ORIGINAL ARTICLE

ASSOCIATION OF HIGH SENSITIVITY C-REACTIVE PROTEIN, GLYCATED HAEMOGLOBIN, BODY MASS INDEX AND BLOOD PRESSURE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Diabetes is characterized by hyperglycaemia resulting from defective secretion, defective action, or both of insulin. The aim of this study was to determine the high sensitivity C-Reactive Protein (hs-CRP) levels in type 2 diabetics and correlate hs-CRP levels with glycaemic control (Glycated Haemoglobin HbA1c levels), body mass index (BMI) and blood pressure. **Methodology:** It was a cross-sectional study carried out at Endocrinology Unit of Hayatabad Medical complex (HMC) and samples were analyzed in the laboratory of Rehman Medical Institute, Peshawar. A total of 125 known diabetic patients were recruited by non-probability convenience sampling. HbA1c, and hs-CRP were measured through immunoassay method besides Fasting Blood Glucose, Blood Pressure, Height and Weight. **Results:** Out of 125 patients, 68% were females and 32% were males, 16% had normal BMI, 48% were overweight and 36% were obese. In the male patients, 4% had good, and 28% had poor glycaemic control. In females, 8.8% had good glycaemic control and 59.2% had poor glycaemic control. There was significant small positive correlation of HbA1c and hs-CRP (r=0.207, p=0.020), significant weak positive correlation of hs-CRP and BMI (r=0.299, p=0.001), and no correlation of hs-CRP and systolic blood pressure in the data (r=0.059, p=0.555). **Conclusion:** There is a positive association of hs-CRP with HbA1c and BMI. If better glycaemic control is maintained, chances of getting cardiovascular diseases are reduced.

Keywords: HbA1C, hs-CRP, BMI, Blood Pressure, Type 2 Diabetes

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INTRODUCTION

Diabetes is characterized by hyperglycaemia resulting from defective secretion, defective action, or both of insulin.[1] A survey conducted by WHO estimated that in year 2025, Pakistan will be on the 4th position with 14.5 million people having diabetes.[2] The prevalence of diabetes had reached to 16.98% in Pakistan during 2019.[3] The prevalence of type 2 diabetes was 4.0% in Nepal and 8.8% in India in 2017.[4]

C-Reactive Protein (CRP), an acute phase protein is produced in the liver in response to interleukin-6 (IL-6).[5] IL-6 is stimulated by Interleukin-1 (IL-1) and tumour necrosis factor-α (TNF-α) produced during inflammation. The physiological role of CRP is activation of complement system.[6] CRP levels are below 1 mg/L in normal healthy individuals.[7] CRP >3 mg/L is considered as high risk for cardiovascular events. Various clinical trials and epidemiological studies have reported CRP as an independent predictor of cardiovascular risk.[8] In the recent decades the researchers are emphasizing on hs-CRP which simply refers to the detection of lower limits of the assay procedures used for CRP.[9,10]

Apart from playing an important role in plaque deposition, CRP also inhibits endothelial nitric oxide synthase and impairs both vasodilation and vasoconstriction.[11] Even in apparently healthy men, increased levels of High sensitivity C-Reactive Protein (hs-CRP) showed positive association with stroke and myocardial infarction.[10]

Various prospective studies in women have shown the association of hs-CRP with obesity and diabetes mellitus.[12,13] Exercise, reduction of weight, and cessation of smoking as recommended for individuals with cardiovascular risk and patients with diabetes have shown to lower the levels of hs-CRP.[14,15]

The objectives of this study were to determine the hs-CRP levels in type 2 diabetics, and to correlate hs-CRP levels with glycaemic control (HbA1c levels), BMI, and blood pressure.

MATERIAL AND METHODS

This was a cross-sectional study carried out in Endocrinology Unit of Hayatabad Medical Complex (HMC) and samples were analyzed in the laboratories of Rehman Medical Institute (RMI), Peshawar. The study was completed in 3 months. Non-probability convenience sampling was done. The sample size was calculated with WHO formula with prevalence of hs-CRP=37% or 0.37.[16] Calculated sample size was 110. A larger sample size of 125 patients was taken to exclude the co-morbidities and outliers.

Type 2 diabetics visiting Endocrinology Unit of HMC who gave informed consent were included in

the study. Patients having type 1 diabetes mellitus or having any acute infection or chronic inflammatory disease like osteoarthritis, rheumatoid arthritis, gout, and bronchial asthma, renal disease, thyroid disease, genetic abnormalities, anaemia, taking NSAIDS or lipid lowering drugs were excluded. A 3 ml fasting blood sample was collected from 125 patients after taking a medical history and physical examination. The patient's body weight and height were measured through a weight and height scale present in OPD of HMC. Body mass index (BMI) was calculated as BMI=Weight in Kg/(Height in meter)^2. Obesity was stratified with recognised standards.

