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RESEARCH ARTICLE

Correlation of high-sensitivity C-reactive protein with blood sugar level in patients with Type 2 diabetes

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ABSTRACT

Background: The prevalence of diabetes is rapidly rising all over the globe at an alarming rate. Complications of diabetes include microvascular and macrovascular complications. High-Sensitivity C-reactive protein (hs-CRP) is an acute phase reactant and a sensitive marker of inflammation. In addition to traditional cardiovascular risk factors, elevation in hs-CRP can be used to predict increased cardiovascular risk in diabetic patients. **Aims and Objectives:** This study was planned to estimate hs-CRP and fasting blood glucose (FBG) levels in diabetic and non-diabetic participants and to find out if there is any correlation between blood glucose and hs-CRP levels in diabetic and non-diabetic participants. **Materials and Methods:** In this study, hs-CRP and FBG levels of 120 participants were estimated. Among which 60 were diabetic, and 60 were non-diabetic participants. Participants were chosen based on inclusion and exclusion criteria. FBG was estimated by glucose oxidase peroxidase method and hs-CRP was estimated chemiluminescence immunoassay method. Data analysis were analyzed by unpaired t-test using Statistical Package for the Social Sciences Version 19.0. **Results:** The results of this study showed that hs-CRP increased as FBG increased. There was positive correlation seen between hs-CRP and blood glucose levels in both study and control group. Hs-CRP was seen to be much higher in diabetic participants than in non-diabetic participants. **Conclusion:** Thus, proving that hyperglycemia itself is a factor that can cause increase of serum hs-CRP levels in Type 2 diabetic participants.

KEY WORDS: Diabetes Mellitus; Fasting Blood Glucose; High-sensitivity C-reactive Protein

INTRODUCTION

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate.[1] Complications of diabetes include microvascular and macrovascular complications.[2,3] High-sensitivity C-reactive protein (hs-CRP) is an acute phase reactant and a sensitive marker of inflammation. In addition to traditional cardiovascular risk factors, elevation in hs-CRP can be used to predict increased cardiovascular risk in diabetic patients.[4] Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. Lack or deficiency of insulin affects the metabolism of carbohydrate, protein, and fat. Long-standing metabolic derangement is associated with functional and structural changes in many organs, such as heart, kidneys, brain, and eyes.[5] Hyperglycemia itself is a pro-inflammatory condition leading to an increase in inflammatory markers in blood.[6]

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The newer "hs-CRP" is a measure of low-grade chronic inflammation measured by a highly sensitive method. As the name suggests, it is more sensitive than CRP. Hyperglycemia can potentially promote the production of CRP. A higher level

of hs-CRP in diabetic patients indicates that micro- or macro-vascular changes have occurred in the patient. In addition to inflammation, increased levels of CRP in male and female participants could indicate risk of cardiovascular disease (CVD) in patients with Type 2 DM. Studies have suggested that the biomarker of inflammation can suggest increased risk of CVD in men than in female patients.[7]

Hs-CRP has been estimated in diabetic participants in several studies.[8,9] Elevated levels of hs-CRP in patients with Type 2 DM were observed in some studies.[7,8] However, in these studies, the diabetic participants were either obese having a high lipid profile or hypertensive. Obesity and hypertension leads to an increase in hs-CRP levels.[8] Therefore, in this study, we chose non-obese, normotensive participants to make sure that there is no other triggering factors to cause an increase in hs-CRP other than DM. The current study was planned to estimate hs-CRP and fasting blood glucose (FBG) levels in Type 2 diabetic and non-diabetic male and female participants. We also planned to explore if there is any correlation between levels of hs-CRP and FBG levels in diabetic and non-diabetic participants.

MATERIALS AND METHODS

The present study was conducted from May 2013 to May 2014 in a local Medical College and Hospital. As per revised Helsinki Declaration, institutional ethical committee approval was obtained for the study. Protocol was explained to the participants and written consent was obtained.

Study was conducted on 120 volunteers (60 males and 60 females) in the age group of 50-65 years. Participants with history of isolated Type 2 DM for more than 5 years and under treatment were included in study group. Participants with habit of smoking and alcohol, pregnant and lactating women, overweight, and obese participants were excluded from the study. In addition, participants having recent history of fever, any acute or chronic infection, allergic reaction, insect bite, those suffering from any autoimmune disease such as rheumatoid arthritis or suffering from any hepatic and renal or CVDs were excluded from this study.

Blood sample of 3 ml was drawn in the morning following 8 h of fasting under all aseptic precautions. To avoid the effect of any diurnal variations on hs-CRP, the time of collection of blood was constant between 9 and 11 am.

Participants were divided into two groups based on FBG levels:

1. Study group: It consisted of 60 participants (30 males and 30 females)
2. Control group: It consisted of 60 healthy individuals (30 males and 30 females), with no history of DM and normal body mass index (BMI).

