Section: General Medicine

Original Research Article

HIGHLY SENSITIVE C-REACTIVE PROTEIN (HSCRP) IN TYPE 2 DIABETES AND ITS RELATIONSHIP TO FASTING, POST PRANDIAL BLOOD SUGAR VALUES IN TERTIARY CARE CENTER: A CROSS-SECTIONAL STUDY

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Abstract

Background: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Currently, there are no available studies showing correlation between hsCRP and FBS or HbA1c in the Kerala setting. The objective was to assess the correlation of hsCRP and with that of FBS, PPBS in adults with Type 2 diabetes mellitus. **Materials and Methods:** This was a cross sectional study. The sample size was calculated to be 74, using correlation coefficient from previous study. All consecutive patients based on the inclusion and exclusion criteria during the period of study was included in study. The demographic and clinical data was obtained as per the proforma. The data obtained-coded and entered in Microsoft excel and was analyzed using statistical software. **Result:** Out of the 74 participants included in the study, the age of patients ranged from 24 to 85 years of age. The mean age of participants in the study was found to be 55.1 years. It was noted that majority of the participants in the study were males (55.4.%). Majority of patients had a duration of diabetes between 5-10 years (31.1%). No patient had any physical examination suggestive of recent infections or stress. There was a statistically significant positive correlation between hsCRP and FBS(Pearson correlation coefficient – 0.027) and a high positive correlation with HbA1c (Pearson correlation coefficient – 0.699, $p<0.001$). **Conclusion:** In our study, it was observed that there is a correlation between hsCRP and Fasting blood sugar values, and also a strong positive correlation between hsCRP and HbA1c. Elevated levels of hsCRP, indicates the presence of ongoing inflammation in subjects with Type 2 Diabetes.

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia[1].There has been an increasing interest in the involvement of low-grade inflammation in the pathogenesis of Type 2 Diabetes Mellitus and it is the leading cause of death and morbidity, and the reason for a high prevalence of vascular disorders such as stroke, myocardial infarction, and peripheral vascular disease.[2-4] Diabetes disease burden is high and rising in every country, spurred by a global increase in obesity and unhealthy lifestyles. According to the most recent estimates, there were 382 million diabetics worldwide in 2013, with the number expected to rise to 592 million by 2035. Diabetes can cause multisystem complications such as retinopathy, nephropathy, and neuropathy, as well as ischemic heart disease, stroke, and peripheral vascular disease. Diabetes is a serious public health problem because of its premature morbidity, mortality, reduced life expectancy, and financial and other costs.[5]

hsCRP levels are higher in people with diabetes compared with those without diabetes. Less is known about whether hsCRP in people with diabetes is related to level of glycemic control.[6] Prevalence of diabetes is as high as 20 % in Kerala, the southern most state of India.[7] Currently, there are no available studies showing correlation between hsCRP and FBS or PPBS and HbA1C in the Kerala setting. Because of the dearth of such

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research and the high disease burden of Type 2 Diabetes Mellitus, this study was conducted to find any association between hsCRP and Fasting/Post prandial blood sugar values as well was HbA1c levels.

MATERIALS AND METHODS

It was a Cross Sectional Study done in Department of General Medicine, Pushpagiri Institute of Medical Science and Research Centre, Tiruvalla, Kerala, India for a period of 18 months. All consecutive patients based on the inclusion and exclusion criteria during the period of study was included in study until sample size is attained. Sample size was calculated using correlation coefficient between hsCRP and HbA1C in adults with Type 2 Diabetes Mellitus from previous study8, confidence level (1-α) as 95%, power of the study (1-β) as 80%. The sample size obtained was 74 using the formula

$$n = \frac{[Z(1-\alpha) + Z(1-\beta)]^2}{[C]^2} + 3$$

Inclusion Criteria

- Adults (more than 18 years age) attending the General Medicine OPD of Pushpagir Medical College Hospital during the period of study (January 2021 to June 2022), who are not having any symptoms or signs of acute or recent infection over the last 2 weeks, and who have not undergone any acute or recent stress (surgery, acute coronary syndrome, acute stroke, trauma).
- Known cases of Type 2 Diabetes Mellitus diagnosed by ADA CRITERIA irrespective of disease duration and treatment.
- The patients meeting the above criteria will be included in the study after obtaining informed consent.

