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A CROSS- SECTIONAL STUDY OF HIGHLY SENSITIVE C-REACTIVE PROTEIN IN TYPE 2 DIABETES MELLITUS AND PREDICTION OF CARDIOVASCULAR RISK WITH GLYCEMIC STATUS.

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ABSTRACT

Background

High-sensitivity C-Reactive Protein (hs-CRP) measurement may be useful for the assessment of the risk of complications in diabetes patients. So, the present study is conducted to measure plasma hs- CRP levels in type 2 diabetes mellitus (T2DM) and to determine whether adequate glycaemic control reduces hs-CRP levels.

Aims and objectives

The objectives of this study were to correlate HbA1c and hs-CRP in T2DM and predict cardiovascular risk with glycaemic status.

Methods

The authors took 50 diabetic patients. The investigation includes Fasting Blood Sugar, Postprandial Blood Sugar, hs- CRP, and Hemoglobin A1c (HbA1c). hs-CRP is measured by the immunoturbidimetry method. The reports were collected and compared with the normal reference range.

Results

The correlation between hs-CRP levels and HbA1c level after six months (<0.001) shows a significant relationship where mean HbA1c values on day 1 and after 6 months were 8.088±1.219 and 7.518±0.693 respectively. The hs-CRP values were 2.508±1.050 on day 1 and 2.15±0.927 after 6 months proving that better glycaemic controls decrease hs-CRP thereby decreasing cardiovascular risk.

Conclusions

hs-CRP values are directly related to HbA1c and better glycaemic control reduces the risk of cardiovascular disease.

Recommendations

The study recommends prioritizing effective glycemic control in Type 2 Diabetes Mellitus patients to lower High-Sensitivity C-Reactive Protein (hs-CRP) levels and reduce cardiovascular risk. It suggests regular monitoring of HbA1c and hs-CRP and further research to include additional factors like BMI and lipid profiles to better understand their impact on hs-CRP levels.

Keywords: *Glycaemic Control, Diabetes, High-Sensitivity C-Reactive Protein, Cardiovascular Risk, Hemoglobin A1c, Insulin Resistance.*

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INTRODUCTION

Diabetes is a global endemic with rapidly increasing prevalence in both developing and developed countries.1 Elevated hs –CRP levels have frequently clustered with well-established risk factors of type 2 diabetes mellitus such as obesity and insulin resistance.2,3 HbA1c is an important indicator of long-term diabetic control with the ability to reflect the cumulative glycemic history of the preceding two to three months. HbA1c provides a reliable measure of chronic glycemia and correlates with the risk of long-term diabetes complications so it is currently considered the test of choice for monitoring and chronic management of diabetes.4-7 Elevated levels of high sensitivity c-reactive protein (hs-CRP) & HbA1C levels have frequently been shown to be associated with type 2 Diabetes. C-reactive protein (CRP) is a liver-derived pattern recognition molecule that is increased in inflammatory states.8-10 It rapidly increases within hours after tissue injury, and it is suggested that it is part of the innate immune system and contributes to host defense.11,12 Since cardiovascular disease is at least in part an inflammatory process, CRP has been investigated in the context of arteriosclerosis and subsequent vascular disorders. The present study aims to observe the relationship between hs-CRP and HbA1c levels in patients with Type 2 Diabetes Mellitus, predicting cardiovascular risk based on glycemic status.

METHODS

Study design:

This study was a cross-sectional study.

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Study setting:

The study was performed in the Clinical Biochemistry Laboratory of Nalanda Medical College and Hospital, Patna, Bihar, India with follow-up. The present study was conducted over 6 months between July 2019 to December 2019.

Participants:

The sample size of patients was 50 after implying all the selection criteria.

Inclusion criteria:

The inclusion criteria are adult patients of type 2 diabetes mellitus diagnosed according to American diabetic association criteria 2015.13

Exclusion criteria:

• The exclusion criteria are heart failure infection acute febrile illness, renal disorders, hepatic disorders, and malignant disorders.

• Patients on hormone replacement therapy, statins, thiazolidinediones, and anti-inflammatory drugs like NSAIDs, type 1 DM.

