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Original Research Article

A Prospective Research to Assess the Association of type 2 Mellitus Diabetes with HbA1c, Lipid Profile, and CRP

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Abstract

Aim: The aim of this study to determine the relation between HbA1c, Lipid profile and CRP in individuals with type 2 diabetes mellitus.

Methods: This prospective observational study was carried out in the Department of General Medicine Nalanda Medical College and Hospital, Patna, Bihar, India .The patients above 28 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: Total cholesterol was compared to CRP. Number of patients with total cholesterol <100 was 5, 100-200 were 35 between 200-300 were 22 with mean CRP of 1.78, 0.81, 2.87. There was a significant positive correlation between CRP and total cholesterol ($p<0.05$). LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 12, between 60-80 were 26, between 80-100 were 15, between 100-120 were 24, between 120-140 was 1, >140 were 12 with mean CRP levels of 1.85, 0.84, 1.82, 0.75, 1.34, 2.29. There was no significant correlation between CRP and LDL cholesterol ($p>0.05$). HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 3, between 20-40 were 43, between 40-60 were 41 and HDL cholesterol >60 were 3 with mean CRP levels of 2.14, 1.41, 1.22, 1.16, respectively. There was a negative correlation between HDL cholesterol and CRP triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 45, between 200-300 were 30, between 300-400 were 8, between 400-500 was 3 and with levels >500 were 4 with mean CRP levels of 0.71, 0.84, 1.84, 2.45, 2.45, respectively. There was significant positive correlation between CRP and triglyceride levels ($p<0.05$).

Conclusion: The CRP is an additional marker of better Glycaemic control and also correlates with the dyslipidaemia profile seen in type 2 diabetes mellitus. Keywords: C-reactive protein, Glycemic control, Hemoglobin A1C, Type 2 diabetes mellitus.

Keywords: CRP, diabetes, HbA1c

Introduction:

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia due to an absolute or relative lack of insulin and/or insulin resistance, resulting mainly in dysregulation of carbohydrate, protein, and lipid metabolism, which account for the symptoms and complications of diabetes[1].

Diabetes is increasingly emerging as a major public health burden across the world. In 2013, the global prevalence of diabetes was estimated to be 8.4%, with

382 million people living with diabetes and over 5 million diabetes-related deaths; it is expected that the number of people living with diabetes will more than double between 2000 and 2030[2,3]. 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[2].

Type 2 diabetes mellitus (T2DM) accounts for approximately 90% of the diabetes cases worldwide and is linked mainly to excess body weight and physical inactivity[2]. The glucotoxicity and lipotoxicity that occur in diabetic patients could be reversed early by good management, which may assist in preventing or delaying the long-term complications of T2DM, particularly vascular complications[5].

It is recognized that the risk of cardiovascular events is amplified in patients with T2DM, and dyslipidemia is a contributing factor.[6] Weight gain and obesity are key factors in increasing the prevalence of both cardiovascular disease (CVD) and T2DM[7].CVD is more likely to develop at a younger age in patients with diabetes than in nondiabetics, with an increasing risk over the duration of the disease[8]. It has been documented that diabetics are more likely to die of cardiovascular-related causes than nondiabetics[9]. Data on mortality in diabetic patients showed that 52% of people with T2DM died of CVD, primarily heart disease and stroke[10]. According to a recent World Health Organization report, age-standardized death rates for ischemic heart disease and cerebrovascular disease in Sudan were 212 and 118 per 100,000 respectively[11]. C-reactive protein (CRP) is a 115 kDa pentamer synthesized and released mainly by hepatocytes under the control of cytokines such as interleukin-6, interleukin-1, and tumor necrosis factor-α[12]. CRP is an acute-phase protein produced as part of innate nonspecific physiological and biochemical responses to a number of pathophysiological conditions including tissue damage, infection, inflammation, and malignancy[13]. CRP can be used as a marker of systemic inflammation because circulating levels of CRP increase up to 1,000-fold within hours of a tissue injury[14]. Currently, CRP is recognized as an indicator of vascular inflammation. Recently, the role of inflammation in the Pathophysiology of CVD has been

emphasized, and CRP, an inflammatory marker, has been reported to be related to different cardiovascular diseases[13,14]. CRP is recognized as a predictor of cardiovascular conditions secondary to atherosclerosis[15], and is suggested to be a stronger predictor of Cardiovascular events when compared with low-density lipoprotein cholesterol (LDL-C)[16]. Experiments demonstrated that CRP as a sensitive physiological marker of subclinical systemic inflammation is associated with hyperglycemia, insulin resistance, and overt T2DM[17]. It is well established that a link exists between diabetes and systemic inflammation, an association that could be reflected in circulating levels of CRP.18–20 Increased concentrations of CRP have been reported in adult patients with T2DM[18].

Material and Methods

This prospective observational study was carried out in the Department of General medicine Nalanda Medical College and Hospital, Patna, Bihar, India.

The patients above 28 years with fasting venous blood glucose value equal or more than 100 mg/dl and postprandial glucose >140 mg/dl were included in this study.

