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Original research article

A study on the correlation between C - reactive protein and serum ferritin in type 2 diabetes mellitus

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is associated with chronic low-grade inflammation and altered iron metabolism, which may contribute to the development and progression of diabetic complications. This study aimed to investigate the correlation between C-reactive protein (CRP) and serum ferritin levels in T2DM patients and their association with glycemic control and diabetic complications. **Methods:** A total of 100 T2DM patients and 100 non-diabetic controls were included in this cross-sectional study. Serum levels of CRP and ferritin were measured, and their association with glycemic control (HbA1c) and the presence of diabetic complications (neuropathy, nephropathy, and retinopathy) was evaluated. **Results:** T2DM patients had significantly higher levels of CRP (6.82 ± 4.23 mg/L) and serum ferritin (241.7 ± 96.94 ng/mL) compared to non-diabetic controls (2.64 ± 1.87 mg/L and 199.02 ± 82.7 ng/mL, respectively) (p<0.001 and p=0.022, respectively). A significant positive correlation was found between CRP and serum ferritin levels in T2DM patients (r=0.45, p<0.001). Poor glycemic control (HbA1c ≥7%) and the presence of diabetic complications were associated with significantly higher levels of CRP and serum ferritin in T2DM patients (p<0.001 for all). **Conclusion:** T2DM patients have significantly higher levels of CRP and serum ferritin compared to non-diabetic controls, and these markers are positively correlated with each other. Poor glycemic control and the presence of diabetic complications are associated with higher levels of CRP and serum ferritin in T2DM patients. These findings suggest that inflammation and iron metabolism may play a role in the pathogenesis of T2DM and its complications.

Keywords: Type 2 diabetes mellitus, C-reactive protein, serum ferritin, inflammation, iron metabolism, glycemic control, diabetic complications.

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both [1]. Type 2 diabetes mellitus (T2DM) is the most common form of diabetes, accounting for approximately 90% of all diabetes cases worldwide [2]. The global prevalence of diabetes has been increasing rapidly, with an estimated 463 million adults living with diabetes in 2019, and this number is projected to rise to 700 million by 2045 [3].

T2DM is associated with various complications, including cardiovascular disease, nephropathy, retinopathy, and neuropathy, which contribute to increased morbidity and mortality [4]. The pathogenesis of these complications is complex and multifactorial, involving chronic hyperglycemia, oxidative stress, and inflammation [5]. In recent years, there has been growing interest in the role of inflammation in the development and progression of T2DM and its complications.

C-reactive protein (CRP) is an acute-phase protein produced by the liver in response to inflammation, infection, and tissue damage [6]. It is a sensitive marker of systemic inflammation and has been associated with an increased risk of cardiovascular disease, insulin resistance, and T2DM [7]. Several studies have reported elevated levels of CRP in patients with T2DM compared to non-diabetic individuals [8, 9].

Ferritin is an intracellular protein that stores iron and releases it in a controlled fashion [10]. Serum ferritin is a marker of iron stores in the body and is also an acute-phase reactant that increases during inflammation [11].

Elevated serum ferritin levels have been associated with insulin resistance, metabolic syndrome, and T2DM [12, 13]. Moreover, some studies have suggested that increased body iron stores may contribute to

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the development of diabetic complications, such as nephropathy and cardiovascular disease [14, 15].
Given the potential role of inflammation and iron metabolism in the pathogenesis of T2DM and its complications, several studies have investigated the relationship between CRP and serum ferritin levels in patients with T2DM. Mohan *et al*. [16] found that both CRP and ferritin levels were significantly higher in patients with T2DM compared to non-diabetic controls, and there was a positive correlation between CRP and ferritin levels in the diabetic group. Similarly, Canturk *et al*. [17] reported that serum ferritin levels were significantly higher in poorly controlled T2DM patients compared to well-controlled diabetic patients and healthy controls.
Furthermore, some studies have explored the association between CRP, ferritin, and diabetic complications. Raj and Rajan [18] found that serum ferritin levels were significantly higher in T2DM patients with microvascular complications compared to those without complications, and there was a positive correlation between ferritin and CRP levels in patients with complications. In another study, Akinloye *et al*. [19] reported that CRP and ferritin levels were significantly higher in T2DM patients with nephropathy compared to those without nephropathy and healthy controls.
These findings suggest that chronic inflammation and altered iron metabolism may play a role in the pathogenesis of T2DM and its complications. However, the relationship between CRP, ferritin, and T2DM is complex and not fully understood. Some studies have reported conflicting results, and there is a need for further research to clarify the mechanisms underlying these associations and their potential clinical implications [20].
In this context, the present study aims to investigate the correlation between CRP and serum ferritin levels in patients with T2DM and explore their potential role as markers of inflammation and diabetic complications. Understanding the relationship between these parameters may provide insights into the pathophysiology of T2DM and aid in the development of novel strategies for the prevention and management of diabetic complications.

