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Original Research Article

Correlation between HbA1c and high sensitivity C-reactive protein in type 2 diabetes mellitus patients: a cross-sectional study at tertiary care hospital in western Rajasthan

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with chronic low-grade inflammation, increasing cardiovascular risk. High-sensitivity C-reactive protein (HSCRP) is a reliable inflammatory biomarker. This study aimed to evaluate the correlation between HbA1c and HSCRP and its association with lipid profile in T2DM patients.

Methods: This cross-sectional study was conducted at Government Medical College and Bangur Hospital, Pali, Rajasthan, over one year. A total of 123 patients aged 18-75 years with T2DM were included. Patients were categorized into controlled (HbA1c<7.5%) and uncontrolled (HbA1c≥7.5%) groups. HbA1c, HSCRP, and lipid profile were measured using standard laboratory methods. Statistical analysis was performed using SPSS version 25, and Pearson's correlation was applied.

Results: Among 123 patients, 50.4% had controlled and 49.6% had uncontrolled diabetes. Mean HSCRP levels were significantly higher in the uncontrolled group (4.86±2.37 mg/L vs 2.63±0.43 mg/L; p<0.001). Uncontrolled diabetes was associated with significantly higher total cholesterol and triglycerides and lower HDL levels (p<0.001). A strong positive correlation was observed between HSCRP and HbA1c (r=0.961, p<0.001), triglycerides (r=0.889), and total cholesterol (r=0.731), while a negative correlation was seen with HDL (r=−0.827).

Conclusions: Poor glycemic control is strongly associated with increased systemic inflammation and adverse lipid profile. HSCRP can serve as an important marker for cardiovascular risk assessment in T2DM patients.

Keywords: Type 2 diabetes mellitus, HbA1c, HSCRP, Lipid profile, Inflammation

INTRODUCTION

Diabetes is one of the types of metabolic disorders and is defined as the complain of hyperglycemia due to some malfunctioning in the secretion and or action of insulin. Over the last twenty years, the number of diabetic people in the world has increased rapidly. in 1985, it was estimated to be 30 million, but in 2019, this figure has jumped to 463 million. According to the most recent data, this figure is predicted to be 642 million in 2040. According to the available data, the number of people with diabetes, regardless of the type, is increasing in the entire world, but the number of people with type 2 diabetes is increasing at a faster rate due to changes in diet, increased obesity, decreased physical activity due to industrialization in many countries and aging of the population. In 2019, India had the highest number of people with diabetes, 77 million and a very high rate of increase in cases of type 2 diabetes. The Framingham Heart Study reported that the presence of diabetes increased the risk of cardiovascular disease in men by 2 times and in women by 3 times, and this risk was independent, even in the presence of primary hypertension, smoking, high cholesterol, left ventricular hypertrophy, and the person's age.[1,2]

Moreover, there is an increase in hyperglycemia-related cardiovascular incidents in patients with diabetes. Meta-analysis of 13 prospective cohort studies indicates that out of all cardiovascular incidents, there is an increase in odds of 1.18 (95% CI 1.1-1.26) of any cardiovascular incident with each 1% increase in glycosylated hemoglobin (HbA1c) targets 33. About eighty (80) percent of patients with diabetes die of cardiovascular disease. In terms of life span, there is an average reduction of 15 years in patients with type 1 diabetes and 7 years in patients with T2DM. It is not in dispute that with better glycemic control, cardiovascular benefits materialized in patients with diabetes. [3,4] Chronic hyperglycemia is associated with an increased risk of morbidity and mortality due to diseases like myocardial infarction and stroke, and it is accompanied by a disease that has a high level of morbidity and mortality.[5] Diabetes is characterized by a considerable presence of reactive oxygen species (ROS) and there is an interaction with inflammation and aberrant immune response. The most prominent pro-inflammatory cytokines, which are produced by adipose tissue, are TNF-α, IL-1, and IL-6.[6]

