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Original research article

Determining the association between HbA1C, Lipid profile and CRP in individuals with type 2 diabetes mellitus: an observational study

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Abstract

Background: Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of cardiovascular diseases (CVD). This study is an attempt to evaluate the diagnostic value of Glycated haemoglobin (HbA1c) in predicting diabetic dyslipidemia.

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

Material and methods: This prospective observational study was carried out in the Department of General Medicine, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India for 1 year. 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 include in this study. 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 3-6 months.

Results: There was no significant difference between gender, age and BMI ($p>0.05$). 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 ($p<0.05$). There was significant correlation between CRP and HbA1C ($p<0.05$).

Conclusion: Timely screening and early detection of the increased hs-CRP in the first-degree relatives of T2DM subjects may help clinicians enable to intervene early in the course of disease and to 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.

Keywords: C-reactive protein, Glycemic control, Hemoglobin A1C, Type 2 diabetes mellitus.

Introduction

Diabetes mellitus (DM) consists of a group of metabolic disorders that share common phenotype of hyperglycemia. India has the highest prevalence of people with diabetes in the world which is predicted to increase to 120.9 million by 2030.

Chronic, systemic subclinical inflammation has also been identified as a driving force for insulin resistance, metabolic syndrome, and type 2 DM. The process of inflammation induces hepatic synthesis of various acute phase proteins such as serum ferritin and high sensitivity C-reactive protein (HsCRP), which is believed to play a role in insulin resistance as well as atherosclerosis. Serum levels of HsCRP have been found to be a strong predictor for increased

cardiovascular disease risk associated with type 2 DM. Higher incidence of type 2 DM has been observed with high levels of HsCRP.[1,2]

C-reactive protein measured by highly sensitive assays (hsCRP), is a very sensitive marker of the inflammatory activity in the arterial wall.[3,4] It is an important predictor of cardiovascular risk apart from the traditional risk factors.[5,6] It is interesting to note that chronic hyperglycaemia stimulates the release of various inflammatory cytokines (IL 6; TNF α) and induces the secretion of acute phase reactants by liver, which in turn results in elevation of CRP in association with elevated fasting plasma glucose.[7] Studies had shown that elevated CRP levels is associated with an increased risk of future development of diabetes mellitus.[8] Also, people with diabetes mellitus had elevated levels of CRP than non -diabetics.[9,10] We understand that both chronic systemic inflammation and hyperglycaemia contribute to the development and progression of atherosclerotic cardiovascular disease. Experimental and clinical studies have confirmed the inter-relationship between CRP, hyperglycaemia and atherosclerosis.[11,12] In states of elevated CRP, hyperglycaemia exaggerates the proatherogenic effects of CRP.[12,13] Few studies which had assessed the relationship between CRP levels and the level of glycaemic status showed conflicting results; some studies had proven the positive co-relation between glycaemic control and CRP levels.[14-16] while some failed to do so.[6] Also, the effect of good glycaemic control on CRP levels is not clear. The aim of this study to determine the relation between HbA1C, Lipid profile and CRP in individuals with type 2 diabetes mellitus.

Material and methods

This prospective observational study was carried out in the Department of General Medicine, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar for 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

Inclusion criteria

- The patients above 30 years with fasting venous blood glucose value equal or more than 100 mg/dl and postprandial glucose >140 mg/dl.

Exclusion criteria

- Patients on statins, thiazolidinedione's (TZDs), and anti-inflammatory drugs that are known to reduce CRP levels
- Patients with heart failure
- Acute febrile illness, renal,
- Hepatic and malignant disorders,
- Type 1 diabetes,
- Amino-glycosides

Methodology

Informed consent was taken from the patients. Detailed history, physical examination, which includes height, weight, body mass index (kg/m^2), 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 3-6 months. Patients were put on OHA/insulin for control of blood sugar along with dietary control and exercise.

Results

120 T2DM cases were collected from both out patients and inpatients visiting Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, for estimation of glycemic status, lipid profile and various parameters related to diabetes mellitus were studied, and they were

correlated with CRP levels in this study. Cases were followed with a minimum gap of 3 months, and the parameters were repeated.

Table 1: CRP in males and females

CRP	Number=120	Mean
Males	85	1.26±1.37
Females	35	1.24±0.90

In this study of 120 patients, 85 patients were males, and 35 were females with mean CRP levels of 1.26±1.37 and 1.24±0.90, respectively. There was no significant difference between male and female patients ($p>0.05$) (Table 1).

Table 2: Age distribution and CRP and HbA1C

Age	Number	HbA1C	CRP
Below 35	10	10.47	1.7
35-45	29	10.67	2.1
45-55	56	9.07	1.5
55-65	20	9.02	0.6
Above 65	5	7.39	0.0

In this study of 120 patients, HbA1C and CRP were correlated with age. Patients between age below 35 years were 10 with mean HbA1C and CRP of 10.47 and 1.7, respectively. Patients between age 35-45 years were 29 with mean HbA1C and CRP of 10.67 and 2.1, respectively. Patients between age 45-55 years were 56 with mean HbA1C and CRP of 9.07 and 1.5, respectively. Patients between 55-65 years were 20 with mean HbA1C and CRP of 9.02 and 0.6, respectively. Patients above 65 was 5 with mean HbA1C and CRP of
7.39 and 0, respectively. There was no significance between different age groups in this study ($p>0.05$) (Table 2).

