C-reactive protein and glycemic control in adults with type 2 diabetes mellitus

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Abstract

Objective: To find a correlation between glycemic control and C-reactive protein (CRP) in patients with type 2 diabetes mellitus (T2DM) and to assess if good control of glycosylated hemoglobin (HbA1c) decreases the CRP values.

Materials and Methods: The study included 50 patients with T2DM whose detailed clinical history and physical examination were done. Evaluation of parameters such as height, weight, waist–hip ratio, body mass index, Hb, total blood count, differential count, erythrocyte sedimentation rate, blood urea, and serum creatinine was done. Urine examination and blood samples were obtained for analysis of CRP, fasting blood sugar, postprandial blood sugar, HbA1c, serum total cholesterol, serum triglycerides, high-density lipoprotein, and low-density lipoprotein. CRP was correlated with HbA1c statistically.

Result: The study reveals that levels of CRP and HbA1c were bi-directionally correlated with P < 0.05. Better glycemic control is leading to the reduction in HbA1c also resulted in a decrease in CRP levels (P = 0.000).

Conclusion: There exists a strong correlation between HbA1c and CRP in T2DM. Hence, CRP is an additional marker of better glycemic control.

Keywords
C-reactive protein, glycosylated hemoglobin, type 2 diabetes mellitus

Introduction

The presence of type 2 diabetes mellitus (T2DM) is on an upward trend in all populations worldwide. It is increasingly the main risk factor for mortality and numerous non-fatal complications. Several latest interventional studies have undoubtedly proven that T2DM can be effectively prevented by the modifying lifestyle in high-risk category patients. According to the World Health Organization, 19% of the world’s diabetic population currently resides in India, and there may be increment from 35 million to nearly 80 million by 2030.¹ According to The International Diabetes Federation, the diabetic population in India would increase from 41 million in 2006 to 70 million by the year 2025.² This rising trend predicts significant health problem to the population as a result of diabetes in India.³ But unfortunately due to lack of awareness, more than 50% of the diabetics in India are unaware of their diabetic status which in turn adds to the disease affliction.⁴

Asian Indians tend to have a greater degree of central obesity despite having lower prevalence of obesity.⁵,⁶ Insulin resistance with visceral fat is more among Asian Indians. Data from the Bangalore DM registry group reported an incidence rate of 1.68/10,000 in 1997.⁷ Clinical and biochemical abnormalities among Asian Indians are one of the major contributing factors toward T2DM.⁸⁻¹⁰ C-reactive protein (CRP), synthesized in the liver and is one of the most sensitive acute phase reactants after tissue damage of inflammation which activates the classical complement pathway as a response to the inflammatory reaction is regulated by circulating levels of interleukin-6 and may cause coronary heart disease incidence in healthy subjects.¹¹ CRP levels in serum can rise dramatically after myocardial infarction, stroke, stress, trauma, infection, inflammation, surgery, or neoplastic proliferation and this increase occurs within 6 h of the start of inflammation, and the level may be up to 2000 times the normal.¹² High-sensitive CRP (hs-CRP) indicated as inflammation is a measurement of CRP of lower concentration. Elevated CRP levels and poor glycemic control leads to
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1.128±1.1758

Materials and Methods

This study included 50 type 2 diabetic patients whose detailed clinical history and physical examination were done. Their height, weight, waist circumference, waist–hip ratio, body mass index (BMI), Hb, total count, differential count, erythrocyte sedimentation rate, blood urea, serum creatinine were evaluated. Urine examination and blood samples were obtained for analysis of CRP, fasting blood sugar (FBS), postprandial blood sugar (PPBS), HbA1c, serum total cholesterol, serum triglycerides, high-density lipoprotein (HDLC) and low-density lipoprotein (LDL). CRP was correlated with HbA1c statistically. In the study, the inclusion criteria were patients with fasting blood glucose >126 mg/dl and postprandial glucose >200 mg/dl, and exclusion criteria were patients on statins, thiazolidinediones, and anti-inflammatory drugs. All the values of FBS, PPBS, CRP, and HbA1c were measured at baseline and a follow-up of these patients was done at an interval of 3 months. After collecting, all the samples patients were put on oral hypoglycemic agents and insulin along with exercise and diet control. For CRP, the diagnostic reagent kit for the in vitro detection of CRP in human serum by qualitative and semi-quantitative rapid latex slide test was used. The basis of the detection is immunologic reaction between CRP which acts as an antigen and latex particles coated with monospecific anti-human CRP sensitized to detect levels of CRP greater than 6 µg/ml.