The pro-inflammatory cytokines which have an impact on atherosclerosis promote the release of proteins associated with the acute phase of the inflammatory response. There are numerous processes within the body that are affected by the insulin-resistant state which include reactive species, the activity of the lipase that acts on lipoproteins, and the function of the fat cell. These also involve pro-inflammatory cytokines and acute phase reactants.[7] One of these acute phase reactants is the C-reactive protein which is also raised with the presence of other inflammatory conditions such as diabetes and cancer as well as coronary heart disease and other infections. Within the C-reactive protein, there is a more sensitive variety of it called high sensitivity C-reactive protein (HSCRP). For inflammatory conditions and even cancers it has been described as the gold biomarker.[6,8] With powerful detection methods, HSCRP can be measured even down to the low range of 0.01 mg/L. In the presence of low grade inflammatory states, even mild inflammatory conditions can be detected HSCRP ranges. hCRP has a range of greater than 10 mg/L is an indicator of an acute state. With high sensitivity C-reactive protein, <1 mg/L is indicated as low risk for cardiovascular disease and 1-3 mg/L moderate risk and >3 mg/L high risk.[9-11] Cytokines also affect the liver contributing to the characteristic lipoprotein abnormalities seen in T2DM.[12] HSCRP and cardiovascular diseases have been the subject of some studies. However, very few studies examined the relationship between HSCRP and T2DM. This study was undertaken to determine the HSCRP and consequential cardiovascular risk in patients with T2DM sufferinig from chronic hyperglycemia.

METHODS

Study design and setting

This was a hospital-based observational cross-sectional study conducted at Government Medical College and Bangur Hospital, Pali, Rajasthan, over a period of one year.

Study population

A total of 123 patients diagnosed with T2DM, aged between 18 and 75 years, were included in the study.

Inclusion and exclusion criteria

Patients diagnosed with T2DM as per world health organization criteria were included. Patients with type 1 diabetes mellitus, gestational diabetes, haemoglobinopathies, chronic inflammatory diseases, malignancy, recent surgery, severe infection, or trauma were excluded.

Study procedure

After obtaining informed consent, detailed clinical history and examination were performed. Blood samples were collected for biochemical analysis. HbA1c was measured using turbidimetric immunoinhibition method, and HSCRP was measured using chemiluminescence assay. Lipid profile including total cholesterol, triglycerides, and HDL was also assessed using standard laboratory techniques.

Patients were categorized into two groups based on HbA1c levels: controlled diabetes (HbA1c <7.5%) and uncontrolled diabetes (HbA1c≥7.5%). HSCRP levels were classified as low (<1 mg/L), moderate (1-3 mg/L), and high (>3 mg/L) cardiovascular risk.

Ethical approval

The study was conducted after obtaining approval from the Institutional Ethics Committee of Government Medical College, Pali.

Statistical analysis

Data were analyzed using Microsoft excel and SPSS version 25. Qualitative variables were expressed as proportions and percentages and analyzed using Chi-square test. Quantitative variables were expressed as mean±standard deviation and compared using appropriate parametric or non-parametric tests. Pearson’s correlation coefficient was used to assess the relationship between HbA1c and HSCRP. A $p<0.05$ was considered statistically significant.

RESULTS

A total of 123 patients with T2DM were included in the study. Among them, 60.1% were males and 39.9% were females, indicating a male predominance. The mean age of the study population was 56.07±9.81 years, reflecting a predominantly middle-aged to elderly cohort.

Table 1 shows gender distribution of the study participants (n=123). The gender-wise distribution showed that males constituted the majority (60.1%), while females accounted for 39.9% of the study population. A considerable proportion of participants had associated lifestyle and clinical risk factors. Nearly 46.3% reported at least one risk factor, with smoking present in 44.7% and alcohol consumption in 11.4% of participants. Hypertension was observed in 36.6% of cases.

Table 1: Gender distribution of the study participants, (n=123).

Gender	N	Percentage (%)
Male	74	60.1
Female	49	39.9

This Table 2 highlights the prevalence of modifiable and non-modifiable risk factors, emphasizing the high burden of cardiovascular risk among diabetic patients.

The overall clinical and biochemical profile of participants indicated the presence of metabolic dysregulation. Mean systolic and diastolic blood pressures were 122.35±24.47 mmHg and 75.67±13.44 mmHg, respectively. Lipid profile parameters showed elevated total cholesterol and triglycerides, along with relatively low HDL levels. The mean HbA1c and HSCRP values were 6.72±1.24% and 3.74±2.03 mg/L, respectively.

