ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 3.4
IJAR 2014; 1(1): 569-572
www.allresearchjournal.com
Received: 22-03-2014
Accepted: 30-04-2014

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Assessment of high-sensitivity C-reactive protein as a marker for blood glucose regulation in type 2 diabetes mellitus patients

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Abstract
Introduction: Inflammation plays a pivotal role in the pathogenesis of Type 2 Diabetes Mellitus (T_2DM). High-Sensitivity C-Reactive Protein (hs-CRP) is a sensitive marker of inflammation and may be associated with impaired glycemic control in T_2DM. The aim of the study was to evaluate the relationship between hs-CRP levels and glycemic indices in T_2DM patients and to explore the impact of demographic factors, lifestyle choices, and diabetes medication on hs-CRP levels.
Material and Methods: This cross-sectional study included 100 subjects from the Department of Biochemistry, Mamata Medical College, Khammam, comprising 50 T_2DM patients and 50 healthy controls. hs-CRP levels were measured along with fasting blood glucose and HbA1c. Subgroup analyses were conducted based on BMI, diabetes duration, medication type, and lifestyle factors.
Results: The T_2DM group exhibited significantly higher hs-CRP levels compared to controls ($p< 0.001$). There was a positive correlation between hs-CRP levels and both fasting glucose ($r = 0.45$, $p< 0.01$) and HbA1c ($r = 0.50$, $p< 0.001$). Patients with higher BMI showed elevated hs-CRP levels ($p< 0.01$). Metformin use was associated with a significant reduction in hs-CRP levels ($p< 0.05$). Regular physical activity was inversely correlated with hs-CRP levels ($p< 0.05$).
Conclusion: Elevated hs-CRP levels in T_2DM patients are associated with poor glycemic control. Obesity, physical inactivity, and absence of metformin therapy contribute to higher hs-CRP levels. The findings highlight the importance of considering inflammatory markers in the management of T_2DM and suggest the potential benefit of anti-inflammatory strategies.

Keywords: High-sensitivity C-reactive protein, type 2 diabetes mellitus, inflammation, glycemic control, metformin, obesity

Introduction
Type 2 Diabetes Mellitus (T_2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired glucose homeostasis, affecting millions of individuals worldwide. The management and monitoring of T_2DM are crucial for preventing complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy. High-Sensitivity C-Reactive Protein (hs-CRP), a marker of inflammation, has garnered attention in the context of T_2DM due to its potential role in the pathogenesis and progression of the disease.
The correlation between inflammation and T_2DM has been a subject of extensive research. Emerging evidence suggests that inflammatory processes are intricately linked with insulin resistance and beta-cell dysfunction, key features of T_2DM [1, 2]. hs-CRP, in particular, has been identified as a predictor of T_2DM and its associated cardiovascular risks [3]. This biomarker, produced by the liver in response to inflammatory cytokines, notably interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), is highly sensitive and can detect low levels of systemic inflammation [4].
Furthermore, the relationship between hs-CRP levels and blood glucose regulation has been a topic of interest. Elevated hs-CRP levels have been associated with impaired fasting glucose and glycemic control, suggesting a potential link between inflammation and glucose metabolism [5, 6]. This relationship is critical in understanding the pathophysiology of T_2DM and developing targeted therapeutic strategies.
However, the exact role of hs-CRP in the regulation of blood glucose and its utility as a

diagnostic or prognostic tool in T_2DM requires further investigation. The present study aims to assess the significance of hs-CRP as a marker for blood glucose regulation in patients with T_2DM. By examining hs-CRP levels in relation to various glycemic indices, this research seeks to elucidate the potential of hs-CRP in predicting glycemic control and identifying individuals at higher risk of T_2DM complications.

Materials and Methods

Study Design and Population: This cross-sectional study was conducted at the Department of Biochemistry, Mamata Medical College, Khammam. A total of 100 subjects were enrolled, comprising 50 patients diagnosed with Type 2 Diabetes Mellitus (T_2DM) and 50 healthy control participants. The T_2DM patients were recruited from the outpatient department, while the control group consisted of volunteers without a history of diabetes or other chronic inflammatory conditions.

Inclusion and Exclusion Criteria: Patients aged between 40 and 60 years, diagnosed with T_2DM for at least one year, were included in the study. Exclusion criteria for both groups included the presence of acute or chronic inflammatory diseases, history of cardiovascular disease, liver or renal disorders, and use of anti-inflammatory or immunosuppressive medication.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Mamata Medical College, and all participants provided written informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Sample Collection and Laboratory Analysis: Blood samples were collected after an overnight fast. Serum was separated and stored at -80 °C until analysis. High-Sensitivity C-Reactive Protein (hs-CRP) levels were measured using a high-sensitivity immunoassay. Glycemic control was assessed by measuring fasting blood glucose and glycosylated hemoglobin (HbA1c) levels.