Data sources/measurement:

The investigation includes complete blood count, urine albumin, renal function test, FBS, PPBS, and HbA1c. The immunoturbidimetric method was used for the measurement of hs- CRP. The American Heart Association and U.S. Centers for Disease Control and Prevention have defined risk groups as follows: Low risk: less than 1.0mg/L, average risk: 1.0 to 3.0mg/L, high risk: above 3.0mg/L.14

Bias:

There was a chance that bias would arise when the study first started, but it was avoided by giving all participants identical information and hiding the group allocation from the nurses who collected the data.

Statistical analysis:

For statistical analysis, SPSS version 22.0 was used to calculate the p-value and x2 value. p-value <0.05 is taken as statistically significant.

Ethical considerations:

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULTS

The present study was conducted with a sample size of 50 patients who were ages 30 years and above with the majority of them in 41-50 years. The sample consisted of 27 males and 23 females. The authors compared the HbA1c value with hs-CRP on day 1 and followed them up after 6 months. During day 1, the patients with HbA1c values of <7 were 8, 7-8 were 20 and >8 was 22. The patients with hs-CRP values of <1 were 5; 1-3 were 32 and >3 were 13. The p values were statistically proving that both HbA1c and hs-CRP are significantly related and out of 22 patients with HbA1c >8, 10 had raised hs-CRP proving an increased CV risk. During the follow-up after 6 months, the patients with HbA1c values in ranges of <7,7-8,>8 were 9, 32, and 9 respectively and the number of pt for hs-CRP values of <1,1-3,>3 were 7, 36, and 7; proving the hypothesis that a glycemic value (HbA1c) has a direct influence on cardiovascular risk and good glycemic control reduces the cardiovascular risk significantly.

The correlation between hs-CRP levels and HbA1c level after six months shows a significant relationship where mean HbA1c values on day 1 and after 6 months were 8.088±1.219 and 7.518±0.693 respectively. The hs-CRP values were 2.508±1.050 on day 1 and 2.15±0.927 at the end of 6 months. (Table: 1)

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ANALYTES	*n*	INITIAL		AT 6TH MONTHEND		p value
		MEAN	SD	MEAN	SD	
HbA1c (%)	50	8.088	1.219	7.518	0.693	<0.001
hs-CRP (mg/L)	50	2.508	1.050	2.15	0.927	<0.001

Table 1: Comparison between hs-CRP levels and HbA1c level on day 1 and after six months

Comparison between hs-CRP level and HbA1c on day 1 and follow-up after 6 months showed 78% cases had HbA1c level under control after 6 months and 22% cases had HbA1c not under control. 82% of cases had decreased hs-CRP levels and 18% had increased hs-CRP levels. After 6 months also, there is a significant correlation between hs-CRP level and HbA1c level. So, these values also suggest that adequate glycemic control can decrease the hs-CRP level.

DISCUSSION

Diabetes is a global pandemic causing substantial comorbidities affecting multiple systems cardiovascular, cerebrovascular, respiratory systems, etc. Vascular co-morbidities including atherosclerosis, account for virtually 80% of diabetes deaths.15 Inflammation plays a major role in the formation of atherosclerotic plaques. The possible mechanisms are activated glycation products, reactive oxygen species, and PKC activation.16-18 Based on multiple epidemiological studies and interventional studies, increased concentrations of hs- CRP are associated with future cardiovascular risk.19 Many studies have investigated the relationship between hs-CRP-DM and hs-CRP-CVD. As DM and inflammation play an important role in CVD development, the present study aims to correlate HbA1c and hs-CRP to predict cardiovascular risk with glycemic status.

The present study was conducted with 50 diabetic patients who were screened on day 1 and followed up after 6 months and results were compared providing the effect of glycemic status on hs-CRP. As the results suggested, the present study showed that patients in whom glycemic control was poor had 18% increased hs-CRP, and patients with good glycemic control had 78% decreased hs-CRP which proves that good glycemic control reduces CVD risk substantially.