Table 2: Personal history distribution of the study participants, (n=123).

Risk factor	N	Percentage (%)
Present	57	46.3
Absent	66	53.7
Smoker		
Yes	55	44.7
No	68	55.3
Alcoholic		
Yes	14	11.4
No	109	88.6
Hypertension		
Present	45	36.6
Absent	78	63.4

Table 3 outlines the disease profile of the participants. The mean systolic and diastolic blood pressures were 122.35±24.47 mmHg and 75.67±13.44 mmHg, respectively. Dyslipidemia was evident with mean total cholesterol at 210.63±44.86 mg/dL, triglycerides at 176.35±50.14 mg/dL, and HDL at 42.22±10.20 mg/dL. Mean random blood sugar was 189.32 mg/dL, while the mean HbA1c and HSCRP values were 6.72±1.24% and 3.74±2.03 mg/L, respectively. These biochemical values point toward chronic metabolic inflammation and increased atherosclerotic risk.

Table 3: Disease profile of study participants, (n=123).

Variables	Mean±SD
Systolic blood pressure	122.35±24.47
Diastolic blood pressure	75.67±13.44
Heart rate	88.50±19.66
Serum triglyceride	176.35±50.14
Serum total cholesterol	210.63±44.86
Serum HDL	42.22±10.20
Random blood sugar	189.32±78.582
HbA1c	6.72±1.24
HSCRP	3.742±2.03

As per Table 4, 50.4% of participants had controlled diabetes (HbA1c<7.5) while 49.6% were classified as uncontrolled (HbA1c>7.5). This near-equal division permits a valid comparative assessment between the two glycemic categories.

Table 4: Diabetes status of the study participants using HbA1c, (n=123).

Diabetes status	N	Percentage (%)
Controlled	62	50.4
Uncontrolled	61	49.6

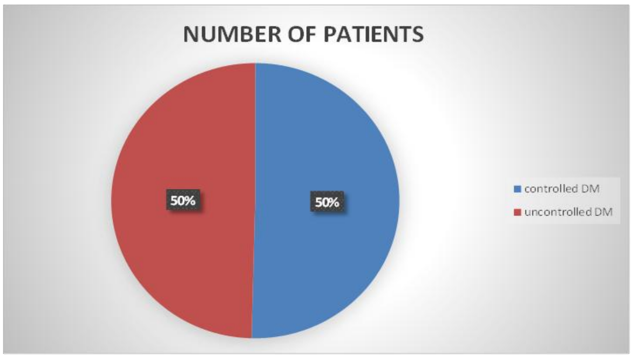

Figure 1: Prevalence of controlled (HbA1c <7.5) and uncontrolled diabetes (HbA1c >7.5).

The Table 5 illustrates that certain demographic and lifestyle factors may influence glycemic control, although not all associations were statistically significant.

Comparison of clinical and biochemical parameters between controlled and uncontrolled diabetes groups revealed significant differences. Patients with uncontrolled diabetes had significantly higher systolic and diastolic blood pressure levels. Additionally, total cholesterol and triglyceride levels were markedly elevated, while HDL levels were significantly reduced in the uncontrolled group (p<0.001). HSCRP levels were also significantly higher in uncontrolled diabetics (4.86±2.37 mg/L) compared to controlled diabetics (2.63±0.43 mg/L).

The findings of Table 6 indicate that poor glycemic control is associated with worsening lipid profile and increased systemic inflammation. Correlation analysis demonstrated a very strong positive relationship between HSCRP and HbA1c (r=0.961, p<0.001). HSCRP also showed strong positive correlations with triglycerides (r=0.889) and total cholesterol (r=0.731), while a strong negative correlation was observed with HDL (r=-0.827).

Table 5: Association of diabetes status with demographic and risk factors, (n=123).