Table 3: CRP and BMI

BMI	Number	CRP
<18	3	1.32
18-23	43	1.21
23-25	51	1.31
25-30	20	1.62
>30	3	1.30

In this study of 120 patients, patients with BMI below 18 was 3 with mean CRP of 1.32, BMI between 18 -23 were 43 with mean CRP of 1.21, BMI between 23-25 were 51 with mean CRP of 1.31, BMI 25-30 were 20 with mean CRP of 1.62, with BMI>30 was 3 with mean CRP of 1.30. There was no significant correlation between CRP and BMI in this study (Table 3

Table 4: FBS with HbA1C and CRP

FBS	Number	HbA1C
<100	5	7.96
100-200	54	8.44
200-300	40	10.74
>300	21	11.59

In this study of 120 patients, FBS was correlated to HbA1C and CRP in different groups. Patients with FBS 0f 100 was 5 with HbA1C and CRP were 7.96 and 0.42,between 100-

200 were 54, between 200-300 were 40,>300 were 21 had HbA1C of 8.44, 10.74, 11.59 and CRP of 0.62, 1.43, 2.23, respectively. FBS and HbA1C were directly correlated (Table 4).

Table 5: PPBS with HbA1C and CRP.

PPBS	Number	HbA1C	CRP
140-200	21	7.85	0.28
200-300	40	9.15	0.63
300-400	38	10.26	1.78
400-500	16	11.43	2.45
>500	5	13.79	2.98

In this study of 120 patients, PPBS was correlated to HbA1C and CRP. Patients with PPBS between 140-200 were 21, between 200-300 were 40, between 300-400 were 38, between 400-500 were 16, and >500 were 5 had HbA1C 7.85, 9.15, 10.26, 11.43, 13.79 and CRP of 0.28, 0.63, 1.78, 2.45, 2.98, respectively. PPBS showed a direct correlation with both HbA1C and CRP in this study (Table 5).

Table 6: CRP and total cholesterol

TC	Number	CRP
<100	8	1.77
100-200	50	0.87
200-300	30	1.69
Above 300	32	0.81

In this study of 120 patients, total cholesterol was compared to CRP. Number of patients with total cholesterol <100 was 8, 100-200 were 50 and 200-300 were 30 with mean CRP of 1.77, 0.87, 2.69. There was a significant positive correlation between CRP and total cholesterol ($p<0.05$) (Table 6).

Table 7: CRP and LDL cholesterol

LDL	Number	CRP
<60	15	1.87
60-80	38	0.98
80-100	20	1.68
100-120	30	0.77
120-140	2	1.33
>140	15	2.27

In this study of 120 patients, LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 15, between 60-80 were 38, between 80-100 were 20, between 100-120 were 30, between 120-140 was 2, >140 were 15 with mean CRP levels of 1.87, 0.98, 1.68, 0.77, 1.33, 2.27. There was no significant correlation between CRP and LDL cholesterol ($p>0.05$) (Table 7)

Table 8: CRP and HDL cholesterol

HDL	Number	CRP
0-20	5	2.12
20-40	58	1.27
40-60	54	1.09
>60	3	1.13

In this study of 120 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 5, between 20-40 were 58, between 40-60 were 54 and

HDL cholesterol >60 were 3 with mean CRP levels of 2.12, 1.27, 1.09, 1.13, respectively. There was a negative correlation between HDL cholesterol and CRP (Table 8)

Table 9: CRP and triglycerides

Triglycerides	Number	CRP
100-200	60	0.92
200-300	40	0.97
300-400	11	1.83
400-500	4	2.42
>500	5	2.43

In this study of 120 patients, triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 60, between 200-300 were 40, between 300-400 were 11, between 400-500 was 4 and with levels >500 were 5 with mean CRP levels of 0.92, 0.97, 1.83, 2.42, 2.43, respectively. There was significant positive correlation between CRP and triglyceride levels ($p<0.05$) (Table 9).

Table 10: CRP and HbA1C

HbA1C	Number	CRP
<7	20	0.41
7-9	30	0.61
9-10	28	1.52
>10	42	2.36

In this study of 120 patients, patients with HbA1C <7 were 20 between 7-9 were 30, between 9-10 were 28, HbA1C >10 were 42 with mean CRP of 0.41, 0.61, 1.52, 2.36, respectively. There was significant correlation between CRP and HbA1C ($p<0.05$) (Table 10). The mean HbA1C of 120 patients initially was 9.87±1.92, and the mean CRP was 1.142±0.9684. A follow-up of 60 cases was done on patients who were not on statin therapy. On follow-up, the mean HbA1C of 60 cases had reduced to 7.53±1.36 ($p<0.05$) and mean CRP of those 60 patients reduced to 0.29±0.51.($p<0.05$). A comparison was made between initial HbA1C, CRP levels with HbA1C, CRP levels of follow up cases among 60 cases. The initial mean HbA1C of 60 patients was 9.54±1.677, and the mean HbA1C on follow up was 7.62±1.36. The initial mean CRP of 60 patients was 0.92±0.915 and mean CRP on follow up was 0.34±0.45. 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.

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.

This study has therefore gone into the various factors that are related both to CRP and T2DM.

King and others in unadjusted analyses demonstrated that a higher HbA1C is significantly associated with a higher CRP levels.[17].[17] 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.[18].[18]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.[19] 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.

In this study, it was found that CRP levels significantly increase with an elevation of total cholesterol. Michelle and others stated that CRP levels were significantly related to 10-year Framingham coronary heart disease risk categories.[20]

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.[21] 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.[22]

Ana et al found that hs-CRP levels were positively correlated with triglycerides.[23] This study also showed a positive correlation similar to other studies.

Conclusion

Timely screening and early detection of the increased hs-CRP in the first-degree relatives of T2DM subjects may help clinicians enable to intervene early in the course of disease and to 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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