Following parameters were assessed in the participants of both groups:

1. FBG level by glucose oxidase peroxidase method, using fully automated EM 360 Biochemistry analyzer/ colorimeter.[10]
2. Hs-CRP by chemiluminescence immunoassay system.[11]

RESULTS

There was no statistically significant difference in the height, weight, waist circumference, and BMI between the male and female participants in both study and control group. All the parameters were within normal limits. Figure 1 shows that there significant and positive correlation between FBG levels and hs-CRP in male control group participants ($r = 0.577$, $P < 0.001$). Figure 2 shows that there is significant and positive correlation between FBG levels and hs-CRP in male study group participants ($r = 0.825$, $P < 0.001$). Figure 3

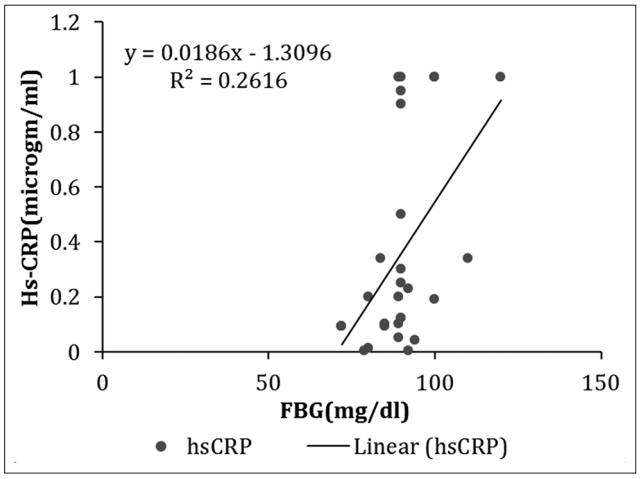

Figure 1: Scatter diagram showing correlation of fasting blood glucose with high-sensitivity C-reactive protein in male participants of control group

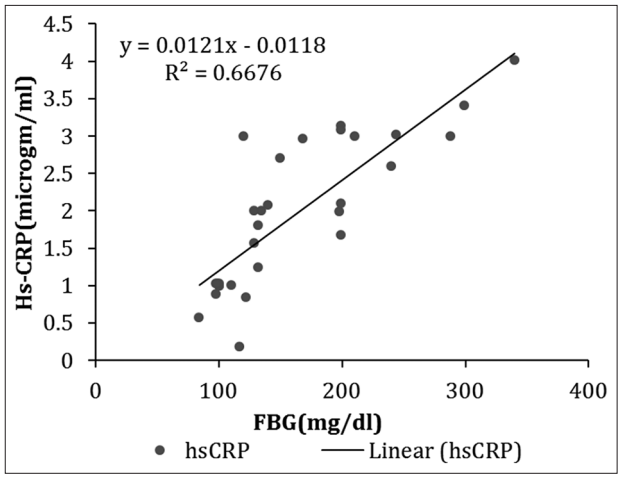

Figure 2: Scatter diagram showing correlation of fasting blood glucose with high-sensitivity C-reactive protein in male participants of study group

shows that there is significant and positive correlation between FBG levels and hs-CRP in female control group participants (r =0.522, P < 0.001). Figure 4 shows that there is significant and positive correlation between FBG levels and hs-CRP in female study group participants (r = 0.898, P < 0.001) (Tables 1 and 2).

Statistical Analysis[12]

Data analysis were analyzed by unpaired *t*-test using Statistical Package for the Social sciences version 19.0. Data were expressed as mean ± standard deviation. P < 0.05 means that value of the corresponding test was statistically significant. Scatter plot was used to find the correlation between FBG and hs-CRP levels of male and female participants in study and control group. Pearson correlation coefficient was done and '*r*' value was determined.

DISCUSSION

Diabetes is a metabolic disorder associated with insulin resistance resulting in hyperglycemia. It is considered that hyperglycemia is itself an inflammatory condition.[1] Further classical risk factors such as obesity, smoking, and hyperlipedemia also exacerbates the condition of inflammation.

However, inflammatory process is difficult to measure directly. Use of imaging technique or arterial biopsy is not practical. Hence, inflammatory biomarkers have been proved to be useful to provide awareness on the inflammatory process. Inflammation in any tissue or organ raises the levels of inflammatory biomarkers in the plasma and is associated with the degree of inflammation. Thus, a high-sensitive method to detect even small variations of these biomarkers in the blood is of choice.[13-15]

Among the several markers of inflammation hs-CRP is significantly associated with diabetic population.[16] The present study was planned to estimate the levels of hs-CRP and FBG levels in diabetic and non-diabetic participants. It

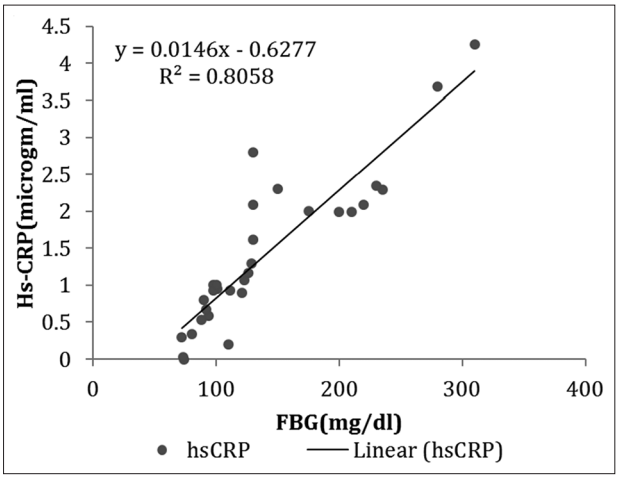

Figure 3: Scatter diagram showing correlation of fasting blood glucose with high-sensitivity C-reactive protein in female participants of control group

