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Original Research Article

A Hospital-Based Prospective Evaluation of the Correlation between Glycemic Control, Lipid Profile and C-Reactive Protein in Adults with Type 2 Diabetes Mellitus

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Abstract

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

Methods: This was a hospital-based prospective study comprised of 60 patients with type 2 diabetes mellitus reporting to Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India for the period of one year.

Results: In this study of 60 patients, 40 patients were males, and 20 were females with mean CRP levels of 1.19±1.25 and 1.12±0.99, respectively. There was no significant difference between male and female patients ($p>0.05$). In this study of 60 patients, HbA1C and CRP were correlated with age. Patients between age 30-40 years were 5 with mean HbA1C and CRP of 10.43 and 1.2, respectively. Patients between age 40-50 years were 15 with mean HbA1C and CRP of 10.59 and 1.8, respectively. Patients between age 50-60 years were 25 with mean HbA1C and CRP of 9.22 and 1.2, respectively. Patients between 60-70 years were 12 with mean HbA1C and CRP of 9.2 and 0.6, respectively. Patients above 70 were 3 with mean HbA1C and CRP of 8.0 and 0, respectively.

Conclusion: 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 (DM) with its complication has become the most important and challenging contemporary health problem. Globally, the estimated number of adults with diabetes in 2007 was 246 million and 380 million adults worldwide will have diabetes by 2025. India has 41 million diabetics and this number is expected to increase to 70 million by 2025. [1] Over the past 30

years, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle-aged people. [2] Onset of type 2 diabetes mellitus (T2DM) at early age heralds many years of disease and an increased risk that the full range of both microvascular and macrovascular complications will occur when affected individuals are still relatively young. Thus, further generations may be burdened with morbidity and mortality at the height of their productivity, potentially affecting workface, and healthcare systems of countries across the world. [3]

The primary task of health management in Type 2 diabetes (T2D) patients is to prevent diabetes-related complications. Previous studies have shown that good control of lipid profiles and glycemic levels can effectively prevent complications such as cardiovascular disease, diabetic nephropathy and diabetic retinopathy. [4,5] Lipid profiles referred to lipids in plasma, generally including triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL), and low density lipoprotein (LDL) clinically. [6] For patients with cardiovascular disease and T2D, lipid profiles should be strictly controlled to reduce mortality and complications. [7]

Factors associated with an increase in mortality rates among those with diabetes mellitus include male gender, longer duration of diabetes, insulin use. [8] It is perceived that chronic low grade inflammation might potentially be a cause underlying the etiology and manifestations of T2DM. [9]

Endothelial dysfunction, subclinical inflammation, and impaired fibrinolysis might contribute to the progression of macrovascular as well as microvascular complications Pickup and crook analyzed the role of the innate immune system from several studies and found that T2DM is associated with increased blood concentration of markers of acute-phase response including C-reactive protein and cortisol, the main cytokine mediator, interleukin 6. [10]

Patients with T2DM have a two to four-fold higher risk of cardiovascular events. The progression of coronary artery disease appears faster when compared with non-diabetic patients. [11] Since inflammation is believed to have a role in the pathogenesis of cardiovascular events, measurement of markers of inflammation has been proposed as a method to improve the prediction of the risk of these events. C-reactive protein is the most reliable marker of inflammation. [12] CRP is produced by hepatocytes largely under the regulatory control of inflammatory cytokines, including IL-6, TNF-α. Diabetes exposure can be characterized by the level of glycosylated hemoglobin (HbA1C) which is an accurate, precise measure of chronic glycemic levels and correlates well with risk of diabetic complications. C-reactive protein and glycated hemoglobin (HbA1C) are established risk factors for the development of cardiovascular diseases.

The purpose of this study was to determine the relation between HbA1C, Lipid profile and CRP in individuals with type 2 diabetes mellitus.

Materials and Methods

This was a hospital-based prospective study comprised of 60 patients with type 2 diabetes mellitus reporting to Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India for the period of one year.