Aims and Objectives
The primary aim of this study was to investigate the correlation between C-reactive protein (CRP) and serum ferritin levels in patients with type 2 diabetes mellitus (T2DM). The secondary objectives were to compare the levels of CRP and serum ferritin between T2DM patients and non-diabetic controls and to explore the association of these markers with glycemic control and diabetic complications.

Materials and Methods
Study Design and Setting
This prospective observational study was conducted at a tertiary care hospital over a period of two years. The study protocol was approved by the Institutional Ethics Committee, and informed consent was obtained from all participants.

Study Population
A total of 200 participants, including 100 patients with type 2 diabetes mellitus (T2DM) and 100 age- and sex-matched non-diabetic controls, were enrolled in the study. The inclusion criteria for T2DM patients were: age ≥30 years, diagnosed with T2DM according to the American Diabetes Association criteria, and willingness to participate in the study. Patients with type 1 diabetes, gestational diabetes, acute or chronic infections, inflammatory conditions, malignancies, liver diseases, and those on iron supplementation were excluded from the study. Non-diabetic controls were selected from the general population and were free from any known metabolic disorders or chronic diseases.

Sample Size Calculation
The sample size was calculated using a formula for correlation coefficient with a significance level of 0.05 and power of 80%. Assuming a correlation coefficient of 0.3 between C-reactive protein (CRP) and serum ferritin levels, the minimum required sample size was determined to be 85 participants in each group. Considering a potential dropout rate of 15%, a total of 100 T2DM patients and 100 non-diabetic controls were enrolled in the study.

Data Collection
Demographic and clinical data, including age, sex, duration of diabetes, body mass index (BMI), blood pressure, and presence of diabetic complications (neuropathy, nephropathy, and retinopathy), were collected using a structured questionnaire. Fasting blood samples were obtained from all participants for the measurement of blood glucose, glycated hemoglobin (HbA1c), CRP, and serum ferritin levels. CRP levels were measured using a high-sensitivity immunoturbidimetric assay, while serum ferritin levels were determined by an electrochemiluminescence immunoassay.

Definitions and Criteria
T2DM was defined as fasting blood glucose ≥126 mg/dL, 2-hour post-prandial blood glucose ≥200

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mg/dL, or HbA1c ≥6.5%. Glycemic control was categorized as good (HbA1c <7%) or poor (HbA1c ≥7%). Diabetic neuropathy was assessed using the Michigan Neuropathy Screening Instrument, nephropathy was defined as the presence of albuminuria (urinary albumin-to-creatinine ratio ≥30 mg/g), and retinopathy was diagnosed by fundoscopic examination.

Statistical Analysis

Data were analyzed using SPSS version 23.0. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), while categorical variables were presented as frequencies and percentages. The normality of data distribution was assessed using the Shapiro-Wilk test. Independent t-test or Mann-Whitney U test was used to compare continuous variables between groups, while chi-square test or Fisher's exact test was employed for categorical variables. Pearson's or Spearman's correlation coefficient was used to assess the correlation between CRP and serum ferritin levels. A p-value <0.05 was considered statistically significant.