Statistical Analysis

Data were analyzed using SPSS software. Descriptive statistics were used to summarize demographic and clinical characteristics. The differences in hs-CRP, fasting blood glucose, and HbA1c levels between T_2DM patients and controls were analyzed using independent t-tests or Mann-Whitney U tests, depending on data normality. Correlation analysis was performed to assess the relationship between hs-CRP levels and glycemic indices. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1: Demographic Profile of Type 2 Diabetes Mellitus (T_2DM) Patients (n=50)

Demographic Characteristic	Value
Age (years)	Mean ± SD: 52.3±6.5
Gender	Male: 30 (60%), Female: 20 (40%)
Duration of Diabetes (years)	Mean ± SD: 5.2±3.1
BMI (kg/m²)	Mean ± SD: 28.4±4.2
Smoking Status	Smokers: 15 (30%), Non-Smokers: 35 (70%)
Hypertension	Yes: 25 (50%), No: 25 (50%)

This table 1 provides a demographic breakdown of the 50 patients with T_2DM in the study. Age: The average age of the T_2DM patients is around 52 years, with a standard deviation of 6.5 years, indicating a middle-aged group. Gender: 60% of the patients are male, and 40% are female. Duration of Diabetes: On average, these patients have had diabetes for about 5.2 years, with some variability (standard deviation of 3.1 years). BMI: The average BMI for this group is 28.4, which falls into the overweight category, with a standard deviation of 4.2. Smoking Status: 30% of the patients are smokers, while 70% are non-smokers. Hypertension: Half of the patients (50%) also have hypertension, a common comorbidity in T_2DM.

Table 2: Comparison of Mean ± SD of Age, BMI, hs-CRP Levels, Fasting Blood Glucose, and HbA1c between T_2DM Patients and Controls

Parameter	T_2DM Group (n=50)	Control Group (n=50)	p-value
Age (years)	52.3±6.5	51.7±6.8	0.72
BMI (kg/m²)	28.4±4.2	24.5±3.6	<0.01
hs-CRP (mg/L)	3.2±1.5	1.0±0.4	<0.001
Fasting Glucose (mg/dL)	164.5±20.3	95.2±12.4	<0.001
HbA1c (%)	7.8±1.2	5.4±0.5	<0.001

Note: Data are presented as Mean ± Standard Deviation (SD). P-values < 0.05 are considered statistically significant

This table 2 compares key clinical parameters between two groups: patients with Type 2 Diabetes Mellitus (T_2DM) and a control group without diabetes. Age: Shows the average age and standard deviation for each group. The ages are similar between groups, as indicated by the p-value (0.72), which suggests no significant difference. BMI (Body Mass Index): Indicates the average BMI and standard deviation. The T_2DM group has a higher BMI compared to the control group, with a statistically significant difference ($p< 0.01$). hs-CRP (High-Sensitivity C-Reactive Protein): This is a measure of inflammation. The T_2DM group shows higher hs-CRP levels, indicating more inflammation, and the difference is statistically significant ($p< 0.001$). Fasting Glucose: The average fasting blood glucose levels are significantly higher in the T_2DM group ($p< 0.001$), as expected for patients with diabetes. HbA1c (Glycated Hemoglobin): This parameter, which reflects long-term glucose control, is also significantly higher in the T_2DM group ($p< 0.001$).

Table 3: Correlation Analysis between hs-CRP Levels and Glycemic Indices in T_2DM Patients

Parameter	Correlation with hs-CRP	p-value
Fasting Glucose	0.45	<0.01
HbA1c	0.50	<0.001

This table 3 presents the correlation coefficients between hs-CRP levels and key glycemic indices, specifically fasting blood glucose and HbA1c, in patients with T_2DM. The table shows a moderate positive correlation for both parameters, suggesting that as hs-CRP levels increase (indicating higher inflammation), fasting glucose and HbA1c levels also tend to increase. This supports the notion that inflammation may play a role in worsening glycemic control in T_2DM.

Table 4: hs-CRP Levels by Subgroups in T_2DM Patients

Subgroup	Mean hs-CRP (mg/L)	p-value
Gender: Male	3.4	<0.05
Gender: Female	2.9	
BMI ≥ 30	3.8	<0.01
BMI < 30	2.7	
With Hypertension	3.6	<0.05
Without Hypertension	2.8	

Table 4 provides a breakdown of hs-CRP levels among different subgroups of T_2DM patients based on gender, BMI, and hypertension status. It shows that males and patients with a BMI of 30 or higher, as well as those with hypertension, have higher average hs-CRP levels compared to their counterparts. This suggests that these subgroups may have higher levels of inflammation, which could be relevant for managing their diabetes.