Variables		Diabetes controlled, n (%)	Diabetes uncontrolled, n (%)	P value
Gender	Male	43 (58.1)	31 (41.9)	0.044
	Female	19 (38.8)	30 (61.2)	
Risk factor	Present	34 (59.6)	23 (40.4)	0.071
	Absent	28 (42.4)	38 (57.6)	
Smoker	Yes	33 (60.0)	22 (40.0)	0.070
	No	29 (42.6)	39 (57.4)	
Alcoholic	Yes	12 (85.7)	2 (14.3)	0.009
	No	50 (45.9)	59 (54.1)	
Hypertension	Yes	21 (46.7)	24 (53.3)	0.577
	No	41 (52.6)	37 (47.4)	

Table 6: Association of diabetes status with examination and investigation findings, (n=123).

Variables	Diabetes controlled, mean±SD	Diabetes uncontrolled, mean±SD	P value
Systolic blood pressure	114.76±22.32	130.07±24.30	0.000
Diastolic blood pressure	73.13±13.96	78.26±12.48	0.034
Heart rate	88.21±19.89	88.79±19.57	0.871
Serum triglyceride	139.81±27.11	213.50±39.77	0.000
Serum total cholesterol	178.29±22.86	243.51±37.16	0.000
Serum HDL	50.21±6.26	34.10±6.24	0.000
Random blood sugar	176.92±56.26	201.92±0.36	0.078
HbA1c	5.911±0.36	7.55±1.27	0.000
HSCRP	2.63±0.43	4.866±2.37	0.000

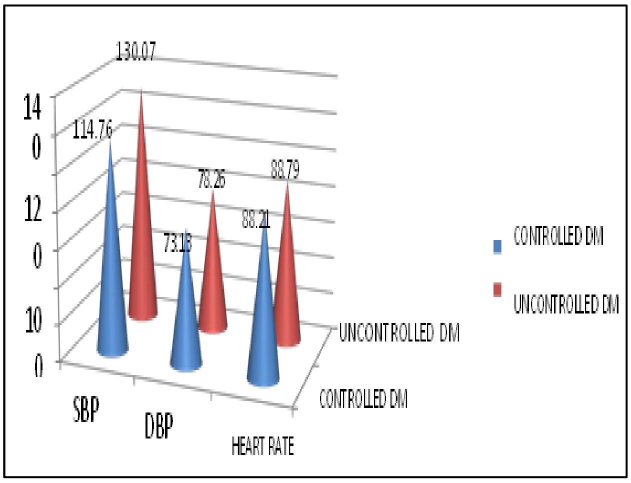

Figure 2: Association of diabetes status with blood pressure and heart rat.

Table 7 reveals that HSCRP demonstrated a very strong positive association with HbA1c (r=0.961), and a strong positive correlation with triglycerides (r=0.889) and total cholesterol (r=0.731). Conversely, a strong negative correlation was observed with HDL levels (r=-0.827). These findings collectively emphasize that worsening glycemic status and lipid imbalance amplify systemic inflammatory response in T2DM.

Table 7: Correlations of HSCRP with other investigation parameters.

Variables	Pearson's correlation	P value
HSCRP and triglycerides	0.889	0.000
HSCRP and total cholesterol	0.731	0.000
HSCRP and HDL	-0.827	0.000
HSCRP and HbA1c	0.961	0.000

Table 8 highlights that patients with HSCRP>3 mg/L (high-risk category) also demonstrated the highest mean HbA1c values (7.48±1.26%), whereas those with HSCRP between 1-3 mg/L showed moderate HbA1c elevation, and patients with HSCRP <1 mg/L had the lowest HbA1c levels. This graded rise reflects a direct proportional relationship between chronic inflammation and poor glycemic control.

Table 8: Correlations of HSCRP with hb1Ac.