Exclusion Criteria

- Patients who are unwilling for the study
- Gestational Diabetes Mellitus
- Known Chronic Inflammatory conditions- TB, Sarcoidosis, vasculitis, hemolytic anemias, Acute or chronic cardiovascular disease
- Chronic Liver disease
- Chronic Kidney disease
- Those having symptoms and/or signs of recent infections in the last 2 weeks
- Those who have undergone acute or recent stress (Acute coronary syndrome, Acute stroke, surgery, or trauma)
- Patients on drug therapy with Statins, Non-steroidal anti-inflammatory drugs

Methods of data collection

Clearance from the institutional ethics and research committee was obtained to conduct the proposed study. T2DM subjects fulfilling the above criteria were enrolled to the study. Data collection was entirely done by the principal investigator. The demographic and clinical data was be obtained as per the proforma. Blood investigations prescribed for the study (FBS, PPBS, HbA1C, hsCRP, CBC, ESR) was collected at the OPD laboratory by trained nursing and health personnel of the hospital itself. HbA1C was performed by high performance liquid chromatography and High sensitivity CRP was analyzed using SIEMENS BN PROSPEC device.

Statistical Analysis

The data obtained-coded and entered in Microsoft excel and was analyzed using statistical software. The data was analyzed and presented as frequency and percentages for categorical data and descriptive statistics (mean, SD, median and range) for continuous data. Pearson Correlation Coefficient between hsCRP and HbA1C; between hsCRP and fasting and between hsCRP and postprandial blood sugar values was calculated and presented with significance level. A p value of less than 0.05 will be considered as statistically significant.

RESULTS

Among the study subjects 40.5% was in the age group of 61-80 years, 29.7% was in 41-60 years, 27% in 20-40 years group and only 2.7% was in the age group greater than 80 years. A total of 74 participants were included in the study. The mean age of participants in the study was found to be 55.1 years. It was noted that majority of the participants in the study were males (55.4%).

Table 1: Age and Gender Distribution

Age group	Frequency	Percent
20-40 years	20	27
41-60 years	22	29.7
61-80 years	30	40.5
>80 years	2	2.7
Total	74	100

Table 2: Abnormal ESR or CRP

Abnormal ESR or CRP	Frequency	Percent
Yes	7	9.5
No	67	90.5
Total	74	100

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As per [Table 2] abnormal ESR or CSP was found in 9.5% of subjects.

Table 3: hsCRP in mg/L

hsCRP in mg/L	Frequency	Percent
≤1	9	12.2
1-3	16	21.6
≥ 3	49	66.2
Total	74	100

In our study 9 (12.2%) patients had low hsCRP levels, 16 (21.6%) had intermediate and 49 (66.2%) had high hsCRP levels.

Table 4: Table Showing Association between hsCRP and Fasting Blood Sugar

hsCRP in mg/L	N	FBS (Mean±SD)	Median(IQR)	P value
≤1	9	145.2±12.5	141(134.5-157)	0.027
1-3	16	158.3±19.7	155(144-174)	
≥ 3	49	164±19.7	165(145-179)	
Total	74	160.5±19.8	159(142-174.25)	

As per [Table 4] here the mean FBS of subjects with hsCRP of ≤1 is 145.2±12.5, mean FBS of subjects with hsCRP of 1-3 is 158.3±19.7 and mean FBS of subjects with hsCRP of ≥ 3 is 164±19.7.The difference in mean was statistically significant since p value is less than 0.05.

Table 5: Table Showing Association between hsCRP and Post Prandial Blood Sugar

hsCRP in mg/L	N	PPBS (Mean±SD)	Median(IQR)	P value
≤1	9	187.1±26.1	180(169.5-199)	0.069
1-3	16	203.1±29.7	198.5(187.25-207.5)	
≥ 3	49	214.5±36.1	201(193-237.5)	
Total	74	208.7±34.6	199.5(187-227.5)	

As per [Table 5] here the mean PPBS of subjects with hsCRP of ≤1 is 187.1±26.1, mean PPBS of subjects with hsCRP of 1-3 is 203.1±29.7 and mean PPBS of subjects with hsCRP of ≥ 3 is 214.5±36.1.The difference in mean was not statistically significant since p value is greater than 0.05.

Table 6: Table Showing Association between hsCRP and HbA1c

hsCRP in mg/L	N	HbA1c (Mean±SD)	Median(IQR)	P value
≤1	9	6.9±0.2	7(6.8-7.1)	0.001
1-3	16	7.2±0.3	7.1(6.92-7.47)	
≥ 3	49	7.8±0.8	7.6(7.15-8.45)	
Total	74	7.6±0.8	7.35(7-7.93)	

Here the mean HbA1c of subjects with hsCRP of ≤1 is 6.9±0.2, mean HbA1c of subjects with hsCRP of 1-3 is 7.2±0.3 and mean HbA1c of subjects with hsCRP of ≥ 3 is 7.8±0.8. The difference in mean was statistically significant since p value is less than 0.05.

