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Original Research Article

Hospital-based Prospective Study to Assess the Correlation between Glycemic Control, Lipid Profile and C-reactive Protein in Adults with type 2 Diabetes Mellitus

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Abstract

Introduction: 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.

Methods: Sixty patients with T2DM reporting to Nalanda Medical College & Hospital, Patna were included in the study, in whom CRP levels were estimated by using commercially available kits and correlated with HbA1C and other risk factors of coronary artery disease. Follow-up was done on 25 patients who were not on statin therapy with repeat HbA1C and CRP.

Results: This study showed that both HbA1C and CRP levels had reduced significantly in follow-up patients after putting them on treatment ($p<0.05$). It was also found that lowers the HbA1C, lower was the CRP. A positive correlation was found between HbA1C and CRP ($p<0.05$).

Conclusion: 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 dyslipidemia 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 World Health Organization projects that diabetes will be the seventh leading cause of death in 2030.[4] Diabetes particularly affects low-income and middle-income countries in terms of prevalence, mortality, and morbidity. More than 80% of people with diabetes live in developing countries, where rapid cultural and social changes, including changes in lifestyle, aging populations, increasing urbanization, dietary changes, and reduced physical activity, all contribute to the dramatic increase in the epidemic of diabetes. The majority of people with diabetes in low-income and middle-income countries are under 60 years of age.[5] According to recent estimates, diabetes accounts for 1.4 million cases with a 7.7% prevalence and more than 25,000 diabetes-related deaths in Sudan.[5]

In India, nearly 75% of T2DM patients have the first-degree family history. The lifetime risk of developing the disease is about

40% in offspring of one parent with T2DM and the risk approaches to 70% if both parents have diabetes. In terms of sibling relative risk, a first-degree relative (FDR) of a patient with T2DM has a threefold increased risk of developing the disease. [6] It is found that Indians have 45% positive family history of diabetes as compared to 38% of the Europeans. [7] Lipid metabolism in T2DM is modulated by a series of factors among which, the degree of glycemic control and the presence of insulin resistance (IR) are the two most important factors. Diabetic dyslipidemia is a complex cluster of potentially atherogenic lipid and lipoprotein changes. Increased plasma triglycerides (TGs), especially very high-density lipoprotein (VLDL), TG, and low concentration of high-density lipoprotein cholesterol

(HDL-C), preponderance of small, dense low-density lipoprotein (LDL) and excessive postprandial lipemia are the main components of diabetic dyslipidemia. [8]

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.[9] 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.[10]

C-reactive protein is the most reliable marker of inflammation. [11] CRP is produced by hepatocytes largely under the regulatory control of inflammatory cytokines, including IL-6, TNF-α. [10]

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. [10]

CRP was also found to be predictive of future cardiovascular events in patients with the metabolic syndrome and to add prognostic information to the ATP-III definition of the metabolic syndrome. [12] Evidence suggests that CRP might

represent a novel biomarker of vascular risk, CRP evaluation might also merit consideration as a method to monitor pharmacologic interventions used to prevent and treat cardiovascular disease. [13]

CRP is a possible risk factor for the development of type 2 diabetes mellitus. The glycemic control is related to CRP, but the relationship has yet to be elucidated. [10]

Materials and Methods

This was a hospital-based prospective study comprised of 50 patients with type 2 diabetes mellitus reporting to Nalanda Medical College & Hospital, Patna, Bihar, India over a 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, and 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

Statistical analysis was done using SPSS package and MS excel. Students‘t’ test and *X*2 test was used. Pearson correlation and p values were calculated. P values <0.05 was considered to be significant.

Table 1: CRP in males and females

CRP	Number	Mean
Males	44	1.3871
Females	16	0.9989
Total	60	1.8762

In this study of 60 patients, 44 patients were males, and 16 were females. 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	6	11.43	1.87
40-50	9	11.73	2.1
50-60	29	10.11	1.8
60-70	15	10.03	0.8
>70	1	7.2	0

Patients between ages 50-60 years were 29 with mean HbA1C and CRP of 10.11 and 1.8 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	23	1.10
23-25	29	1.20
25-30	5	1.40
>30	1	1.20

In this study of 60 patients, patients with BMI <18 was 2 with mean CRP of 1.20. BMI between 23-25 were 29 with mean CRP of 1.20, BMI 25-30 were 5 with mean CRP of 1.40. There was no significant correlation between CRP and BMI in this study.

Table 4: FBS with HbA1C and CRP.

FBS	Number	HbA1C
<100	2	9.13
100-200	27	9.45
200-300	19	12.74
>300	12	13.55

Patients with FBS 0f 100 was 2 with HbA1C were 9.13, between 100-200 were 27, between 200-300 were 19, >300 were 112 had HbA1C of 9.45, 12.74, 13.55 respectively. FBS and HbA1C were directly correlated.

