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Research Article

STUDY TO DETERMINE THE ASSOCIATION BETWEEN INFLAMMATORY MARKER (C-REACTIVE PROTEIN) AND HBA1C IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objectives: Patients with type 2 diabetes exhibit subclinical inflammation and nearly all signs of systemic inflammation, which characterized by high circulating levels of inflammatory parameters. The present study aimed to assess the levels of the inflammatory markers such as C-reactive protein (CRP) in patients with type 2 diabetes mellitus and to correlate their values with the hemoglobin A1c (HbA1c) levels.

Methods: This cross-sectional study was conducted on 78 patients with type 2 diabetes in Patna Medical College and Hospital, Patna. All patients had laboratory investigations including HbA1C and CRP, patients were assessed according to glycemic status, patients with under control of diabetics (HbA1C level was equal to or <6.5%), and patients with poorly-controlled diabetics (HbA1c level was >6.5%).

Results: Statistically significant association was observed between CRP levels and level of HbA1c. The CRP level was significantly higher in poorly-controlled diabetic patient than who with well-controlled diabetics (p=0.017).

Conclusions: There is positive correlation between the level of glycemic control (HbA1c) and CRP levels; better glycemic control results in significant reduction in the highly sensitive C-reactive protein levels.

Keywords: C-reactive protein, Correlation, Glycemic control, Highly sensitive C-reactive protein, Hemoglobin A1c.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by the 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 glycemic control is assessed by the measurement of glycated hemoglobin (HbA1c) which has its own advantages and disadvantages [1]. Till date, HbA1c is the widely used tool to assess the glycemic status. Poor glycemic 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 hyperglycemia stimulates the release of various inflammatory cytokines (IL6; TNFα) 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 are associated with an increased risk of future development of DM [8]. Furthermore, people with DM had elevated levels of CRP than non-diabetics [9,10]. We understand that both chronic systemic inflammation and hyperglycemia contribute to the development and progression of atherosclerotic cardiovascular disease. Experimental and clinical studies have confirmed the inter-relationship between CRP, hyperglycemia, and atherosclerosis [11,12]. In states of elevated CRP, hyperglycemia exaggerates the proatherogenic effects of CRP [12,13]. Few studies which had assessed the relationship between CRP levels and the level of glycemic status showed conflicting results; some studies had proven the positive corelation between glycemic control and CRP levels [14,15], while some failed to do so [6]. Furthermore, the effect of good glycemic control on CRP levels is not clear. The aim of this study was to determine the relationship between HbA1C, lipid profile, and CRP in individuals with type 2 DM (T2DM).

METHODS

This prospective observational study was carried out in the Department of pathology, PMCH, Patna, 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 were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

- Patients on statins, thiazolidinediones, 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
- Aminoglycosides.

Methodology

Informed consent was taken from the patients. Detailed history, physical examination, which includes height, weight, and body mass index (kg/m^2), were measured. Resting pulse rate, blood pressure, and body temperature were recorded. HbA1c was measured by the HPLC method on Hb-Vario and a CRP level was measured by the quantitative method on the vitros chemistry 4600 system. In accordance with the American Diabetes Association, diabetes is diagnosed at an HbA1c of ≥6.5% (Table 1).

CRP values were divided into normal (<6 mg/L), borderline (6–10 mg/L), and high (>10 mg/L).

The relationship between CRP with HbA1c was recorded by Pearson's correlation coefficient. The data were entered into an Microsoft Excel spreadsheet and analysis was performed using the Statistical Package for the Social Sciences version 26.0. Statistical analysis was done using Pearson's correlation test and data were expressed as mean±Standard deviation for each parameter. $p<0.05$ was considered to be significant.

RESULTS

A total of 78 patients were included in the study, of whom 36 (46.3%) were male and 42 (53.7%) were female. The mean age was 59.12±12.39 years and the mean weight was 85.80±15.90 kg. The demographic characteristics of the study population are shown in (Table 2).

When the patients were assessed according to HbA1C, of these 78 patients, 15 (18.8%) had their diabetes under control (HbA1C level was <5.7%), whereas 20 (25.3%) patients were in a prediabetic state and 43 (55.8%) were poorly-controlled diabetics (HbA1c level >6.5%) (Table 3).