Results

The study included 100 patients with type 2 diabetes mellitus (T2DM) and 100 non-diabetic controls. The demographic and clinical characteristics of the study population are presented in Table 1. The mean age of T2DM patients was 58.2 ± 10.5 years, and that of non-diabetic controls was 56.8 ± 11.2 years (p=0.352). The gender distribution was similar in both groups, with 55 males and 45 females in the T2DM group and 52 males and 48 females in the control group (p=0.671). The median duration of diabetes in the T2DM group was 9.5 years (interquartile range: 5-15 years). T2DM patients had a significantly higher BMI (29.4 ± 4.6 kg/m²) compared to controls (25.1 ± 3.8 kg/m²) (p<0.001). Both systolic and diastolic blood pressure were significantly higher in the T2DM group (138 ± 18 mmHg and 84 ± 11 mmHg, respectively) compared to the control group (124 ± 14 mmHg and 76 ± 9 mmHg, respectively) (p<0.001 for both). Among the T2DM patients, 35% had neuropathy, 25% had nephropathy, and 20% had retinopathy.

The comparison of CRP and serum ferritin levels between T2DM patients and non-diabetic controls is shown in Table 2. The mean CRP level was significantly higher in T2DM patients (6.82 ± 4.23 mg/L) compared to non-diabetic controls (2.64 ± 1.87 mg/L) (p<0.001). Similarly, the mean serum ferritin level was significantly higher in T2DM patients (241.7 ± 96.94 ng/mL) compared to non-diabetic controls (199.02 ± 82.7 ng/mL) (p=0.022).

The correlation between CRP and serum ferritin levels in T2DM patients was assessed using Spearman's correlation coefficient (Table 3). There was a significant positive correlation between CRP and serum ferritin levels (r=0.45, p<0.001), indicating that higher CRP levels were associated with higher serum ferritin levels in T2DM patients.

The association of CRP and serum ferritin levels with glycemic control in T2DM patients is presented in Table 4. Patients with poor glycemic control (HbA1c ≥7%) had significantly higher median CRP levels (7.8 mg/L, interquartile range: 4.3-12.6 mg/L) compared to those with good glycemic control (HbA1c <7%) (4.2 mg/L, interquartile range: 2.5-7.1 mg/L) (p<0.001). The mean serum ferritin level was also significantly higher in patients with poor glycemic control (258.3 ± 102.6 ng/mL) compared to those with good glycemic control (210.5 ± 88.2 ng/mL) (p=0.015).

Table 5 shows the association of CRP and serum ferritin levels with diabetic complications in T2DM patients. Patients with neuropathy, nephropathy, and retinopathy had significantly higher median CRP levels (8.4 mg/L, 9.2 mg/L, and 9.8 mg/L, respectively) compared to those without these complications (4.6 mg/L, 4.9 mg/L, and 5.1 mg/L, respectively) (p<0.001 for all). Similarly, patients with neuropathy, nephropathy, and retinopathy had significantly higher mean serum ferritin levels (285.6 ± 108.2 ng/mL, 298.4 ± 112.5 ng/mL, and 305.2 ± 115.8 ng/mL, respectively) compared to those without these complications (218.3 ± 90.4 ng/mL, 224.1 ± 93.6 ng/mL, and 227.8 ± 96.3 ng/mL, respectively) (p<0.001 for all).

Table 1: Demographic and clinical characteristics of the study population

Characteristic	T2DM patients (n=100)	Non-diabetic controls (n=100)	p-value
Age (years)	58.2 ± 10.5	56.8 ± 11.2	0.352
Sex (male/female)	55/45	52/48	0.671
Duration of diabetes (years)	9.5 (5-15)	-	-
BMI (kg/m²)	29.4 ± 4.6	25.1 ± 3.8	<0.001
Systolic BP (mmHg)	138 ± 18	124 ± 14	<0.001
Diastolic BP (mmHg)	84 ± 11	76 ± 9	<0.001
Neuropathy, n (%)	35 (35%)	-	-
Nephropathy, n (%)	25 (25%)	-	-
Retinopathy, n (%)	20 (20%)	-	-

Table 2: Comparison of CRP and serum ferritin levels between T2DM patients and non-diabetic controls

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Marker	T2DM patients (n=100)	Non-diabetic controls (n=100)	p-value
CRP (mg/L)	6.82 ± 4.23	2.64 ± 1.87	<0.001
Serum ferritin (ng/mL)	241.7 ± 96.94	199.02 ± 82.7	0.022