Inclusion criteria

Inclusion criteria were; the 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

Exclusion criteria were; patients on statins, thiazolidinediones (TZDs), and anti-inflammatory drugs that are known to reduce CRP levels excluded from the study. 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.

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

Statistical analysis was done using SPSS package and MS excel. Students' 't' test and X2 test was used. Pearson correlation and p values were calculated. P values <0.05 was considered to be significant.

Results

Table 1: CRP in males and females

CRP	Number	Mean
Males	40	1.2514
Females	20	0.9954
Total	60	1.1759

In this study of 60 patients, 40 patients were males, and 20 were females with mean CRP levels of 1.19±1.25 and 1.12±0.99, 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	5	10.43	1.2
40-50	15	10.59	1.8
50-60	25	9.22	1.2
60-70	12	9.20	0.6
>70	3	8.00	0.0

In this study of 60 patients, HbA1C and CRP were correlated with age. Patients between age 30-40 years were 5 with mean HbA1C and CRP of 10.43 and 1.2, respectively. Patients between age 40-50 years were 15 with mean HbA1C and CRP of 10.59 and 1.8, respectively. Patients between age 50-60 years were 25 with mean HbA1C and CRP of 9.22 and 1.2, respectively. Patients between 60-70 years were 12 with mean HbA1C and CRP of 9.2 and 0.6, respectively. Patients above 70 were 3 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: CRP and BMI

BMI	Number	CRP
<18	2	1.20
18-23	22	1.12
23-25	23	1.20
25-30	10	1.50
>30	3	1.20

In this study of 60 patients, patients with BMI <18 was 2 with mean CRP of 1.2, BMI between 18 -23 were 22 with mean CRP of 1.2, BMI between 23-25 were 23 with mean CRP of 1.20, BMI 25-30 were 10 with mean CRP of 1.5, with BMI>30 was 3 with mean CRP of 1.2. There was no significant correlation between CRP and BMI in this study.

Table 4: FBS with HbA1C and CRP

FBS	Number	HbA1C
<100	2	8.00
100-200	30	8.25
200-300	20	10.56
>300	18	11.33

In this study of 60 patients, FBS was correlated to HbA1C and CRP in different groups. Patients with FBS 0f 100 was 2 with HbA1C and CRP were 8.0 and 0.4, between 100-200 were 30, between 200-300 were 20, >300 were 18 had HbA1C of 8.25, 10.56, 11.33 and CRP of 0.6, 1.41, 2.04, respectively. FBS and HbA1C were directly correlated.

Table 5: PPBS with HbA1C and CRP

PPBS	Number	HbA1C	CRP
140-200	10	7.77	0.26
200-300	15	8.85	0.48
300-400	18	10.13	1.65
400-500	12	11.36	2.1
>500	5	13.40	2.4

In this study of 60 patients, PPBS was correlated to HbA1C and CRP. Patients with PPBS between 140-200 were 10, between 200-300 were 15, between 300-400 were 18, between 400-500 were 12, and >500 were 5 had HbA1C 7.77, 8.85, 10.13, 11.63, 13.40 and CRP of 0.26, 0.4, 1.6, 2.1, 2.4, respectively. PPBS showed a direct correlation with both HbA1C and CRP in this study.

Table 6: CRP and LDL cholesterol

LDL	Number	CRP
<60	5	1.71
60-80	25	0.86
80-100	15	1.70
100-120	10	0.65
120-140	3	1.20
>140	2	2.00

In this study of 60 patients, LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 5, between 60-80 were 25, between 80-100 were 15, between 100-120 were 10, between 120-140 was 3, >140 were 2 with mean CRP levels of 1.71, 0.86, 1.7, 0.65, 1.2, 2.0. There was no significant correlation between CRP and LDL cholesterol ($p>0.05$).

Table 7: CRP and HDL cholesterol

HDL	Number	CRP
0-20	2	2.00
20-40	30	1.25
40-60	25	1.08
>60	3	1.02

In this study of 60 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 2, between 20-40 were 30, between 40-60 were 25 and HDL cholesterol >60 were 3 with mean CRP levels of 2.00, 1.25, 1.08, 1.02, respectively. There was a negative correlation between HDL cholesterol and CRP.