Table 7: Correlation Coefficient of HbA1c and hsCRP

Variables	Mean±SD	Pearson Correlation Coefficient	P value
hsCRP	31.1±49.1	0.699	<0.001
HbA1c	7.6±0.8		

There is a statistically significant high positive correlation between hsCRP and HbA1c.

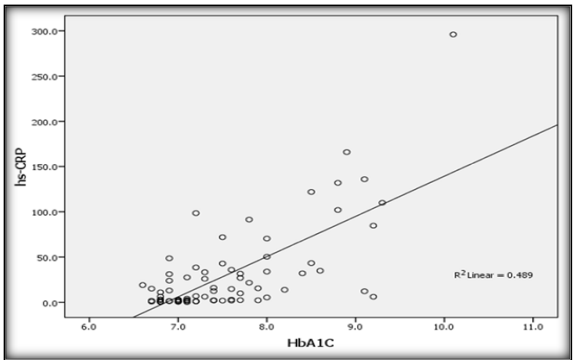

Figure 1: Scatter plot Showing Correlation between hsCRP and HbA1c

DISCUSSION

This was a cross sectional study over 18 months conducted in Pushpagiri Institute of Medical Sciences and Research Center, Tiruvalla, Kerala. The study was aimed to find out the correlation between High sensitivity C reactive protein (hsCRP) and fasting and post prandial blood sugar values as well as glycated hemoglobin (HbA1c) levels among Type 2 Diabetes Mellitus patients. In this study, 44.6% of the participants were females, whereas the remaining (55.4%) were males. The age groups of

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the study participants varied from 24 years to 85 years of age and hence, they were divided into age groups of 4: 20 to 40, 41 to 60, 61-80 and those more than 80 years of age. Amongst the subjects, maximum number of participants came within the 61-80 years age group (40.5%). Study done by Yildiz Tutuncu et al on comparison of hsCRP levels in new Diabetes groups observed a positive correlation between hsCRP levels and age.[9] Study done by Ramesh SS et al also demonstrated correlation between hsCRP and HbA1c but could not establish a relation between hsCRP with FBS or PPBS, which thereby indicates that these variables may not be as effective as HbA1c in monitoring and prognostication of the disease.[3]

From our analysis, the mean HbA1c of subjects with hsCRP of ≤1 was 6.9±0.2, mean HbA1c of subjects with hsCRP of 1-3 was 7.2±0.3 and mean HbA1c of subjects with hsCRP of ≥ 3 was 7.8±0.8. The difference in mean was statistically significant since p value was less than 0.05. The Pearson Correlation Coefficient between hsCRP and HbA1c was found to be 0.699 and a strong positive correlation between the two was established, with a statistically significant p value of <0.001. Our findings are consistent with some of the studies. In a national survey study, subjects with HbA1C levels ≥ 9% had a significantly higher rate of elevated CRP than those with HbA1C levels < 7%. This suggests an association between poor glycemic control and systemic inflammation in people with established diabetes.[10]

Analysis done by Krishnamurthy V et al also demonstrated similar positive correlation between HbA1c and hsCRP, where among 35 patients with good glycemic control were noted to have correlation between the two variables (R2=0.17, p=00.03).[11] Similar results were obtained from study done by Petchiappan V et al, where they analyzed correlation between hsCRP and HbA1c in 30 participants at baseline, sugars were monitored and medications were optimized and it was repeated after 6 months. The baseline median hsCRP was 3.33mg/L and at the end of 6 months, it was 2.08mg/L.[8]

A study conducted by KV et al in 3534 subjects, hsCRP, and HbA1c were performed at baseline and after 2 years of follow-up and they observed that subjects with HbA1c and hsCRP in the upper 2 quartiles had an increased risk for new vascular events (adjusted hazard ratio in diabetics: 4.3 [1.8, 7.3]; P=0.001). This suggests the combination of hyperglycemia and inflammation is associated with an increased risk of new vascular events in diabetic subjects.[11]

CONCLUSION

In our study, it was observed that there was a positive correlation between hsCRP and Fasting blood sugar values, but not with that of Post prandial blood sugar values. There was also a strong positive correlation between hsCRP and HbA1c. Elevated levels of hsCRP, along with HbA1c indicates that there is a relation between level of glycemic control and the presence of ongoing inflammation in subjects with Type 2 Diabetes Mellitus. Hence, hsCRP may be used as a prognostic tool to assess degree of inflammation in patients with Type 2 Diabetes and which in turn indicates the future risk for Cardiovascular events or other complications related with Diabetes Mellitus.

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