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General Medicine

# C-REACTIVE PROTEIN AND GLYCEMIC CONTROL IN ADULTS WITH TYPE 2 DIABETES MELLITUS - A PROSPECTIVE STUDY

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**ABSTRACT** **Background & Objectives:** Recent evidence suggests that poor glycemic control is significantly associated with the development of macrovascular complications of diabetes. Studies have indicated that C-reactive protein (CRP) is a significant risk factor for cardiovascular disease. Elevated CRP levels have also been linked to an increased risk of later development of diabetes. This study aims to determine the relation between CRP and HbA1c in individuals with Type 2 Diabetes Mellitus. **Methods:** Fifty patients with T2DM reporting to government general hospital, Vijayawada were included in the study. CRP levels were estimated by using commercially available kits and correlated with HbA1c. Other risk factors of Coronary artery disease were also associated with CRP Follow up was done on patients who were not on statin therapy with repeat HbA1c and CRP **Results:** In this study of 50 diabetic patients, there were 36 males and 14 females. The mean HbA1c of the follow-up patients was 7.3952 ± 1.3155, and mean CRP of the followed-up cases was 0.2857 ± 0.5237. It showed that both HbA1c and CRP levels had significantly reduced follow-up patients after putting them on treatment ($P<0.05$). It was also found that the lower the CRP level, the lower was the HbA1c. A positive correlation was found between CRP and HbA1c ($P<0.05$). **Interpretation & Conclusion:** In this study of 50 patients with T2DM, it was found that CRP is significantly correlated with HbA1c level. The decrease in the level of HbA1c also caused a decline in C - reactive protein level. A positive correlation was found between serum CRP and HbA1c in the initial group. A positive correlation of CRP and HbA1c was also found in the follow-up patients, showing that CRP levels were lower with better glycaemic control.

**KEYWORDS :** C-reactive protein; HbA1c; Glycaemia control; T2DM

## INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by defects in insulin secretion or action; chronic hyperglycemia can lead to microvascular and macrovascular complications if the blood sugars are not under optimal control. The glycaemic control is assessed by measuring glycated hemoglobin (HbA1c), its advantages and disadvantages.[1] To date, HbA1c is the widely used tool to determine the glycaemic status. As indicated by elevated HbA1c levels, poor glycemic control accelerates the atherosclerosis process and significantly increases the risk of cardiovascular events.[2] C-reactive protein measured by highly sensitive assays (hs-CRP) is a very sensitive marker of the arterial wall's inflammatory activity.[3,4] It is a significant predictor of cardiovascular risk apart from the traditional risk factors.[5,6]It is interesting to note that chronic hyperglycemia stimulates the release of various inflammatory cytokines (IL 6; TNF α) and induces the secretion of acute-phase reactants by the liver, which in turn results in elevation of CRP in association with elevated fasting plasma glucose.[7]C-reactive protein (CRP) and glycated-hemoglobin(HbA1c) are established risk factors for developing the cardiovascular disease. Patients with both hs-CRP and HbA1c in the upper quartiles (>0.44 mg/dl and >6.2%, respectively) are at exceptionally high risk for poor cardiovascular outcome.[8] Hence; this study was taken up to determine the relation between CRP and HbA1cin individuals with Type 2 Diabetes Mellitus.

## METHODS AND MATERIALS

The study was conducted in the Department of Medicine, a government general hospital. Vijayawada Patients with type 2 diabetes mellitus diagnosed based on WHO criteria were prospectively enrolled in the study from March 2019 to April 2020 of disease duration and treatment. A detailed history, Physical examination, height, weight, waist circumference, waist-hip ratio, body mass index, Hb, TC, DC, ESR, Blood Urea, Serum Creatinine, Urine examination, Blood sample for analysis for CRP, FBS, PPBS, HbA1c, Serum total cholesterol, Serum triglycerides, High-density lipoprotein, Low-density lipoprotein were taken. CRP was correlated with HbA1c statistically.