Table 8: CRP and HbA1C

HbA1C	Number	CRP
<7	10	0.40
7-9	15	0.51
9-10	15	1.41
>10	20	2.15

Table 9: HbA1C and CRP of 50 initial and 20 follow-up cases

	HbA1c	HbA1c	CRP	CRP
	Initial (50)	Follow-up (20)	Initial (50)	Follow-up (20)
Mean	9.6500	7.39	1.1520	0.30
SD	1.8816	1.31	0.9984	0.50
P value	0.0001		0.0003	

The mean HbA1C of 60 patients initially was 9.56±1.88, and the mean CRP was 1.152±0.9984. A follow-up of 20 cases was done on patients who were not on statin therapy. On follow-up, the mean HbA1C of 20 cases had reduced to 7.39±1.31 ($p<0.05$) and mean CRP of those 20 patients reduced to 0.28±0.52 ($p<0.05$).

Discussion

There is growing evidence supporting the concept that chronic, low-grade, inflammatory states may have a pathogenic role in IR. Several studies have shown that proinflammatory cytokines and acute-phase reactants are correlated with measures of IR, BMI, waist circumference, circulating TG, and HDL cholesterol concentration. Inflammatory cytokines, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), have been linked to IR, and their expression is increased in adipose tissue. Type 2 diabetes mellitus is a major risk factor for death, and numerous nonfatal complications. C-reactive protein, a marker of systemic inflammation, is emerging as an independent risk factor for cardiovascular disease and has been linked to an increased risk of thrombotic events. CRP levels are higher in people with diabetes compared to those without. Not much is known whether CRP in people with diabetes is related to the level of glycemic control.

King and others in unadjusted analyses, demonstrated that a higher HbA1C is significantly associated with a higher CRP level. [13] This study showed that a rise in HbA1C, higher glycemic levels significantly correlated with increasing values of CRP. Hu et al 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. [14] 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.

Williams et al showed that obesity was independently related to CRP, an increase in CRP is associated with an increase in BMI. [15] The findings in this study, contrary to others, suggest that CRP was not significantly associated with BMI and that inflammation as a potential mechanism in T2DM may be independent of obesity and leads to increase risk of cardiovascular events.

Steven et al found that the correlation between the reduction in LDL cholesterol and CRP levels was weak but significant in the group as a whole. [16] In this study, there was no significant correlation between CRP and LDL cholesterol. Takiko et al showed that CRP negatively correlated with HDL cholesterol which were similar to the findings observed in this study. [17] Ana et al found that hs-CRP levels were positively correlated with triglycerides. [18] This study also showed a positive correlation similar to other studies.

T2D patients had an increased risk of death and disability due to associated complications, suggesting the significance of good control for lipid profiles and glycemic level. [19] High-sensitivity C-reactive protein levels are positively influenced more by W/H ratio than BMI. Visceral adipocytes play key role in regulating inflammation. C-reactive protein is synthesized in the liver and is regulated by proinflammatory cytokines, such as IL-6 and TNF-α. This suggests that, association of increased hs-CRP concentration with increased insulin levels could be due to the presence of chronic systemic subclinical inflammation. [20]

C-reactive protein bound to membranes of damaged vascular cells activates complement proteins. [21] Inflammation disturbs pancreatic β-cell function in genetically susceptible individuals who are at high risk to develop diabetes. Inflammation could also promote hepatic IR in individuals who are genetically susceptible to develop diabetes. Insulin resistance exacerbates fasting glycemia and hypertriglyceridemia. [22,23]

Conclusion

The present study concluded 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.

Timely screening and early detection of the increased hs-CRP in the FDRs of T2DM subjects may help clinicians enable to intervene early in the course of disease and prevent further complications and outcomes. Therefore, primary prevention by target screening among high-risk individuals to prevent transition to overt T2DM by therapeutic lifestyle changes is a feasible and attractive alternative to reduce diabetes-related morbidity and mortality.

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