etiology and manifestations of T2DM. [3] T2DM is associated with increased blood concentration of markers of acute-phase response including C-reactive protein and cortisol, the main cytokine mediator, interleukin. [4,5] These cytokines promote the release of acute-phase proteins, which are atherosclerotic risk factors. Cytokines act on liver to produce characteristic dyslipidemia in type 2 diabetes mellitus. TNF-α is a major factor in causing insulin resistance, and long-term hypersecretion of cytokines may impair beta-cell insulin secretion. [5]

Cardiovascular morbidity and mortality is high in the majority of patients with diabetes, in particular with Type 2 diabetes mellitus (T2DM), who are at a 2- to 4- fold higher risk of cardiovascular mortality compared with non-diabetic subjects. [6] Up to 90% of CVD may be preventable if established risk factors are avoided. [3] Patients

with T2DM often exhibit an atherogenic lipid profile, characterized by high plasma levels of triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), but low level of high-density lipoprotein cholesterol (HDL-C) [7] as well as increased free fatty acids, increased small dense LDL (sdLDL), which greatly increases their risk for CVD via the process of atherosclerosis. Worsening of glycaemic control deteriorates lipid and lipoprotein abnormalities as a growing body of evidence suggests that dyslipidaemia is secondary to insulin resistance or factors closely related to insulin resistance, such as adiposity. [8]

The combination of hyperglycaemia and dyslipidaemia produces an enhanced atherogenic environment within the circulation which accelerate the progression to atherosclerosis. [9] C-reactive protein and glycated hemoglobin (HbA1C) are established risk factors for the development of cardiovascular diseases. CRP levels were found to be related to insulin resistance, obesity, endothelial dysfunction in a cross-sectional study done by Yudkin et al. [11] It is known to play a direct role in atherosclerosis and thrombosis. [12,13] CRP was also found to be predictive of future cardiovascular events in patients with the metabolic syndrome and to add prognostic information to the ATPIII definition of the metabolic syndrome. [14]

CRP might represent a novel biomarker of vascular risk and CRP is a possible risk factor for the development of type 2 diabetes mellitus. Hence this study was undertaken to determine the relation between HbA1C, Lipid profile and CRP in individuals with type 2 diabetes mellitus. [10]

Material & Methods

This was a hospital-based prospective study comprised of 100 patients with type 2 diabetes mellitus reporting to Department of General Medicine, Jannayak Karpuri Thakur Medical College and Hospital Madhepura, Bihar, India for the duration of 12 months.

Inclusion Criteria

- Patients above 30 years with fasting venous blood glucose value equal or more than 100 mg/dl and postprandial glucose >140 mg/dl were included in the study.

Exclusion Criteria

- Patients on statins, thiazolidinediones (TZDs), and anti-inflammatory drugs that are known to reduce CRP levels.
- Patients with heart failure, acute febrile illness, renal, hepatic and malignant disorders, chronic illnesses, asymptomatic infections, type1diabetes, gestational diabetes, alcoholism, pancreatitis, other endocrinal disorders, those on diuretic therapy, amino-glycosides and smokers were also excluded from the study.

Methodology

Informed consent was taken from the patients. Detailed history, physical examination, which includes height, weight, body mass index (kg/m2), were measured. Resting pulse rate, blood pressure, body temperature was recorded. FBS and PPBS, CRP (immunoturbidimetric method), and HbA1C (ion exchange chromatography using HPLC) lipid profile samples were drawn at entry and at subsequent follow-up with a minimum gap of 3 months. Patients were put on OHA/insulin for control of blood sugar along with dietary control and exercise.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages and means.

Results

Table 1: CRP in males and females

CRP	Number	Mean
Males	70	1.2420
Females	20	0.9926
Total	50	1.1730

In this study of 100 patients, 70 patients were males, and 20 were females with mean CRP levels of 1.18±1.22 and 1.14±0.98, respectively. There was no significant difference between male and female patients ($p>0.05$).

Table 2: Age distribution and CRP and HbA1C

Age	Number	HbA1C	CRP
30-40	8	10.38	1.4
40-50	25	10.52	1.7
50-60	45	9.21	1.3
60-70	20	9.24	0.7
>70	2	8.00	0.0

In this study of 100 patients, HbA1C and CRP were correlated with age. Patients between age 30-40 years were 8 with mean HbA1C and CRP of 10.38 and 1.4 respectively. Patients between age 40-50 years were 25 with mean HbA1C and CRP of 10.52 and 1.7 respectively. Patients between age 50-60 years were 45 with mean HbA1C and CRP of 9.21 and 1.3 respectively. Patients between 60-70 years were 20 with mean HbA1C and CRP of 9.24 and 0.7 respectively. Patients above 70 were 2 with mean HbA1C and CRP of 8.0 and 0, respectively. There was no significance between different age groups in this study ($p>0.05$).