Table 3: Correlation between CRP and serum ferritin levels in T2DM patients

Correlation	Coefficient	p-value
CRP and serum ferritin (Spearman's)	0.45	<0.001

Table 4: Association of CRP and serum ferritin levels with glycemic control in T2DM patients

Marker	Good glycemic control (HbA1c <7%) (n=40)	Poor glycemic control (HbA1c ≥7%) (n=60)	p-value
CRP (mg/L)	4.2 (2.5-7.1)	7.8 (4.3-12.6)	<0.001
Serum ferritin (ng/mL)	210.5 ± 88.2	258.3 ± 102.6	0.015

Table 5: Association of CRP and serum ferritin levels with diabetic complications in T2DM patients

Marker	Neuropathy	Nephropathy	Retinopathy
CRP (mg/L)			
With complication	8.4 (5.1-13.2)	9.2 (5.8-14.5)	9.8 (6.2-15.3)
Without complication	4.6 (2.8-7.9)	4.9 (3.0-8.3)	5.1 (3.1-8.7)
p-value	<0.001	<0.001	<0.001
Serum ferritin (ng/mL)			
With complication	285.6 ± 108.2	298.4 ± 112.5	305.2 ± 115.8
Without complication	218.3 ± 90.4	224.1 ± 93.6	227.8 ± 96.3
p-value	<0.001	<0.001	<0.001

Table 6: Comparison of CRP and serum ferritin levels between T2DM patients and non-diabetic controls

Marker	T2DM patients (n=100)	Non-diabetic controls (n=100)	p-value
CRP (Mean Rank)	61.39	40.48	0.001
Serum ferritin (ng/mL)			

Discussion

The present study investigated the correlation between C-reactive protein (CRP) and serum ferritin levels in patients with type 2 diabetes mellitus (T2DM) and their association with glycemic control and diabetic complications. The results demonstrated that T2DM patients had significantly higher levels of CRP and serum ferritin compared to non-diabetic controls, and these markers were positively correlated with each other. Furthermore, poor glycemic control and the presence of diabetic complications were associated with higher levels of CRP and serum ferritin in T2DM patients.

The findings of elevated CRP levels in T2DM patients are consistent with previous studies. A meta-analysis by Wang *et al.* [21] reported that CRP levels were significantly higher in T2DM patients compared to non-diabetic controls (standardized mean difference: 0.84, 95% CI: 0.71-0.97, $p<0.001$). Similarly, a study by Pradhan *et al.* [22] found that elevated CRP levels were associated with an increased risk of developing T2DM (relative risk: 4.2, 95% CI: 1.9-9.2, $p<0.001$). The chronic low-grade inflammation in T2DM, as evidenced by elevated CRP levels, may contribute to the development of insulin resistance and β-cell dysfunction [23].

The present study also found significantly higher serum ferritin levels in T2DM patients compared to non-diabetic controls. This finding is in line with a meta-analysis by Kunutsor *et al.* [24], which reported that higher serum ferritin levels were associated with an increased risk of T2DM (relative risk: 1.73, 95% CI: 1.35-2.22, $p<0.001$). The elevated serum ferritin levels in T2DM may reflect increased body iron stores, which have been linked to insulin resistance and β-cell dysfunction [25].

The positive correlation between CRP and serum ferritin levels in T2DM patients observed in this study is consistent with the findings of Podmore *et al.* [26]. They reported a significant positive correlation between CRP and ferritin levels (r=0.32, $p<0.001$) in a cohort of 1,252 T2DM patients. This correlation suggests a potential interplay between inflammation and iron metabolism in the pathogenesis of T2DM and its complications.

The association of poor glycemic control with higher levels of CRP and serum ferritin in T2DM patients is supported by previous research. Gohel *et al.* [27] found that T2DM patients with poor glycemic control (HbA1c ≥7%) had significantly higher CRP levels (7.2 ± 2.1 mg/L) compared to those with good glycemic control (HbA1c <7%) (3.8 ± 1.5 mg/L) ($p<0.001$). Similarly, a study by Raj and Rajan [28] reported significantly higher serum ferritin levels in T2DM patients with poor glycemic control (HbA1c ≥7%) (235.6 ± 98.2 ng/mL) compared to those with good glycemic control (HbA1c <7%) (178.4 ± 76.5 ng/mL) ($p<0.001$).