### Inclusion criteria

Patients with fasting venous blood glucose value equal to or more than 126mg/dl and postprandial glucose >200mg/dl

### Exclusion criteria

Patients on statins, thiazolidinediones (TZDs), and anti-inflammatory drugs, known to reduce CRP levels were excluded from the study. Patients with heart failure, acute febrile illness, renal, hepatic& malignant disorders, chronic illnesses, asymptomatic infections, and smokers were also excluded from the study

### Methods

FBS and PPBS were drawn at entry, CRP and HbA1c at entry and subsequent follow-up with a minimum gap of 3 months. All samples were drawn on the same day. Patients were put on OHA / insulin to control blood sugar and dietary control and exercise. Those who had to be started on statins and TZDs were excluded from the study.

### Statistical Analysis

Statistical analysis was done using the SPSS package and MS Excel. Student's t-test is used. Pearson correlation and p values are calculated. P values < 0.005 were considered to be significant.

## RESULTS

Fifty T2DM cases were collected from both outpatients and inpatients visiting the government general hospital, Vijayawada, to estimate Glycemic status and was correlated with CRP levels.

Out of 50 patients in this study, there were 36 males and 14 female patients. The minimum age was 34 years old, and the maximum age was 75 years old. In this study, the minimum waist-hip ratio was 0.84. Maximum waist-hip ratio was 1.09 with a mean of 0.99 ± 0.04, minimum body mass index was 17, and maximum 32 with a mean of 23.77 ± 2.64, and minimum FBS 88. The maximum was 400 with mean 228.62 ± 83.165, minimum PPBS was 143 and maximum was 624 with mean 310.08 ± 104.47, minimum HbA1c was 7.0 and maximum HbA1c was 14.0 with mean 9.65 ± 1.88, minimum Total cholesterol was 97.0 and maximum was 297 with a mean of 180.70 ± 35.39, minimum LDL cholesterol was 0 and maximum was 202 with mean 92.72 ± 37.227, minimum HDL was 12 and maximum was 82 with mean 39.32 ± 10.77, minimum Triglyceride was 100 and maximum 759 with mean 233 ± 120.20, minimum Creatinine was 0.60 and maximum 1.20 with mean 0.94 ± 0.15, minimum CRP was 0 and maximum was 2.4 with mean 1.218 ± 1.1759.These values are given in the following Table:

**Minimum, Maximum Mean and Standard Deviation of Parameters studied.**

| | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| WAIST HIP RATIO | 0.84 | 1.09 | 0.99 | 0.04 |
| BODY MASS INDEX | 17.00 | 32.00 | 23.77 | 2.64 |
| FBS | 88 | 400 | 228.62 | 83.165 |
| PPBS | 143 | 624 | 310.08 | 104.47 |
| HbA1c | 7.0 | 14.0 | 9.65 | 1.88 |
| TOTAL.CHOL | 97.00 | 297.00 | 180.70 | 35.39 |
| LDL-CHOL | 0 | 202 | 92.72 | 37.227 |
| HDL-CHOL | 12.00 | 82.00 | 39.32 | 10.77 |
| TRIGLYCERIDE | 100.00 | 759.00 | 233.30 | 120.20 |
| CREATININE | 0.60 | 1.20 | 0.94 | 0.15 |
| CRP | 0.00 | 2.4 | 1.218 | 1.1758 |

**HbA1c and CRP.**

The patients were divided into four groups: HbA1c less than 7, 7 to 9, 9 to 10, and more than 10. The number of Patients with HbA1c less than 7 was 9 with a mean CRP of 0.40, number of patients with HbA1c between 7 and 9 were 14, with mean CRP 0.51, patients with HbA1c between 9 and 10 were 11 with mean CRP of 1.41 and patients with HbA1c more than ten were 16 with mean CRP 2.15. This showed that the level of CRP positively related to increase in glycosylated hemoglobin (HbA1c). There was a significant correlation between CRP and HbA1c ($P<0.05$). Values are shown in Table

**CRP AND HbA1c**

| HbA1c | No: of patients | CRP |
|---|---|---|
| <= 7 | 9 | 0.40 |
| 7 – 9 | 14 | 0.51 |
| 9 – 10 | 11 | 1.41 |
| >10 | 16 | 2.15 |

**CRP and Lipid Profile (Correlation Coefficient)**

CRP was correlated with lipid profile (Total cholesterol, Triglyceride, LDL and HDL) statistically with Pearson's correlation. CRP had a significant positive correlation with total cholesterol and Triglyceride ($P<0.05$), and there was no significant correlation with LDL cholesterol ($P>0.05$). But there was a negative correlation with HDL cholesterol.

