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Original Article

Study to determine between HbA1c and C-reactive protein in Diabetes mellitus

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ABSTRACT

Background: Studies have shown that C-reactive protein, as an inflammatory marker, is an important risk factor for insulin resistance and type 2 diabetes mellitus. Measurement of inflammatory markers like CRP will improve the prediction of the risk of these events. This study aimed to investigate the relationship between hemoglobin A1c, one of the indicators of diabetes, and the highly sensitive C-reactive protein, one of the indicators of inflammation.

Materials and Methods: This prospective observational study was carried out in the Department of Pathology, Patan Hospital, and included 154 subjects each of Type 2 diabetic patients and healthy control.

Results: Most (57.7%) of the patients were between 40 to 60 years with a female preponderance of (0.5:1). The HbA1c and CRP values were high in the case group compared to the control group and analysis shows statistical significance. There was a statistically significant association between CRP level in the diabetic group (patient with HbA1C > 5.7%) and the control group (patient with HbA1C ≤ 5.7%) (p-value <0.05).

Conclusions: Higher HbA1c levels are associated with increased CRP, demonstrating that poorly controlled diabetes mellitusis associated with increased systemic inflammation. Timely screening and early detection of elevated CRP in diabetes mellituspatients can prevent further complications and consequences.

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INTRODUCTION

The worldwide prevalence of diabetes mellitus is 9.2% in 2020.[1] The burden of diabetes mellitus (DM) has been increasing worldwide. In 2019, approximately 463 million adults aged 2079 years were living with diabetes worldwide, causing an estimated 1.5 million deaths. This number is expected to rise to 700 million by 2045.[2]

Inflammation plays a role in the pathogenesis of cardiovascular events and measuring markers of inflammation will improve the prediction of the risk of

these events. Highly sensitive C-reactive protein is the most reliable marker of cardiovascular inflammation.[3] The hepatic synthesis of several acute-phase proteins, including serum ferritin and highly sensitive C-reactive protein (CRP), thought to contribute to insulin resistance and atherosclerosis, is triggered by inflammation. Type 2 diabetes is associated with an increased risk of cardiovascular disease, and serum levels of CRP are a strong predictor of this risk. A higher rate of type 2 DM was observed with elevated CRPI levels.[4, 5]

Hemoglobin A1c (HbA1c) can be measured in blood samples taken from patients whether they are fasting or not. Thus, it can be used as an indicator of diabetes instead of measuring blood sugar levels before meals or 2 hours after meals. The American Diabetes Association added HbA1c 6.5% as a diagnostic criterion for diabetes.[6, 7]

The presence of dyslipidemia is often observed in individuals with diabetes, and it has been linked to a higher risk of atherovascular events and potentially cardiovascular disease in the future. Diabetes and prediabetes are significant risk factors for cardiovascular disease. Unfortunately, the mortality rate for cardiovascular disease in diabetic patients is alarmingly high at 70%, and the risk of such mortality is 24 times greater in diabetics compared to healthy individuals.[8]

MATERIAL AND METHODS

This was a prospective study conducted in the Department of Pathology of Patan Hospital from April 2020 to May 2022. All patients of both sexes of all age groups with diagnosed diabetes mellitus who consented to participate were included in the study. Patients with acute febrile illness, and malignant disorder. All patients of both sexes of all ages with diagnosed cases of diabetes mellitus were included in the study. The study included 156diabetic patients with increased CRP and 156 control cases with normal glycated hemoglobin and CRP level. HbA1c was measured by the HPLC method on Hb-Varioand a CRP level was measured by the quantitative method on the Vitros chemistry 4600 system. In accordance with the American Diabetes Association (ADA), diabetes is diagnosed at an A1C of greater than or equal to 6.5 percent (Table 1).[9]

Table 1: American Diabetes Association (ADA), HbA1c level

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

CRP values were divided into normal (<6 mg/L), borderline (6-10 mg/L), and high (>10 mg/L).[10] The relationship between CRP with HbA1c was recorded by Pearson's correlation coefficient.