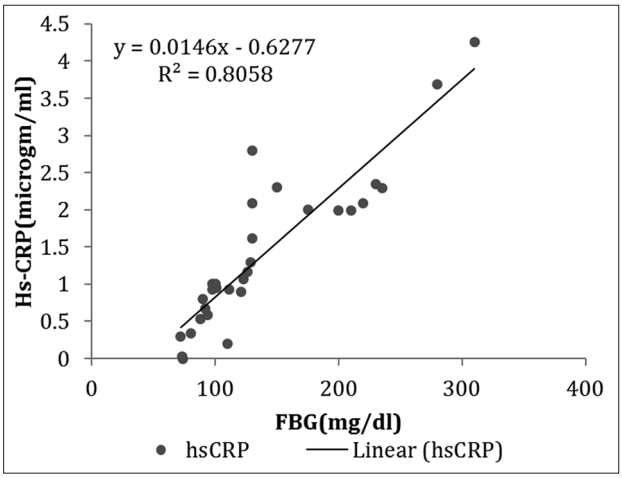

Figure 4: Scatter diagram showing correlation of fasting blood glucose with high-sensitivity C-reactive protein in female participants of study group

Table 1: Correlation between hs-CRP and FBG levels in male and female participants of control group

Gender	Control group, mean±SD		*r* value	*P* value
	hs-CRP (µg/ml)	FBG (mg/dl)		
Male (*n*=30)	0.34±0.37	89.10±10.31	0.577	<0.001**
Female (*n*=30)	0.18±0.28	85.23±9.24	0.522	<0.001**

**P<0.001: Statistically highly significant, hs-CRP: High-sensitivity C-reactive protein, FBG: Fasting blood glucose, SD: Standard deviation

Table 2: Correlation between hs-CRP and FBG levels in male and female participants of study group

Gender	Study group, mean±SD		*r* value	*P* value
	hs-CRP (µg/ml)	FBG (mg/dl)		
Male (*n*=30)	1.96±1.00	162.93±67.53	0.825	<0.001**
Female (*n*=30)	1.41±1.04	139.33±63.84	0.898	<0.001**

**P<0.001: Statistically highly significant, hs-CRP: High-sensitivity C-reactive protein, FBG: Fasting blood glucose, SD: Standard deviation

was planned to find if there was any correlation between the two parameters.

Recent research evidence supports a link between hyperglycemia and inflammation. CRP is known to be higher in people with impaired glucose tolerance and frank diabetes. The results in a study by Kawamoto et al. suggested that hs-CRP levels increased continuously across the FBG spectrum.[16]

In our study, statistically significant difference in the hs-CRP levels in control and study participants (both male and female) as shown in Table 1 and Figure 2. Hs-CRP levels were seen to be higher in the diabetic participants as compared to the non-diabetic participants in our study. The scatter Figures 1-4 show a linear positive correlation between hs-CRP and FBG levels in the diabetic and non-diabetic participants of our study.

Our findings were similar to those in a study done by Haque et al.[17] They observed in their study that plasma hs-CRP levels in Type 2 DM participants was about 3 times higher than in normal participants.

Studies have related hyperglycemia to inflammation by demonstrating simultaneous inflammation, endothelial dysfunction, and insulin resistance at the physiologic level.[18] One of the several mechanisms proposed is oxidative stress on the endothelium, which promotes inflammation and is enhanced by hyperglycemia.[19] Such evidence is consistent with the findings in the current study, which further documents the association between hyperglycemia and inflammation in adults with diabetes.

In a nutshell rise in hs-CRP levels in male than female diabetic participants could be due to, low-grade chronic inflammation leading to production of inflammatory cytokines, formation of advanced glycation end products, and inflammatory cytokines released by adipocytes or decreasing β cell mass through IL-1β-induced apoptosis.[18,19]

Limitations

1. The sample size was very small
2. Hemoglobin A1c was not estimated to assess the glycemic status of the participants
3. Other pro-inflammatory cytokines (interleukin-6, tumor necrosis factor-alpha) were not estimated.

CONCLUSION

The present study was aimed to explore association of hs-CRP and blood sugar levels in Type 2 diabetic patients. The results of this study showed that hs-CRP increased as FBG increased. There was positive correlation seen between hs-CRP and blood glucose levels in both study and control group. Hs-CRP was seen to be much higher in diabetic participants than in non-diabetic participants. Thus proving that hyperglycemia itself is a factor that can cause increase of serum hs-CRP levels in Type 2 diabetic participants.

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