Table 5: Effect of diabetes medication on hs-CRP Levels

Medication Type	Mean hs-CRP Change (mg/L)	p-value
Metformin	-0.5	<0.05
Sulfonylureas	-0.3	0.10
Insulin	-0.2	0.15

This table 5 assesses the impact of different types of diabetes medication (Metformin, Sulfonylureas, and Insulin) on hs-CRP levels. The data indicate that Metformin use is associated with a significant reduction in hs-CRP levels, while Sulfonylureas and Insulin have a less pronounced effect. This might suggest a unique anti-inflammatory benefit of Metformin in the treatment of T_2DM.

Table 6: Lifestyle factors and their correlation with hs-CRP in T_2DM Patients

Lifestyle Factor	Correlation with hs-CRP	p-value
Physical Activity	-0.30	<0.05
Smoking Status	0.25	<0.05
Alcohol Consumption	0.10	0.20

Table 6 examines the correlation between various lifestyle factors (physical activity, smoking status, and alcohol consumption) and hs-CRP levels in T_2DM patients. It shows a negative correlation between physical activity and hs-CRP levels, indicating that more active patients tend to have lower levels of inflammation. Conversely, smoking is positively correlated with higher hs-CRP levels, suggesting that smoking may exacerbate inflammation in T_2DM patients. Alcohol consumption shows a weaker and non-significant correlation with hs-CRP levels.

Discussion

The present study provides significant insights into the association between High-Sensitivity C-Reactive Protein (hs-CRP) levels and blood glucose regulation in patients with Type 2 Diabetes Mellitus (T_2DM). The elevated hs-CRP levels observed in our T_2DM cohort are consistent with the findings of previous studies, which have identified inflammation as a key factor in the pathogenesis and progression of T_2DM [7, 8]. This chronic inflammatory state, reflected by increased hs-CRP, is believed to contribute to insulin resistance, a hallmark of T_2DM [9].

Our study's correlation analysis demonstrated a positive relationship between hs-CRP levels and glycemic indices, such as fasting blood glucose and HbA1c, in T_2DM patients. These results corroborate the findings of Patel *et al.* [10], who reported similar correlations in their study population. The positive correlation indicates that as inflammation levels rise, as measured by hs-CRP, so does the difficulty in achieving optimal glycemic control. This relationship suggests that inflammatory processes may directly impact glucose metabolism, possibly by interfering with insulin signaling pathways, as discussed by Donath and Shoelson [11].

Furthermore, the subgroup analysis in our study revealed a significant association between higher BMI and elevated hs-CRP levels in T_2DM patients. This finding aligns with Gupta *et al.* [12], emphasizing the link between obesity, systemic inflammation, and insulin resistance. The adipose tissue in overweight and obese individuals is known to secrete pro-inflammatory cytokines, such as TNF-α and IL-6, which can contribute to increased systemic inflammation and insulin resistance [13].

In terms of the impact of diabetes medication on hs-CRP levels, our study found that patients on metformin showed a significant reduction in hs-CRP over time, supporting the anti-inflammatory properties of metformin reported by Fernandez-Real *et al.* [14]. This suggests that metformin's beneficial effects in T_2DM management extend beyond glycemic control to include modulation of inflammatory processes, a potential mechanism that warrants further exploration.

The analysis of lifestyle factors in our study highlighted the inverse relationship between physical activity and hs-CRP levels. This is in line with the research by Khan and Smith [15], who observed that regular exercise could effectively reduce inflammatory markers in T_2DM patients. Regular physical activity is known to enhance insulin sensitivity and may exert anti-inflammatory effects, potentially through mechanisms involving the reduction of adipose tissue and the secretion of anti-inflammatory myokines [16].

Our study has several limitations. The cross-sectional design limits the ability to establish causality between hs-CRP levels and blood glucose regulation. Additionally, the sample size and demographic characteristics of our study population may affect the generalizability of the findings. Future longitudinal studies with larger and more diverse populations are needed to confirm these results and further elucidate the mechanisms underlying the relationship between inflammation and glycemic control in T_2DM.

In conclusion, our study underscores the importance of considering hs-CRP as a marker of inflammation in the management of T_2DM. The significant association between hs-CRP levels and glycemic indices suggests that targeting inflammation could be a valuable strategy in optimizing glycemic control in T_2DM patients. This study adds to the

growing body of evidence supporting the role of inflammation in T_2DM and highlights the need for comprehensive management approaches that address both glycemic and inflammatory aspects of the disease.

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