Methodology

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, Type 1 diabetes, Amino-glycosides were

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 3-6 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

90 T2DM cases were collected from both out patients and inpatients visiting Nalanda Medical College and Hospital, 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=90	Mean
Males	64	1.32±1.41
Females	26	1.28±0.94

In this study of 90 patients, 64 patients were males, and 26 were females with mean CRP levels of 1.32±1.41 and 1.28±0.94, 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	6	11.51	1.5
35-45	23	11.71	1.8
45-55	44	10.11	1.4
55-65	15	10.06	0.6
Above 65	2	8.46	0.0

In this study of 90 patients, HbA1C and CRP were correlated with age. Patients between age below 35 years were 6 with mean HbA1C and CRP of 11.51 and 1.5, respectively. Patients between age 35-45 years were 23 with mean HbA1C and CRP of 11.71 and 1.8, respectively. Patients between age 45-55 years were 44 with mean HbA1C and CRP of 10.11 and 1.4, respectively. Patients between 55-65 years were 15 with mean HbA1C and CRP of 10.06 and 0.5, respectively. Patients above 65 was 2 with mean HbA1C and CRP of 8.46 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	2	1.34
18-23	32	1.26
23-25	38	1.34
25-30	16	1.63
>30	2	1.32

In this study of 90 patients, patients with BMI below 18 was 2 with mean CRP of 1.34, BMI between 18 -23 were 32 with mean CRP of 1.26, BMI between 23-25 were 38 with mean CRP of 1.34, BMI 25-30 were 16 with mean CRP of 1.63, with BMI>30 was 2 with mean CRP of 1.32. 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	2	7.99
100-200	40	8.41
200-300	31	10.74
>300	18	11.55

In this study of 90 patients, FBS was correlated to HbA1C and CRP in different groups. Patients with FBS 0f 100 was 2 with HbA1C and CRP were 7.99 and 0.47,between 100-200 were 40, between 200-300 were 31,>300 were 18 had HbA1C of 8.41, 10.74, 11.55 and CRP of 0.59, 1.49, 2.24, respectively. FBS and HbA1C were directly correlated (Table 4).

Table 5: PPBS with HbA1C and CRP

PPBS	Number	HbA1C	CRP
140-200	15	7.88	0.41

200-300	28	9.14	0.65
300-400	30	10.28	1.91
400-500	14	11.43	2.44
>500	3	13.74	2.84

In this study of 90 patients, PPBS was correlated to HbA1C and CRP. Patients with PPBS between 140-200 were 15, between 200-300 were 28, between 300-400 were 30, between 400-500 were 14, and >500 were 4 had HbA1C 7.88, 9.14, 10.28, 11.43, 13.74 and CRP of 0.41, 0.665, 1.91, 2.44, 2.84, 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	5	1.78
100-200	35	0.81
200-300	22	1.87
Above 300	28	0.81

In this study of 90 patients, total cholesterol was compared to CRP. Number of patients with total cholesterol <100 was 5, between 100-200 were 35 between 200-300 were 22 with mean CRP of 1.78, 0.81, 2.87. 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	12	1.85
60-80	26	0.84
80-100	15	1.82
100-120	24	0.75
120-140	1	1.34
>140	12	2.29

In this study of 90 patients, LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 12, between 60-80 were 26, between 80-100 were 15, between 100-120 were 24, between 120-140 was 1, >140 were 12 with mean CRP levels of 1.85, 0.84, 1.82, 0.75, 1.34, 2.29. 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	3	2.14
20-40	43	1.41
40-60	41	1.22
>60	3	1.16

In this study of 90 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 3, between 20-40 were 43, between 40-60 were 41 and HDL

cholesterol >60 were 3 with mean CRP levels of 2.14, 1.41, 1.22, 1.16, respectively. There was a negative correlation between HDL cholesterol and CRP (Table 8)

Table 9: CRP and triglycerides

Triglycerides	Number	CRP
100-200	45	0.71
200-300	30	0.84
300-400	8	1.84
400-500	3	2.45
>500	4	2.45

In this study of 100 patients, triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 45, between 200-300 were 30, between 300-400 were 8, between 400-500 was 3 and with levels >500 were 4 with mean CRP levels of 0.71, 0.84, 1.84, 2.45, 2.45, 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	15	0.47
7-9	22	0.65
9-10	20	1.54
>10	33	2.28

In this study of 90 patients, patients with HbA1C <7 were 15 between 7-9 were 22, between 9-10 were 20, HbA1C >10 were 33 with mean CRP of 0.47, 0.65, 1.54, 2.28, respectively. There was significant correlation between CRP and HbA1C ($p<0.05$) (Table 10). The mean HbA1C of 90 patients initially was 10.12±1.78, and the mean CRP was 1.337±0.8814. A follow-up of 45 cases was done on patients who were not on statin therapy. On follow-up, the mean HbA1C of 45 cases had reduced to 7.55±1.37 ($p<0.05$) and mean CRP of those 45 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 45 cases. The initial mean HbA1C of 45 patients was 10.63±1.757, and the mean HbA1C on follow up was 7.58±1.38. The initial mean CRP of 45 patients was 0.94±0.675 and mean CRP on follow up was 0.42±0.59. HbA1C has significantly reduced in patients, after being put on treatment ($p<0.05$) and CRP levels also reduced ($p<0.05$).

Discussion

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[19]. 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[20]. 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[21]. 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[22].

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[23]. 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[24].

Ana et al found that hs-CRP levels were positively correlated with triglycerides[25]. This study also showed a positive correlation similar to other studies.

Conclusion

The present study concluded that the 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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