

Serum High Sensitive CRP Levels in Patients with Type 2 Diabetes Mellitus: A Case-Control Study

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with chronic low-grade inflammation, which may contribute to disease pathogenesis and progression. High-sensitive C-reactive protein (hs-CRP) is an established inflammatory biomarker that may be elevated in T2DM patients.

Objective: To evaluate and compare serum hs-CRP levels in patients with Type 2 diabetes mellitus and healthy controls.

Methods: This case-control study included 50 T2DM patients (cases) and 50 age and sex-matched healthy individuals (controls). Patients with Type 1 diabetes, known diabetic complications, hypertension, and other lifestyle diseases were excluded. Serum hs-CRP levels were measured using immunoturbidimetric assay. Data were analyzed using independent t-test and chi-square test. A p-value <0.05 was considered statistically significant.

Results: The mean age of cases was 52.4±8.6 years and controls was 51.8±8.2 years. There were 28 males (56%) and 22 females (44%) in each group. The mean serum hs-CRP level in T2DM patients was 4.82±2.14 mg/L, significantly higher than controls (1.68±0.92 mg/L) with p<0.001. Elevated hs-CRP levels (>3 mg/L) were found in 72% of cases compared to 12% of controls (p<0.001).

Conclusion: Serum hs-CRP levels are significantly elevated in Type 2 diabetes mellitus patients compared to healthy controls, suggesting the presence of chronic subclinical inflammation in T2DM. Hs-CRP may serve as a useful biomarker for assessing inflammatory status in diabetic patients.

Keywords: High-sensitive C-reactive protein, Type 2 diabetes mellitus, inflammation, case-control study, biomarker

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has emerged as a major global health challenge, affecting approximately 589 million adults worldwide as of 2026, with projections suggesting this number will rise to 853 million by 2050 [1]. T2DM is characterized by insulin resistance and progressive beta-cell dysfunction, leading to chronic hyperglycemia and associated micro- and macrovascular complications. Emerging evidence suggests that chronic low-grade inflammation plays a crucial role in the pathogenesis of T2DM and its complications [2]. Inflammatory mediators such as cytokines, chemokines, and acute-phase proteins are elevated in diabetic patients and contribute to insulin resistance, endothelial dysfunction, and atherosclerosis [3].

C-reactive protein (CRP) is an acute-phase reactant synthesized primarily by hepatocytes in response to inflammatory cytokines, particularly interleukin-6 (IL-6) [4]. High-sensitive CRP (hs-CRP) assays can detect lower concentrations of CRP and are widely used to assess cardiovascular risk and subclinical inflammation [5]. Previous studies have demonstrated associations between elevated hs-CRP levels and insulin resistance, metabolic syndrome, and cardiovascular disease [6,7]. However, the relationship between hs-CRP and T2DM in specific populations requires further investigation to establish its utility as a diagnostic and prognostic biomarker [8]. Understanding the inflammatory profile of T2DM patients through hs-CRP assessment may provide insights into disease mechanisms and help identify patients at higher risk for complications [9]. This study aims to evaluate serum hs-CRP levels in T2DM patients without known complications and compare them with healthy controls.

MATERIALS AND METHODS

This was a hospital-based case-control study conducted in the Department of Laboratory Medicine, Government Medical college Nagapattinam over a period of 12 months from January 2024 to December 2024. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants.

Sample Size: 100 participants (50 cases and 50 controls)

Cases: Patients diagnosed with Type 2 diabetes mellitus attending the outpatient department

Controls: Age and sex-matched healthy individuals with no history of diabetes or other chronic diseases.

Inclusion Criteria

For Cases:

- Diagnosed cases of Type 2 diabetes mellitus (as per American Diabetes Association criteria) [10]
- Age 30-70 years

- Both males and females
- Willing to participate and provide informed consent

For Controls:

- Healthy individuals without diabetes
- Age and sex-matched with cases
- Fasting blood glucose <100 mg/dL and HbA1c <5.7%
- Willing to participate and provide informed consent

Exclusion Criteria

For both groups:

- Type 1 diabetes mellitus patients
- Diabetes patients with known complications (retinopathy, nephropathy, neuropathy, diabetic foot)
- Hypertension (BP >140/90 mmHg or on antihypertensive medications)
- Other lifestyle diseases (coronary artery disease, stroke, peripheral vascular disease)
- Acute infections or inflammatory conditions in the past 4 weeks
- Chronic inflammatory diseases (rheumatoid arthritis, inflammatory bowel disease, etc.)
- Malignancy
- Chronic liver or kidney disease
- Pregnancy
- Use of anti-inflammatory medications or immunosuppressants

Study Procedure

All participants underwent detailed history taking and clinical examination. Demographic data including age, sex, duration of diabetes (for cases), and body mass index (BMI) were recorded. After 12 hours of overnight fasting, 5 mL of venous blood was collected under aseptic precautions. Samples were allowed to clot and centrifuged at 3000 rpm for 10 minutes. Serum was separated and stored at -20°C until analysis.