Table 3: Association of CRP and BMI and FBS with HbA1C

BMI	Number	CRP
<18	2	1.22
18-23	38	1.14
23-25	42	1.22
25-30	16	1.52
>30	2	1.22
FBS	**Number**	**HbA1C**
<100	2	8.00
100-200	44	8.32
200-300	34	10.52
>300	20	11.44

In this study of 100 patients, patients with BMI <18 was 2 with mean CRP of 1.22, BMI between 18 -23 were 38 with mean CRP of 1.14, BMI between 23-25 were 42 with mean CRP of 1.22, BMI 25-30 were 16 with mean CRP of 1.52, with BMI>30 was 2 with mean CRP of 1.22. There was no significant correlation between CRP and BMI in this study. In this study of 100 patients, FBS was correlated to HbA1C in different groups. Patients with FBS of 100 was 2 with HbA1C were 8.0, between 100-200 were 44, between 200-300 were 34, >300 were 10 had HbA1C of 8.32, 10.52, 11.34 respectively. FBS and HbA1C were directly correlated.

Table 4: PPBS with HbA1C and CRP

PPBS	Number	HbA1C	CRP
140-200	18	7.80	0.28
200-300	30	8.88	0.50
300-400	32	10.18	1.64
400-500	16	11.39	2.2
>500	4	13.48	2.6

In this study of 100 patients, PPBS was correlated to HbA1C and CRP. Patients with PPBS between 140-200 were 18, between 200-300 were 30, between 300-400 were 32, between 400-500 were 16 and >500 were 4 had HbA1C 7.80, 8.88, 10.18, 11.39, 13.48 and CRP of 0.28, 0.50, 1.64, 2.2, 2.6, respectively. PPBS showed a direct correlation with both HbA1C and CRP in this study.

Table 5: Association of CRP and total cholesterol, association of CRP and LDL cholesterol, association of CRP and HDL and association of CRP and triglycerides

Total cholesterol	Number	CRP
<100	2	0.0
101-200	78	0.95
201-300	20	2.13
LDL		
<60	14	1.74
60-80	28	0.88
80-100	18	1.72
100-120	26	0.68
120-140	2	1.22
>140	12	2.00
HDL		
0-20	6	2.00
20-40	46	1.28
40-60	44	1.09
>60	4	1.03

Triglycerides		
100-200	50	0.88
200-300	34	0.96
300-400	8	1.82
400-500	2	2.42
>500	6	2.44

In this study of 100 patients, total cholesterol was compared to CRP. Number of patients with total cholesterol <100 was 2, between 100-200 were 39 between 200-300 were 20 with mean CRP of 0.0, 0.95, 2.13. There was a significant positive correlation between CRP and total cholesterol ($p<0.05$). In this study of 100 patients, LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 14, between 60-80 were 28, between 80-100 were 18, between 100-120 were 26, between 120-140 was 2, >140 were 12 with mean CRP levels of 1.74, 0.88, 1.72, 0.68, 1.22, 2.0. There was no significant correlation between CRP and LDL cholesterol ($p>0.05$). In this study of 50 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 6, between 20-40 were 46, between 40-60 were 44 and HDL cholesterol >60 were 4 with mean CRP levels of 2.00, 1.28, 1.09, 1.03, respectively. There was a negative correlation between HDL cholesterol and CRP. In this study of 100 patients, triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 50, between 200-300 were 34, between 300-400 were 8, between 400-500 was 1 and with levels >500 were 6 with mean CRP levels of 0.88, 0.96, 1.82, 2.42, 2.44, respectively. There was significant positive correlation between CRP and triglyceride levels ($p<0.05$).

Discussion

Diabetes mellitus describes a metabolic disorder of multiple etiology, characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. [15] Type 2 diabetes mellitus is the most common form of diabetes. The prevalence of type 2 diabetes mellitus is increasing in all populations worldwide. It is a major risk factor for death and numerous nonfatal complications. According to the International diabetes federation (IDF) there are approximately 72 million people with diabetes mellitus in India at present and number is expected to rise more than 134 million by 2045. [16] Factors associated with an increase in mortality rates among those with diabetes mellitus include male gender, longer duration of diabetes, insulin use. [17] It is perceived that chronic low grade inflammation might potentially be a cause underlying the etiology and manifestations of T2DM. [18]