The latex slide test is advantageous due to its rapid performance for detection of CRP, and we detect CRP levels milligram per liter by multiplying the highest dilution giving clear cut agglutination with a factor of 6 (sensitivity of antigen 6 mg/l). The detection limit of this test is 0.6 mg/dl. For detecting HbA1c kit used was Teco Diagnostics Glycohemoglobin Reagent Set which was based on hemolyzed preparation, results of the unknown should be determined in the following manner:

Percentage glycohemoglobin (unknown)=R (unknown)×Standard concentration (R)  
R unknown=ratio unknown=absorbent of glycol unknown/absorbent of total Hb unknown.

R standard=Absorbent of glyco standard/Absorbent of total Hb standard.

An unknown sample had glycol Hb absorbent=0.962 and total Hb absorbent=0.76 glyco Hb. Statistical analysis was performed using SPSS package and MS Excel. Student’s t-test and χ² test were used. Pearson correlation and P values were calculated. The significant value considered is found to be P < 0.05.

Results

Around 50 T2DM cases were collected, and various parameters related to diabetes were studied which was further correlated with CRP levels in this study. Cases were followed with a minimum gap of 3 months and the parameters were repeated. The results are tabulated and analysis of the data was done.

Out of 50 patients in this study, there were 36 males and 14 female patients.

The minimum age was 34 years old and maximum age was 75 years old. The mean and standard deviation of the parameters studied were tabulated [Table 1]. On comparing HbA1c and CRP, 50 patients were divided into 4 group. Coronary artery disease (CAD) is a risk factor in patients suffering from T2DM and is considered to be one of the important parameter in this study [Table 2]. CRP was correlated with HbA1c with Pearson correlation, and P values were calculated shown in Table 3 which concluded that CRP is directly related with cardiovascular diseases in patients suffering from T2DM. Numeric tabulation of data for triglyceride and CRP [Table 4], PPBS, HbA1c and CRP [Table 5] and FBS, HbA1c, and CRP [Table 6] were done. HbA1c and Triglyceride showed highly significant correlation with CRP. Other risk factors such as waist–hip ratio, body weight, BMI, LDL cholesterol, and serum creatinine also had positive

Table 1: Minimum, maximum mean and standard deviation of parameters studied

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist–hip ratio</td>
<td>0.84</td>
<td>1.09</td>
<td>0.99±0.04</td>
</tr>
<tr>
<td>Body mass index</td>
<td>17.00</td>
<td>32.00</td>
<td>23.77±2.64</td>
</tr>
<tr>
<td>FBS</td>
<td>88</td>
<td>400</td>
<td>228.62±83.165</td>
</tr>
<tr>
<td>PPBS</td>
<td>143</td>
<td>624</td>
<td>310.08±104.47</td>
</tr>
<tr>
<td>HbA1c</td>
<td>7.0</td>
<td>14.0</td>
<td>9.65±1.88</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>97.00</td>
<td>297.00</td>
<td>180.70±35.39</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>0</td>
<td>202</td>
<td>92.72±37.227</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>12.00</td>
<td>82.00</td>
<td>39.32±10.77</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>100.00</td>
<td>759.00</td>
<td>233.30±120.20</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.60</td>
<td>1.20</td>
<td>0.94±0.15</td>
</tr>
<tr>
<td>CRP</td>
<td>0.00</td>
<td>2.4</td>
<td>1.128±1.1758</td>
</tr>
</tbody>
</table>

FBS: Fasting blood sugar, PPBS: Post prandial blood sugar, HbA1c: Glycosylated hemoglobin, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, CRP: C-reactive protein, SD: Standard deviation