The auscultatory method of blood pressure (BP) measurement was used and BP was measured in a rested sitting state. Whole blood collected in EDTA tube was used to measure HbA1c through immunoassay method on Architect *i1000*SR machine and then centrifuged in *Beckman Allegra TM 6R* centrifuge at 3,000 rpm for 10 minutes to obtain plasma. The plasma was used to measure hs-CRP levels by immuno-turbidimetry method by automated analyzer Architect *ci 8200* machine. Data about age, gender, BMI, fasting blood glucose, HbA1c, and hs-CRP was recorded in SPSS-17. Data was analyzed to measure the frequency, mean and standard deviation. Pearson's correlation coefficients were determined for numerical variables, i.e., hs-CRP with HbA1c, BMI and systolic BP.

RESULTS

Out of 125 patients included in this study, 85 (68%) were females and 40 (32%) were males, 20 (16%) had normal BMI, 60 (48%) were overweight and 48 (36%) were obese (Table-1).

Table-2 shows that 5 male patients (4%) had good glycaemic control while 35 male patients (28%) had poor glycaemic control. The data also indicates that 11 females (8.8%) had good glycaemic control and 74 (59.2%) had poor glycaemic control.

Table-3 shows significant small positive correlation of HbA1c and hs-CRP (r=0.207, p=0.020). There is significant weak positive correlation of hs-CRP and BMI (r=0.299, p=0.001). A weak positive correlation of hs-CRP and systolic blood pressure is also indicated (r=0.059, p=0.555).

Table-1: Gender and baseline Body Mass Index (BMI) of the subjects (n=125)

Variables	Number of Patients (*n*)	Percentage (%)
Females	85	68%
Males	40	32%
Base line BMI (Kg/m^2)		
Normal (18.5–24.9)	20	16%
Overweight (25–29.9)	60	48%
Obese (≥30)	45	36%

Table-2: Gender-wise distribution of HbA1c levels [n (%)]

Sex	HbA1c≤7% *n*=16	HbA1c>7% *n*=109
Male	5 (4)	35 (28)
Female	11 (8.8)	74 (59.2)

Table-3: Correlation of the parameters with hs-CRP

Parameter	Correlation with hs-CRP (*r*)	*p*
HbA1c	0.207	0.020
BMI	0.299	0.001
Systolic blood pressure	0.059	0.555

DISCUSSION

This study was conducted to determine the hs-CRP in type 2 diabetics and to correlate it with HbA1c levels, BMI and systolic blood pressure.

The stratification of type 2 diabetics of our study according to BMI is: 16% had normal weight, 48% were overweight, 36% were obese. In a similar study the stratification of BMI in type 2 diabetics in Indian population reported that out of 240 patients 26.7% were normal weighing, 55% were overweight, 19.3% were obese.[17] In that study most of the participants were among overweight and obese category as that of the current study which shows the same level of unawareness of weight control to improve glycaemic control in both study populations.

There was a significant positive association of hs-CRP with HbA1c (r=0.207, p=0.020); our findings are similar to various studies including a study conducted in India[18] on newly diagnosed type 2 diabetics in which hs-CRP positively correlated to HbA1c. A case control study in which hs-CRP levels were measured in Saudi type 2 diabetics and compared with controls, the correlation of hs-CRP with HbA1c was also measured and reported to be positive (r=0.326, p=0.006).[19] In another study in India[20] in which 400 type 2 diabetics and 400 non-diabetics were studied, the correlation of hs-CRP with HbA1c was found to be the same as that of our study (r=0.307, p=0.001). A Japanese study[21] on 195 elderly type 2 diabetics showed a positive correlation of hs-CRP with HbA1c, the correlation was of same strength as that of our study. The correlation of hs-CRP and HbA1c studied in a Khyber Pakhtunkhawa, Pakistan also reports to be positive.[22]

We found a significant positive correlation of hs-CRP and BMI (r=0.299, p=0.001) in our study. Our findings were similar to studies conducted in overweight and obese diabetics[19,20,23] which showed a positive correlation between the two variables. However Bhaktha *et al*[24] did not notice such a correlation because of little variation in BMI in their study as compared to our study.

The correlation of hs-CRP and systolic BP was (r=0.059, p=0.555), indicating no significance between the two variables in the current study. However the correlation of hs-CRP with systolic BP is reported to be positive by other studies[20,23] but we could not get such a correlation because the patients enrolled in the study were already on antihypertensive medications which might have weakened our correlation strength. Certain studies[21,22,24] supported the findings of our study reporting no correlation between hs-CRP and systolic BP because of the same fact that the study participants were already on antihypertensives.

CONCLUSION

There is a positive association of hs-CRP with HbA1c and BMI. With better glycaemic control there is a lower chance of getting cardiovascular disease.

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