

STUDY TO DETERMINE THE RELATION BETWEEN HbA1C, LIPID PROFILE AND CRP IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

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Article Info: Received 08 February 2021; Accepted 05 March 2021

DOI: <https://doi.org/10.32553/ijmbs.v5i3.1816>

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Conflict of interest: No conflict of interest.

Abstract

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 Medicine in Nalanda Medical College and Hospital at 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: We 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.

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. Poor glycaemic control as indicated by elevated HbA1c levels accelerates the atherosclerosis process and significantly increases the risk of cardiovascular events.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 medicine in Nalanda Medical College and Hospital at Patna, Bihar India for one 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, 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

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.

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

100 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=100 | Mean |
|----------------|------------|-----------|
| Males | 70 | 1.22±1.31 |
| Females | 30 | 1.18±0.84 |

In this study of 100 patients, 70 patients were males, and 30 were females with mean CRP levels of 1.22 ± 1.31 and 1.18 ± 0.84 , 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 | 7 | 10.51 | 1.4 |
| 35-45 | 25 | 10.71 | 1.9 |
| 45-55 | 48 | 9.11 | 1.3 |
| 55-65 | 17 | 9.06 | 0.5 |
| Above 65 | 3 | 7.46 | 0.0 |

In this study of 100 patients, HbA1C and CRP were correlated with age. Patients between age below 35 years were 7 with mean HbA1C and CRP of 10.51 and 1.4, respectively. Patients between age 35-45 years were 25 with mean HbA1C and CRP of 10.71 and 1.9, respectively. Patients between age 45-55 years were 48 with mean HbA1C and CRP of 9.11 and 1.3, respectively. Patients between 55-65 years were 17 with mean HbA1C and CRP of 9.06 and 0.5, respectively. Patients above 65 were 3 with mean HbA1C and CRP of 7.46 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 | 1.24 |
| 18-23 | 36 | 1.16 |
| 23-25 | 43 | 1.24 |
| 25-30 | 17 | 1.53 |
| >30 | 2 | 1.22 |

In this study of 100 patients, patients with BMI below 18 was 2 with mean CRP of 1.24, BMI between 18 -23 were 36 with mean CRP of 1.6, BMI between 23-25 were 43 with mean CRP of 1.24, BMI 25-30 were 17 with mean CRP of 1.53, with BMI>30 was 2 with mean CRP of 1.22. 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 | 3 | 7.89 |
| 100-200 | 45 | 8.31 |
| 200-300 | 33 | 10.64 |
| >300 | 19 | 11.45 |

In this study of 100 patients, FBS was correlated to HbA1C and CRP in different groups. Patients with FBS of 100 was 3 with HbA1C and CRP were 7.89 and 0.37, between 100-200 were 45, between 200-300 were 33, >300 were 19 had HbA1C of 8.31, 10.64, 11.45 and CRP of 0.56, 1.39, 2.14, respectively. FBS and HbA1C were directly correlated (Table 4).

Table 5: PPBS with HbA1C and CRP.

| PPBS | Number | HbA1C | CRP |
|---------|--------|-------|------|
| 140-200 | 17 | 7.78 | 0.31 |
| 200-300 | 31 | 9.04 | 0.55 |
| 300-400 | 33 | 10.18 | 1.81 |
| 400-500 | 15 | 11.33 | 2.34 |
| >500 | 4 | 13.64 | 2.94 |

In this study of 100 patients, PPBS was correlated to HbA1C and CRP. Patients with PPBS between 140-200 were 17, between 200-300 were 31, between 300-400 were 33, between 400-500 were 15, and >500 were 4 had HbA1C 7.81, 8.97, 10.23, 11.45, 13.55 and CRP of 0.28, 0.52, 1.77, 2.4, 2.9, 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 | 6 | 1.68 |
| 100-200 | 39 | 0.91 |
| 200-300 | 25 | 1.77 |
| Above 300 | 30 | 0.71 |

In this study of 100 patients, total cholesterol was compared to CRP. Number of patients with total cholesterol <100 was 6, between 100-200 were 39 between 200-300 were 25 with mean CRP of 1.68, 0.91, 2.77. 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 | 13 | 1.75 |
| 60-80 | 29 | 0.94 |
| 80-100 | 17 | 1.72 |
| 100-120 | 27 | 0.65 |
| 120-140 | 1 | 1.24 |
| >140 | 13 | 2.19 |

In this study of 100 patients, LDL cholesterol was compared with CRP. Patients with LDL cholesterol <60 were 13, between 60-80 were 29, between 80-100 were 17, between 100-120 were 27, between 120-140 was 1, >140 were 13 with mean CRP levels of 1.75, 0.94, 1.72, 0.65, 1.24, 2.19. 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 | 4 | 2.04 |
| 20-40 | 48 | 1.31 |
| 40-60 | 45 | 1.12 |
| >60 | 3 | 1.06 |

In this study of 100 patients, HDL cholesterol was compared with CRP. Patients with HDL cholesterol between 0-20 were 4, between 20-40 were 48, between 40-60 were 45 and HDL cholesterol >60 were 3 with mean CRP levels of 2.04, 1.31, 1.12, 1.06, respectively. There was a negative correlation between HDL cholesterol and CRP (Table 8)

Table 9: CRP and triglycerides

| Triglycerides | Number | CRP |
|---------------|--------|------|
| 100-200 | 51 | 0.81 |
| 200-300 | 33 | 0.94 |
| 300-400 | 9 | 1.74 |
| 400-500 | 3 | 2.35 |
| >500 | 4 | 2.35 |

In this study of 100 patients, triglyceride levels were compared with CRP. Patients with triglyceride levels between 100-200 were 51, between 200-300 were 33, between 300-400 were 9, between 400-500 was 3 and with levels >500 were 4 with mean CRP levels of 0.81, 0.94, 1.74, 2.35, 2.35, 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 | 17 | 0.37 |
| 7-9 | 25 | 0.55 |
| 9-10 | 23 | 1.44 |
| >10 | 35 | 2.18 |

In this study of 100 patients, patients with HbA1C <7 were 17 between 7-9 were 25, between 9-10 were 23, HbA1C >10 were 35 with mean CRP of 0.37, 0.55, 1.44, 2.18, respectively. There was significant correlation between CRP and HbA1C ($p<0.05$) (Table 10). The mean HbA1C of 100 patients initially was 9.69 ± 1.78 , and the mean CRP was 1.137 ± 0.9874 . A follow-up of 50 cases was done on patients who were not on statin therapy. On follow-up, the mean HbA1C of 50 cases had reduced to 7.45 ± 1.27 ($p<0.05$) and mean CRP of those 50 patients reduced to 0.24 ± 0.48 ($p<0.05$). A comparison was made between initial HbA1C, CRP levels with HbA1C, CRP levels of follow up cases among 50 cases. The initial mean HbA1C of 50 patients was 9.314 ± 1.897 , and the mean HbA1C on follow up was 7.48 ± 1.28 . The initial mean CRP of 50 patients was 0.84 ± 0.875 and mean CRP on follow up was 0.32 ± 0.49 . 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.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 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 categories²⁰

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

We 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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