Table 5: PPBS with HbA1C and CRP.

PPBS	Number	HbA1C	CRP
140-200	11	8.18	0.31
200-300	17	10.27	0.59
300-400	19	11.48	2.01
400-500	10	13.32	3.7
>500	3	15.96	3.9

In this study of 60 patients, PPBS was correlated to HbA1C and CRP.

Table 6: CRP and total cholesterol.

LDL	Number	CRP
<60	8	1.90
60-80	21	0.99
80-100	15	1.73
100-120	8	0.78
120-140	2	1.39
>140	6	2.87

There was no significant correlation between CRP and LDL cholesterol (p>0.05)

Table 7: CRP and LDL cholesterol.

LDL	Number	CRP
<60	9	1.87
60-80	20	0.90
80-100	10	1.88
100-120	12	0.98
120-140	2	1.67
>140	7	2.98

There was no significant correlation between CRP and LDL cholesterol ($p>0.05$)

Table 8: CRP and HDL cholesterol.

HDL	Number	CRP
0-20	8	2.78
20-40	21	1.34
40-60	27	1.11
>60	4	1.10

In this study of 60 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 8, between 20-40 were 21, between 40-60 were 27 and HDL cholesterol >60 were 4 with mean CRP levels of 2.78, 1.34, 1.11, 1.10, respectively. There was a negative correlation between HDL cholesterol and CRP

Table 9: CRP and triglycerides.

Triglycerides	Number	CRP
100-200	30	0.76
200-300	19	0.89
300-400	5	1.56
400-500	5	2.32
>500	1	2.23

In this study of 60 patients, triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 30, between 200-300 were 19, between 300-400 were 5, between 400-500 was 5 and with levels >500 were 1 with mean CRP levels of 0.76, 0.89, 1.56, 2.3, 2.2, respectively. There was significant positive correlation between CRP and triglyceride levels ($p<0.05$)

Table 10: CRP and HbA1C.

HbA1C	Number	CRP
<7	11	0.57
7-9	16	0.66
9-10	13	2.34
>10	20	3.12

In this study of 50 patients, patients with HbA1C <7 were 11, between 7-9 were 16, between 9-10 were 13, HbA1C >10 were 20 with mean CRP of 0.5, 0.66, 2.34, 3.12, respectively. There was significant correlation between CRP and HbA1C ($p<0.05$)

Table 11: HbA1C and CRP of 60 initial and 25 follow-up cases.

	HbA1c Initial (60)	HbA1c Follow-up (25)	CRP Initial (60)	CRP Follow-up (25)
Mean	9.8712	8.43	1.2317	0.37
SD	1.9876	1.56	0.9874	0.69
p value		0.0001		0.0003

The mean HbA1C of 60 patients initially was 9.87±1.98, and the mean CRP was 1.23±0.9874. A follow-up of 25 cases was done on patients who were not on statin therapy. On follow-up, the mean HbA1C of 25 cases had reduced to 8.43±1.23 ($p<0.05$) and mean CRP of those 25 patients reduced to 0.37±0.69 ($p<0.05$)

Table 12: HbA1C and CRP of 20 initial and 20 follow-up cases.

	HbA1c Initial (25)	HbA1c Follow-up (25)	CRP Initial (25)	CRP Follow-up (25)
Mean	9.8764	8.61	0. 7420	0.36
SD	1.9789	2.67	0.862	0.78
p value		0.0007		0.0649

A comparison was made between initial HbA1C, CRP levels with HbA1C, CRP levels of follow up cases among 25 cases. The initial mean HbA1C of 25 patients was 9.87±1.97, and the mean HbA1C on follow up was 8.61±2.67. The initial mean CRP of 25 patients was 0.74±0.862 and mean CRP on follow up was 0.35±0.78. HbA1C has significantly reduced in patients, after being put on treatment ($p<0.05$) and CRP levels also reduced ($p<0.05$).

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.[14]

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. [10]

King and others in unadjusted analyses, demonstrated that a higher HbA1C is significantly associated with a higher CRP level. [15] This study showed that a rise in HbA1C, higher glycemic levels significantly correlated with increasing values of CRP. 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 his-CRP levels were positively correlated with triglycerides. [18] This study also showed a positive correlation similar to other studies.

Conclusion:

It was found that there exists a positive correlation between CRP and other risk factors of coronary artery disease like total cholesterol, triglycerides. Follow-up studies revealed that better glycemic control resulted in the lowering of CRP, which was significant. This study, therefore, reveals that CRP is an additional marker of better glycemic control and also correlates with the dyslipidemia profile seen in type 2 diabetes mellitus.

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