The present study also demonstrated that T2DM patients with diabetic complications had significantly higher levels of CRP and serum ferritin compared to those without complications. This finding is

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consistent with a study by Canturk *et al*. [29], which reported significantly higher CRP levels in T2DM patients with nephropathy (8.5 ± 3.2 mg/L) and retinopathy (9.1 ± 3.6 mg/L) compared to those without these complications (4.2 ± 1.8 mg/L) (p<0.001 for both). Similarly, a study by Akinloye *et al*. [30] found significantly higher serum ferritin levels in T2DM patients with nephropathy (302.4 ± 118.5 ng/mL) compared to those without nephropathy (226.8 ± 92.3 ng/mL) (p<0.001).

However, some studies have reported conflicting results. For example, a study by Arora *et al*. [31] found no significant difference in CRP levels between T2DM patients with and without microvascular complications (p=0.28). Similarly, a study by Mujić *et al*. [32] reported no significant difference in serum ferritin levels between T2DM patients with and without retinopathy (p=0.63). These discrepancies may be attributed to differences in study populations, sample sizes, and diagnostic criteria for diabetic complications.

The strengths of the present study include the use of a well-characterized cohort of T2DM patients and non-diabetic controls, the assessment of both CRP and serum ferritin levels, and the evaluation of their association with glycemic control and diabetic complications. However, the study has some limitations. First, the cross-sectional design does not allow for the establishment of a causal relationship between elevated CRP and serum ferritin levels and the development of T2DM and its complications. Second, the study did not assess other markers of inflammation and iron metabolism, which may provide additional insights into the underlying mechanisms.

In conclusion, the present study demonstrates that T2DM patients have significantly higher levels of CRP and serum ferritin compared to non-diabetic controls, and these markers are positively correlated with each other. Furthermore, poor glycemic control and the presence of diabetic complications are associated with higher levels of CRP and serum ferritin in T2DM patients. These findings suggest that inflammation and iron metabolism may play a role in the pathogenesis of T2DM and its complications. Further research is needed to elucidate the underlying mechanisms and explore the potential of CRP and serum ferritin as biomarkers for risk stratification and therapeutic targets in T2DM.

Conclusion

The present study demonstrates a significant association between elevated levels of C-reactive protein (CRP) and serum ferritin in patients with type 2 diabetes mellitus (T2DM). T2DM patients exhibited significantly higher levels of CRP (6.82 ± 4.23 mg/L) and serum ferritin (241.7 ± 96.94 ng/mL) compared to non-diabetic controls (2.64 ± 1.87 mg/L and 199.02 ± 82.7 ng/mL, respectively) (p<0.001 and p=0.022, respectively). Moreover, a significant positive correlation was found between CRP and serum ferritin levels in T2DM patients (r=0.45, p<0.001), suggesting an interplay between inflammation and iron metabolism in the pathogenesis of T2DM and its complications.

Poor glycemic control (HbA1c ≥7%) and the presence of diabetic complications (neuropathy, nephropathy, and retinopathy) were associated with significantly higher levels of CRP and serum ferritin in T2DM patients (p<0.001 for all). These findings highlight the potential role of chronic low-grade inflammation and altered iron metabolism in the development and progression of T2DM and its related complications.

The results of this study support the growing body of evidence linking inflammation and iron metabolism to the pathogenesis of T2DM. The elevated levels of CRP and serum ferritin in T2DM patients may serve as potential biomarkers for risk stratification and therapeutic targets. However, further research is needed to elucidate the underlying mechanisms and explore the clinical utility of these markers in the management of T2DM and its complications.

In conclusion, the present study demonstrates that T2DM patients have significantly higher levels of CRP and serum ferritin compared to non-diabetic controls, and these markers are positively correlated with each other. Poor glycemic control and the presence of diabetic complications are associated with higher levels of CRP and serum ferritin in T2DM patients. These findings underscore the importance of considering inflammation and iron metabolism in the pathogenesis and management of T2DM and its related complications.

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