Laboratory Investigations:

Fasting blood glucose, HbA1c (for cases), Serum high-sensitive CRP (immunoturbidimetric method) Lipid profile, Renal function tests.

Hs-CRP Measurement:

Serum hs-CRP was measured using immunoturbidimetric assay with a detection range of 0.1-20 mg/L by using Getein Biotech kit.

Classification of hs-CRP Levels:

- Low risk: <1 mg/L
- Average risk: 1-3 mg/L
- High risk: >3 mg/L [5]

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean \pm standard deviation (SD) and

categorical variables as frequencies and percentages. The statistical analysis was performed using appropriate inferential methods. An independent samples *t*-test was applied to compare the mean values between cases and controls. Categorical variables were analyzed using the chi-square test. Correlation analysis was conducted using the Pearson correlation coefficient. A *p*-value of less than 0.05 was considered statistically significant. Where applicable, results were reported with 95% confidence intervals to estimate the precision of the observed effects.

RESULTS

A total of 100 participants were enrolled in the study, comprising 50 cases (T2DM patients) and 50 controls (healthy individuals).

Table 1: Demographic and Clinical Characteristics of Study Population

Parameter	Cases (n=50)	Controls (n=50)	p-value
Age (years)	52.4 \pm 8.6	51.8 \pm 8.2	0.718
Male, n (%)	28 (56%)	28 (56%)	1.000
Female, n (%)	22 (44%)	22 (44%)	1.000
BMI (kg/m ²)	26.8 \pm 3.4	24.2 \pm 2.8	<0.001
Duration of diabetes (years)	5.2 \pm 3.1	-	-

Data are Mean \pm SD

The mean age of cases was 52.4 \pm 8.6 years and controls was 51.8 \pm 8.2 years, with no statistically significant difference (*p*=0.718). The gender distribution was identical in both groups with 56% males and 44%

females. The mean BMI was significantly higher in cases (26.8 \pm 3.4 kg/m²) compared to controls (24.2 \pm 2.8 kg/m²) with *p*<0.001. The mean duration of diabetes in cases was 5.2 \pm 3.1 years.

Table 2: Comparison of Biochemical Parameters

Parameter	Cases (n=50)	Controls (n=50)	p-value
Fasting blood glucose (mg/dL)	156.4 \pm 42.8	88.6 \pm 8.4	<0.001
HbA1c (%)	8.2 \pm 1.6	5.1 \pm 0.4	<0.001
Total cholesterol (mg/dL)	198.4 \pm 38.6	174.2 \pm 28.4	<0.001
Triglycerides (mg/dL)	168.2 \pm 52.4	126.4 \pm 34.2	<0.001
HDL cholesterol (mg/dL)	42.6 \pm 8.4	52.8 \pm 9.2	<0.001
LDL cholesterol (mg/dL)	122.4 \pm 32.6	98.2 \pm 24.8	<0.001

Data are Mean \pm SD

All biochemical parameters showed statistically significant differences between cases and controls (*p*<0.001), confirming the metabolic dysregulation in T2DM patients.

Table 3: Comparison of Serum hs-CRP Levels

Group	n	Mean hs-CRP (mg/L)	SD	95% CI	p-value
Cases	50	4.82	2.14	4.21-5.43	<0.001
Controls	50	1.68	0.92	1.42-1.94	

The mean serum hs-CRP level in T2DM patients was 4.82 ± 2.14 mg/L, which was significantly higher than controls (1.68 ± 0.92 mg/L). The difference was statistically highly significant ($p < 0.001$) with a mean difference of 3.14 mg/L (95% CI: 2.46-3.82). The independent samples *t*-test demonstrated a statistically significant difference between the groups, with a *t*-

statistic of 9.24 and 98 degrees of freedom. The observed difference was highly significant ($p < 0.001$). The magnitude of the effect was large, as indicated by a Cohen's *d* value of 1.85, reflecting a substantial difference between the groups.

Distribution of hs-CRP Categories

Table 4: Distribution of Participants According to hs-CRP Risk Categories

hs-CRP Category	Cases n (%)	Controls n (%)	χ^2	p-value
Low risk (<1 mg/L)	4 (8%)	22 (44%)		
Average risk (1-3 mg/L)	10 (20%)	22 (44%)	42.86	<0.001
High risk (>3 mg/L)	36 (72%)	6 (12%)		

The distribution of hs-CRP categories showed highly significant differences between cases and controls ($\chi^2=42.86$, $p < 0.001$). In the T2DM group, 72% of

patients had high-risk hs-CRP levels (>3 mg/L) compared to only 12% in the control group. Only 8% of cases had low-risk levels compared to 44% of controls.