Table 2: CRP and risk factors for CAD

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Number of patients</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤7</td>
<td>9</td>
<td>0.40</td>
</tr>
<tr>
<td>7-9</td>
<td>14</td>
<td>0.51</td>
</tr>
<tr>
<td>9-10</td>
<td>11</td>
<td>1.41</td>
</tr>
<tr>
<td>&gt;10</td>
<td>16</td>
<td>2.15</td>
</tr>
</tbody>
</table>

CRP: C-reactive protein, HbA1c: Glycosylated hemoglobin, CAD: Coronary artery disease

macrovacular damage and causes increased risk of diabetes in future.

Patients with both hs-CRP and glycosylated hemoglobin (HbA1c) in the cardiovascular outcome.[13] Hence, this study was taken up to relate CRP and HbA1c in individuals with T2DM.
correlation but were of lesser significance, whereas HDL showed a negative correlation. According to Pearson correlation, values obtained <0.05 which was highly significant, for total cholesterol was 0.53 with $P < 0.05$, which was again highly significant and for triglyceride was 0.37 with $P < 0.05$ which was also highly significant.

**Discussion**

DM has reached epidemic proportions worldwide. Recent intervention studies have proven that the lifestyle modification can effectively prevent T2DM in high-risk individuals. Increased CRP is an indicator for increased chances for cardiovascular disease. Late development of diabetes has been related to raised CRP. The CRP levels are known to increase under events of myocardial infarction and stroke.

CRP levels are increased in patients with diabetes and also is associated with HbA1c in people without diabetes.\[^{14,15}\] The CRP levels are significantly increased in diabetics. However, literature is obscure about the correlation of glycemic control in terms of HbA1C and levels of CRP. This study has, therefore, gone into the various factors that are related both to CRP and T2DM and the relationship between them. The minimum and maximum values of each parameter were noted before the analysis of results. Although BMI and CRP are strongly related, this association is independent of parameters strongly affiliated to BMI such as age, sex, ethnicity, education, and diabetic status. In this study, a strong correlation is present between CRP and a host of other variables such as age, BMI, waist circumference, waist–hip ratio, systolic and diastolic blood pressure, serum triglyceride, family history of diabetes, physical inactivity, use of antihypertensive drugs, and hormonal replacement therapy. However, a strong positive correlation exists between CRP and risk of developing diabetes in women.\[^{16}\]

The coronary heart disease risk score’ given by Framingham, Michelle and others stated that the CRP levels were significantly related to 10-year Framingham coronary heart disease risk categories.\[^{17}\]

In a study by Ridker related to CRP and markers of inflammation for prediction of cardiovascular disease among women and others in multivariate analyses, it was found the only plasma markers that independently predicted risk of cardiovascular disease were hs-CRP and the ratio of total cholesterol to HDL.\[^{18}\]

Dyslipidemia has been proven as one of the major risk factor for CHD. Both triglyceride and LDL-cholesterol are associated with atherogenic process, and there is increasing evidence that HDL-cholesterol prevents atherogenesis. In a study by Tiejian Wu et al. on “Associations between serum CRP and fasting insulin” the values of CRP were compared with insulin, glucose, and HbA1c after adjusting with age, ethnicity, education, poverty index, cigarette smoking, alcohol use, and leisure time physical activity. After adjustment of mean insulin among men and women, it was found that there is a concomitant increase in HbA1c level with CRP.\[^{19}\]

King et al. found a strong correlation between HbA1c levels and CRP. Besides, they also found that CRP levels were associated with HbA1c levels.\[^{20}\]
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Conclusion

In this study, it is found that there is a positive correlation between serum CRP with HbA1c and other risk factors of CAD. The strongest association of CRP was found with HbA1c, total cholesterol and triglyceride levels.

The finding regarding BMI in this study, contrary to others, suggest that CRP level was not significantly associated with BMI and that inflammation as a potential mechanism in T2DM may be independent of obesity and may lead to an increased risk of cardiovascular events. Follow-up studies revealed that better glycemic control resulted in 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 dyslipidemic profile, seen in T2DM.

References