HSCRP	Diabetic cases, (n=123)	Hb1Ac (Mean±SD)
<1 mg/L, low risk	1	5
1-3 mg/L, intermediate risk	57	5.893±0.339
>3 mg/L, high risk	65	7.486±1.264

DISCUSSION

We aimed to study the correlation between HbA1c and HSCRP levels in diabetic patients. As the quartile levels for HSCRP increased, the levels for the regression coefficient also increased. Therefore, this concludes that HbA1c levels contributed to the levels of HSCRP. The results still showed that, even when multiple covariates were accounted for, HSCRP levels still increased with HbA1c levels (p=0.001). The outcomes of this study align with other studies that demonstrate the relationship between inflammation and blood sugar levels in diabetic patients. On the relationship of HSCRP to HbA1c, it was explained that the regression coefficient value for the HbA1c and HSCRP relationship increased with the quartiles of HSCRP. Therefore, this indicates that the HSCRP levels were able to influence the HbA1c levels. We aimed to identify the association of HbA1c with HSCRP. The sample size (n=123) of this study consisted of only type 2 diabetic patients and were divided into levels of control of the HbA1c; controlled and uncontrolled, with HbA1c<7.5, and >7.5, into 2 groups respectively. Every individual that was recruited was also given an extensive clinical and laboratory examination of which multiple parameters were documented. A comparative study was done between the 2 groups to determine the impact of uncontrolled diabetes on systemic inflammation with HSCRP as one of the predictors.[13]

The participants included in this study were aged 18 to 75 years old with a total average of 56.07±9.815 years. In the controlled group, the average age of subjects is 54.52±10.01 years, while in the group without control, it is 57.64±9.434 years. No meaningful difference was noticed in average age of the patients in the two groups. Thus, the samples were age matched across all groups. A prior study similar in nature by Shen et al whose age of study population was 50.16 years. Controlled group consisted of 19% females and 43% males, whereas uncontrolled group consisted of 31% females and 30% males with no statistical significance difference (p=0.044). Therefore, the various groups may be regarded as similar in terms of their gender distribution and correspond with the gender ratio of the study. The subjects were included in the study without regard to their history of hypertension and smoking. There are 33% smokers in group 1 patients and 22% in group 2 without any statistically significant difference (p=0.071). In group 1, hypertension is present in 21% of subjects while in group 2, 24% of subjects are hypertensive. This difference too is statistically insignificant.[14]

The various divisions were looked at with respect to their lipid profiles. Uncontrolled group's total cholesterol was statistically higher (243.51±37.16 mg/dl) than the controlled group (178.29±22.86 mg/dl) and that discrepancy was found to be statistically significant (p=0.001). Group 2's mean of the triglyceride level was higher (213.50±39.77 mg/dl) than that of group 1 (139.81±27.11 mg/dl) and that was a statistically significant difference (p=0.001). Mean HDL was less than level 1 of group 2 ((34.10±6.24 mg/dl) and greater than of group 1 (50.21±6.26 mg/dl) and disparity that was found was statistically significant (p=0.001). There was a mean heart rate difference of 0.58 beats per second, with it being 88.21±19.89 beats per minute for group 1 and 88.79±19.57 for group 2, however that difference was rendered statistically insignificant (p=0.871).[14]

Above observations reveals that high HbA1c level and dyslipidemia is associated with higher HSCRP and as substantial part of incident MI and stroke is unaccounted for by traditional cardiovascular risk factors, there is a great need to find novel and preferably modifiable factors that can identify subjects at high risk. Considering the combined effect of HbA1c and HSCRP may help to more exactly identify and better treat these patients at high risk these findings underscore the importance of optimized diabetes control particular in diabetic subjects with elevated HSCRP levels.

CONCLUSION

This study demonstrates a clinically meaningful relationship between poor glycemic control and systemic inflammation among people with T2DM. Individuals with uncontrolled diabetes (HbA1c>7.5) had significantly higher levels of HSCRP and had a more atherogenic lipid profile with increased triglycerides and total cholesterol and much lower HDL. From the correlation analysis, HSCRP had a significantly strong positive correlation with both HbA1c and the more adverse lipid parameters. HSCRP strongly suggests that an increase in glycemic level is an inflammatory anti-activation and is an independent contributor to the rise in cardiovascular risk. These results mean that HSCRP is an inflammatory marker and is a strong determinant of cardiovascular risk among people with diabetes, more so with chronic hyperglycemia. Hence, to cut down risk of cardiovascular complications, there is an urgent need to control hyperglycemia, and early management of lipids is to reduce chronic low-grade inflammation in T2DM. Adding HSCRP levels to the standard assessments done in diabetes should aid in better risk evaluation and more preventive strategies.

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