Values are shown in the following Table

**CRP and Lipid Profile**

| | | T.CHOL | TRYGL | LDL | HDL |
|---|---|---|---|---|---|
| CRP | Pearson Correlation | 0.53 | 0.37 | 0.11 | -0.14 |
| | P Value | 0.00 | 0.01 | 0.46 | - |

**Follow-up Cases**

HbA1c and CRP of 50 initial and 20 follow up cases. The mean HbA1c of 50 patients was initially $9.6500 \pm 1.8816$ and meant CRP $1.1520 \pm 0.9984$. A follow-up of 20 subjects was done on patients who were not on statin therapy. On follow-up, the mean HbA1c of 20 cases followed up had reduced to $7.3952 \pm 1.3155$ ($P<0.05$) and mean CRP of those 20 patients reduced to $0.2857 \pm 0.5237$ ($P<0.05$). This shows that HbA1c has decreased significantly in patients after treatment and lower the HbA1c, the CRP levels also reduced. Values are shown in Table

**HbA1c and CRP of 50 initial and 20 follow up cases**

| | (HbA1c 1) Initial (50) | (HbA1c 2) Follow Up (20) | (C.R.P. 1) Initial (50) | (C.R.P. 2) Follow-up (20) |
|---|---|---|---|---|
| Mean | 9.6500 | 7.3952 | 1.1520 | 0.2857 |
| SD | 1.8816 | 1.3155 | 0.9984 | 0.5237 |
| P Value | | 0.0000 | | 0.000359 |

## DISCUSSION

The prevalence of T2DM is increasing in all populations worldwide. It is a major risk factor for death and numerous nonfatal complications. Several recent intervention studies have undisputedly proved that the complications of T2DM can be efficiently prevented by lifestyle modification, in high risk individuals. C-reactive protein (CRP), 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, including myocardial infarction and stroke. CRP has also been linked to an increased risk of later development of diabetes. Previous research has also established that CRP levels are higher in people with diabetes and is associated with HbA1c in people without diabetes.[9,10] CRP concentration distribution among participants with a BMI of 25 to <30, 30 to <35, 35 to <40, and >40 kg/m2 were 1.51 (95% CI 1.23–1.86), 3.19 (2.60–3.91), 6.11(4.67–7.98), and 9.30 (6.43–13.46), respectively, compared with participants with a BMI <25k g / m2. The reasons for the apparent association between C-reactive protein and BMI are not clear, but several explanations are possible. First, individuals with obesity are at increased risk for various chronic diseases, several of which are also characterized by elevated C-reactive protein concentrations. Second, subclinical disease may have been responsible. Third, it is possible that obesity is accompanied by an inflammatory component unrelated to accompanying clinical or subclinical pathology.[9] In this study of 50 patients there were 72% male and 28% female. Male patients had mean CRP of 1.1916 and female patients had mean CRP of 1.2857. The female patients had a higher CRP levels compared to male patients but this difference was not significant statistically ($p>0.05$). This could be attributed to the smaller number of females in this study. In a cross-sectional study conducted by Gohel et al, a significant positive linear relationship was observed between hsCRP and HbA1c.[10] Li et al, Khan DA et al, and Sarinnapakorn V et al, also had similar observation in their studies.[11-13] In the present study, the different cholesterol levels were correlated with the CRP levels. CRP concentration distribution among patients with total cholesterol <100, 100- 200, 200-300 were 0, 0.95, and 2.13. These values show that CRP significantly increases with elevation of total cholesterol ($p<0.05$) and conforms with other studies. In this study mean CRP when correlated with HbA1c at different levels < 7, 7-9, 9-10, >10, were 0.40, 0.51,1.41 and 2.15 respectively. This showed that a rise in HbA1c is significantly correlated with increasing values of CRP ($P < 0.05$). Therefore, this study shows that higher glycaemic levels are associated with higher CRP values.

## CONCLUSION

There is a positive correlation between glycemic control (HbA1c) and CRP levels; Better glycemic control results in significant reduction in the hsCRP levels.

**Limitations of the Study**

The CRP values were measured using a Semi-quantitative method. Patients who had dyslipidaemia and who were put on statins were excluded from follow up. This partially accounted for the low number in the follow up cases.

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