The findings of the study highlight a significant correlation between hs-CRP levels and HbA1c in patients with T2DM. The results indicate that improved glycemic control over six months is associated with a reduction in hs-CRP levels, which in turn suggests a decreased cardiovascular risk. This relationship underscores the inflammatory component of cardiovascular disease (CVD), where hs-CRP serves as a biomarker of systemic inflammation.

In a previous study, statistically significant positive association between dietary glycemic load and plasma hs-CRP.20 The median hs-CRP concentration for the lowest quintile of dietary glycemic load was 1.9mg/L and for the highest quintile was 3.7mg/L; respectively (P for trend <0.01). Dietary glycemic load is significantly and positively associated with plasma hs-CRP in healthy middle-aged women, independent of conventional risk factors for cardiovascular diseases. In the present study, showed elevated hs-CRP levels among cases compared to controls in T2DM.

According to hs-CRP levels, seven cases were in the low-risk (<1mg/l), 32 in the moderate-risk (1-3mg/l), and 21 in the high-risk (3-10mg/l) group. It showed that hs-CRP levels correlate with T2DM. This study also showed that increased HbA1c levels correlate with hs- CRP.21 According to a study, showed that hs-CRP is an independent marker of CVD. They found an association between hs-CRP and DM, metabolic syndrome, and CAD. They found that standardized hs-CRP assays with adequate follow-up duration are required to derive risk cut-off values for CVD from the Indian perspective.22

According to the American Heart Association (AHA) and the Centre for Disease Control and Prevention (CDC) shows that hs-CRP is an independent marker of CAD and CVD risk and may be useful as a prognostic indicator for recurrent events in patients with acute coronary disease.23A study found that hs-CRP levels correlated with HbA1c levels. Mean HbA1c levels were significantly higher in patients who had hs-CRP levels of 1 mg/L or more (p-value <0.001).

Other factors such as age, blood pressure, BMI, LDL, and serum creatinine were not correlated with hs-CRP level.24

All previous studies have concluded that diabetes is one of the risk factors for CVD and hs- CRP is a marker of low-grade inflammation in diabetic patients. So, high hs-CRP values increase cardiovascular risk if adequate glycemic status has not been achieved. In the present study also authors proved that hs-CRP values were high in poor glycemic status. The authors also proved that if adequate glycemic status is achieved, hs-CRP values can be decreased, and it decreases the cardiovascular risk.

Generalizability

The study findings suggest that improved glycemic control, which reduces hs-CRP levels and consequently cardiovascular risk, could be broadly applicable to the larger diabetic population. By integrating regular monitoring of HbA1c and hs-CRP into routine diabetes management, these results could inform public health strategies and healthcare guidelines, potentially improving outcomes across diverse demographic groups suffering from Type 2 Diabetes Mellitus.

CONCLUSION

In present study concluded that hs-CRP level has a statistically significant correlation with high HbA1c levels (>8) and adequate glycemic control will decrease hs-CRP level.

LIMITATIONS

The limitations of this study were authors did not include the BMI and lipid profile of patients, which could have a slight influence on the hs-CRP values. Few studies have been done which have found a significant influence of these factors on the hs-CRP values. If these factors could be included in future studies the outcome of predictability will be better.7

RECOMMENDATIONS

The study recommends prioritizing effective glycemic control in Type 2 Diabetes Mellitus patients to lower High-Sensitivity C-Reactive Protein (hs-CRP) levels and reduce cardiovascular risk. It suggests regular monitoring of HbA1c and hs-CRP and further research to include additional factors like BMI and lipid profiles to better understand their impact on hs-CRP levels.

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LIST OF ABBREVIATIONS

hs-CRP - High-Sensitivity C-Reactive Protein
T2DM - Type 2 Diabetes Mellitus
CVD - Cardiovascular Disease
HbA1c - Hemoglobin A1c
FBS - Fasting Blood Sugar
PPBS - Postprandial Blood Sugar
BMI - Body Mass Index
LDL - Low-Density Lipoprotein
CAD - Coronary Artery Disease
AHA - American Heart Association
CDC - Centers for Disease Control and Prevention

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CONFLICT OF INTEREST

The authors have no competing interests to declare.

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