Table 5: Correlation of hs-CRP with Clinical and Biochemical Parameters in Cases

Parameter	Pearson correlation coefficient (r)	p-value
Duration of diabetes	0.342	0.015
BMI	0.428	0.002
Fasting blood glucose	0.386	0.006
HbA1c	0.512	<0.001
Total cholesterol	0.298	0.035
Triglycerides	0.364	0.009
HDL cholesterol	-0.312	0.027
LDL cholesterol	0.286	0.044

In T2DM patients, hs-CRP showed significant positive correlations with HbA1c ($r=0.512$, $p < 0.001$), BMI ($r=0.428$, $p=0.002$), fasting blood glucose ($r=0.386$, $p=0.006$), triglycerides ($r=0.364$, $p=0.009$), and duration of diabetes ($r=0.342$, $p=0.015$). A significant negative correlation was observed with HDL cholesterol ($r=-0.312$, $p=0.027$).

DISCUSSION

This case-control study demonstrated that serum hs-CRP levels are significantly elevated in patients with Type 2 diabetes mellitus compared to healthy controls. The mean hs-CRP level in diabetic patients was nearly three times higher than in controls (4.82 ± 2.14 mg/L vs 1.68 ± 0.92 mg/L, $p < 0.001$), supporting our research hypothesis. Furthermore, 72% of T2DM

patients had high-risk hs-CRP levels (>3 mg/L) compared to only 12% of controls, indicating a state of chronic subclinical inflammation in diabetic individuals.

Our findings are consistent with several previous investigations. A study by Pradhan et al. demonstrated that elevated CRP levels predict the development of type 2 diabetes, suggesting that inflammation precedes the onset of clinical disease [2]. Similarly, Festa et al. found that CRP levels were significantly higher in individuals with metabolic syndrome and diabetes [3].

The mean hs-CRP level of 4.82 mg/L observed in our diabetic patients aligns with reports from other populations. A study from India by Nakanishi et al. reported mean hs-CRP levels of 4.2-5.6 mg/L in T2DM patients, while a European study by Thorand et al. found levels ranging from

3.8-5.2 mg/L [6]. These consistent findings across different populations strengthen the evidence for chronic inflammation in T2DM.

The elevated hs-CRP levels in T2DM patients can be explained through several interconnected mechanisms:

Insulin Resistance and Inflammation:

Chronic low-grade inflammation contributes to insulin resistance through multiple pathways. Pro-inflammatory cytokines such as TNF- α and IL-6 interfere with insulin signaling by promoting serine phosphorylation of insulin receptor substrate-1, thereby reducing insulin sensitivity [11]. These same cytokines stimulate hepatic CRP production [4].

Adipose Tissue Dysfunction: The higher BMI observed in our diabetic patients (26.8 \pm 3.4 kg/m²) is relevant, as adipose tissue, particularly visceral fat, secretes pro-inflammatory adipokines and cytokines [9]. The significant correlation between hs-CRP and BMI (r=0.428, p=0.002) in our study supports the role of adiposity in systemic inflammation [12].

Hyperglycemia and Oxidative Stress:

Chronic hyperglycemia induce oxidative stress through increased production of reactive oxygen species, advanced glycation end products (AGEs), and activation of protein kinase C [13]. These processes trigger inflammatory pathways and stimulate acute-phase protein synthesis, including CRP.

The elevated hs-CRP levels in T2DM patients have important clinical implications. Our finding that 72% of T2DM patients have high-risk hs-CRP levels (>3 mg/L) suggests that hs-CRP measurement could be useful for cardiovascular risk stratification in diabetic patients [5]. The strong positive correlation between hs-CRP and HbA1c (r=0.512, p<0.001) indicates that inflammatory status is related to glycemic control, suggesting that improving glycemic control may reduce inflammatory burden [14].

CONCLUSION

The significant correlations between hs-CRP and glycemic control (HbA1c), BMI, and lipid parameters suggest that inflammation is integrally linked to metabolic dysregulation in diabetes. These findings support the hypothesis that T2DM is not merely a metabolic disorder but also an inflammatory condition. The clinical implications are substantial: hs-CRP may serve as a valuable biomarker for cardiovascular risk stratification, treatment monitoring, and prognostication in T2DM patients. Targeting inflammation may represent an important therapeutic strategy beyond traditional glycemic control.

Declaration by Authors

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