A significant association was also noted between the level of CRP and HbA1C. The patients who have HbA1C level <7.5% are more likely to have higher CRP level than others with controlled HbA1C ($p<0.05$) (Table 3).

DISCUSSION

T2DM is a major risk factor for death and numerous nonfatal complications. 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. CRP levels are higher in diabetic as compared to non diabetic people . Recently, inflammation has been implicated in the development and progression of atherosclerosis. [11] It is very important to study and monitor inflammatory markers to identify patients at higher risk for vascular complications. This study was conducted to determine the relationship between HbA1c and CRP in diabetic patients. In this study, it was observed that most (57.7%) of the patients were aged 40–60 years. The mean age was found (59.12±12.39) years. In a similar report, Muhammad *et al*. [12] found that the mean age of the study population was 51.5±9.5 years. The majority (55.6%) of the patients were female and (53.7%) are female in the present study which is in concordance with Muhammad *et al*. [12] The present study suggests that the association between CRP and diabetes risk was stronger in women than in men, which is similar to the Hu *et al*. [13] and Pichandi *et al*. [14], and discordance to Ahmed *et al*. [16].

Table 1: American Diabetes Association, HbA1c level

Result	HbA1c
Normal	<5.7%
Prediabetes	5.7% to 6.4%
Diabetes	>6.5%

Table 2: Demographic characteristics of the study population

Variables	Values
Total patients, n (%)	78 (100%)
Age (years)	59.12±12.39
Weight	85.80±15.90
Gender	
Male, n (%)	36 (46.3%)
Females, n (%)	42 (53.7%)

Table 3: Correlation between HBA1C with CRP

HBA1C		CRP			Value	p-value
		Total	Normal CRP level	High CRP level		
Total	n (%)	78	49 (62.8%)	29 (37.2)	5.17	0.017
Well-controlled group	n (%)	35	35	0		
Poorly-controlled group	n (%)	43	17	26		

CRP: C-Reactive protein, HBA1C: Hemoglobin A1c

Gender differences in plasma CRP are well documented, with circulating levels being higher in women [15,17,18]. This difference is not fully understood but could be related to gender differences in both visceral and subcutaneous fat, an important factor in CRP levels [18] or to differences in estrogen, which is known to increase CRP level [19]. In this study, it was found that CRP levels increase significantly with an increase in total cholesterol. Michelle *et al*. [20] indicated that CRP levels were significantly associated with the 10-year Framingham coronary heart disease risk category king and others showed in unadjusted analyzes that higher HbA1C is significantly associated with higher CRP levels [21]. This study showed that increases in HbA1C were significantly correlated with increases in CRP levels. Fawaz *et al*. [22] found a positive correlation between inflammatory markers (CRP) and HbA1c in their study, which supports other studies [23,24]. This can be explained by the fact that HbA1c reflects the biological activities of hyperglycemia and advanced glycation end-products, all of which can trigger inflammation [25]. Hu *et al*. examined the risk ratio of type 2 DM for different serum CRP levels and found that the association between CRP and diabetes risk was stronger in women than in men [13]. In this study, women had higher CRP levels compared to men [15,17,18]. In the present study, 32 (20.8%) of 154 cases had normal CRP observed in prediabetics. The present study shows that 6.4% of the control group have a higher CRP value, which could be due to various forms of inflammatory processes. One of the aims of the study was to investigate the association between CRP and HbA1c in adults with diabetes. Current research shows a link between hyperglycemia and inflammation. This evidence is consistent with the findings of the present study, which further documents the link between hyperglycemia and inflammation in adults with diabetes The limitation of this study is the small sample size. A large sample required community-based assessment. Other inflammatory markers need to be studied with a larger sample size in DM. The lack of statistical significance in multivariate-adjusted analysis with a trend toward an association could be due to the relatively small sample size. As CRP is an inflammatory marker, alteration in its value can occur in several other inflammatory conditions. Those conditions were not analyzed in the study. Hence, a further larger study is necessary taking into consideration of all the confounding factors.

CONCLUSIONS

Our study reported correlations between elevated glycated hemoglobin levels, which reflect poor glycemic control, and CRP levels which are inflammatory markers that reflect the role of glycemic control and subclinical inflammation in patients with T2DM.

CONFLICTS OF INTEREST

None.

SOURCE OF FUNDING

Self.

ETHICAL CLEARANCE

Taken.

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