In this study of 100 patients, 70 patients were males, and 20 were females with mean CRP levels of 1.18±1.22 and 1.14±0.98, respectively. There was no significant difference between male and female patients ($p>0.05$). In this study of 100 patients, HbA1C and CRP were correlated with age. Patients between age 30-40 years were 8 with mean HbA1C and CRP of 10.38 and 1.4 respectively. Patients between age 40-50 years were 25 with mean HbA1C and CRP of 10.52 and 1.7 respectively. Patients between age 50-60 years were 45 with mean HbA1C and CRP of 9.21 and 1.3 respectively. Patients between 60-70 years were 20 with mean HbA1C and CRP of 9.24 and 0.7 respectively. Patients above 70 were 2 with mean HbA1C and CRP of 8.0 and 0, respectively. There was no significance between different age groups in this study ($p>0.05$). King and others [19] in unadjusted analyses, demonstrated that a higher HbA1C is significantly associated with a higher CRP levels. Hu et al [20] studied hazard ratios of T2DM for different levels of serum CRP and found that the association between CRP and risk of diabetes was stronger in women than men. In this study, the females had higher CRP levels compared to males, but this difference was not statistically significant ($p>0.05$); this could be due to a smaller number of the female population in the study.

In this study of 100 patients, patients with BMI <18 was 2 with mean CRP of 1.22, BMI between 18 -23 were 38 with mean CRP of 1.14, BMI between 23-25 were 42 with mean CRP of 1.22, BMI 25-30 were 16 with mean CRP of 1.52, with BMI>30 was 2 with mean CRP of 1.22. There was no significant correlation between CRP and BMI in this study. Williams et al [21] showed that obesity was independently related to CRP, an increase in CRP is associated with an increase in BMI. In this study of 100 patients, triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 50, between 200-300 were 34, between 300-400 were 8, between 400-500 was 1 and with levels >500 were 6 with mean CRP levels of 0.88, 0.96, 1.82, 2.42, 2.44, respectively. There was significant positive correlation between CRP and triglyceride levels ($p<0.05$). Michelle and others stated that CRP levels were significantly related to 10-year Framingham coronary heart disease risk categories. [22] In this study of 100 patients, FBS was correlated to HbA1C in different groups. Patients with FBS of 100 was 2 with HbA1C were 8.0, between 100-200 were 44,

between 200-300 were 34, >300 were 10 had HbA1C of 8.32, 10.52, 11.34 respectively. FBS and HbA1C were directly correlated. In this study of 100 patients, PPBS was correlated to HbA1C and CRP. Patients with PPBS between 140-200 were 18, between 200-300 were 30, between 300-400 were 32, between 400-500 were 16 and >500 were 4 had HbA1C 7.80, 8.88, 10.18, 11.39, 13.48 and CRP of 0.28, 0.50, 1.64, 2.2, 2.6, respectively. PPBS showed a direct correlation with both HbA1C and CRP in this study. In this study of 100 patients, total cholesterol was compared to CRP. Number of patients with total cholesterol <100 was 2, between 100-200 were 39 between 200-300 were 20 with mean CRP of 0.0, 0.95, 2.13. There was a significant positive correlation between CRP and total cholesterol ($p<0.05$). In this study of 100 patients, LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 14, between 60-80 were 28, between 80-100 were 18, between 100-120 were 26, between 120-140 was 2, >140 were 12 with mean CRP levels of 1.74, 0.88, 1.72, 0.68, 1.22, 2.0. There was no significant correlation between CRP and LDL cholesterol ($p>0.05$). Nissen SE et al [23] found that the correlation between the reduction in LDL cholesterol and CRP levels was weak but significant in the group as a whole. In this study of 50 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 6, between 20-40 were 46, between 40-60 were 44 and HDL cholesterol >60 were 4 with mean CRP levels of 2.00, 1.28, 1.09, 1.03, respectively. There was a negative correlation between HDL cholesterol and CRP. Yanagawa T et al [24] showed that CRP negatively correlated with HDL cholesterol which were similar to the findings observed in this study.

Conclusion

In this study of 100 diabetic patients, a positive correlation between CRP and HbA1C was found. Further, it was found that there exists a positive correlation between CRP and other risk factors of coronary artery disease like total cholesterol, triglycerides. At the same time, HDL showed a negative correlation with CRP. The findings regarding BMI in this study, contrary to others, suggest CRP was not significantly associated with BMI, and inflammation as a potential mechanism in T2DM may be independent of obesity. Follow-up studies revealed that better glycaemic control resulted in the lowering of CRP, which was significant. This study, therefore, reveals that CRP is an additional marker of better glycaemic control and also correlates with the dyslipidaemia profile seen in type 2 diabetes mellitus.

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