The data was entered in an MS Excel spreadsheet and analysis was performed using Statistical Package for Social Sciences (SPSS) version 26.0. Statistical analysis was done using Pearson's correlation test and data was expressed as mean ±SD for each parameter. A p-value of < 0.05 was considered to be significant.

RESULTS

This cross-sectional study was performed on 312 patients. The present study group consisted of 154 diabetic patients with increased CRP and 154 matched controls with normal HbA1C levels having CRP test results. Diabetic cases aged < 40 years (17.5%) and >40 years (82.5%) were segregated by gender. Most (57.7%) of the patients were between 40 to 60 years old with a range of 19 to 84 years. The mean age of patients was (53.0%±13) which is significantly higher than the control group (38.8±11.8) followed by the 61-80 age (31.4%) group and 2.5% in the age group over 81 years. The majority (65.6%) of the patients were female and (34.4%) were male with a male-to-female ratio of 0.5:1. The HbA1c and CRP values were high in the case group compared to the control group and analysis shows statistical significance (Table 2). Similarly, diabetic patients had significantly high cholesterol.

Table 2: Comparison of HbA1c and CRP among the patient and control group

Parameters	Control (n=154)	Case (n=154)
HbA1C	5.3±1.2	7.6±2.5
CRP	2.9±1.4	23.6±41.2

When the patients were assessed according to HbA1C, of these 154 patients, 29 (18.8%) had their diabetes under control (HbA1C level was less than 5.7%), whereas 39 (25.3%) patients were in a prediabetic state and 86 (55.8%) poorly controlled diabetics (HbA1c level > 6.5%). (Table 3)

Table 3: HbA1C values according to age group

Age group	Normal	Prediabetic	Diabetic	Total
<40	9/29	3/39	15/86	27/154
>40	20/29	36/39	71/86	127/154

In this study of 154 cases, 32 (20.8%) had normal CRP, and 122 (79.2%) had elevated. There was a statistically significant association between CRP level, cholesterol level, and level of HbA1c. The CRP level was significantly higher in the diabetic than in the control (p-value <0.05).

DISCUSSION

Growing evidence supports the concept that chronic, low-grade, inflammatory states may have a pathogenic role in inflammatory response (IR). Recently, inflammation has been implicated in the development and progression of atherosclerosis.[11] 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. 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 (53.0%±13) years with a range from 19-84 years, significantly higher than the control group. 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 (65.6%) of the patients were female (65.7%) in the present study which is in concordance with Muhammad et al.[11] The present study suggests that the association between CRP and diabetes risk was stronger in women than in men, which is similar to the Huet al.[13] and Pichandi, et al.[14] and discordance to Ahemed et al.[15] Gender differences in plasma CRP are well documented, with circulating levels being higher in women.[16-18] 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 endproducts, 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.[26] In this study, women had higher CRP levels compared to men.[16- 18] In the present study, 32 (20.8%) of 154 cases had normal CRP observed in prediabetics. The current 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 hemoglobin A1c (HbA1c) in adults with diabetes. Current research shows a link between hyperglycemia and inflammation. This evidence is consistent with the findings of the current study, which further documents the link between hyperglycemia and inflammation in adults with diabetes.

The limitation of this study isthe small sample size. A large sample required community-based assessment. Other inflammatory markers need to be studied with a larger sample size in diabetes mellitus. The lack of statistical significance in multivariate-adjusted analysis with a trend towards 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

Higher HbA1c levels are associated with increased CRP, demonstrating that poorly controlled DM is associated with increased systemic inflammation. CRP is an additional marker for better glycemic control and also correlates with dyslipidemia. Timely screening and early detection of elevated CRP in first-degree relatives of DM patients can help physicians intervene early in the course of the disease and prevent further complications and consequences.

Conflict of interest: None

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