

# Correlation of serum ferritin and hemoglobin levels between normal and type 2 diabetic mellitus (DM) individuals

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## ABSTRACT

**Objective:** To investigate the correlation between serum ferritin and hemoglobin levels in Pakistani subjects with type 2 diabetic mellitus (DM) individuals.

**Material and Methods:** This comparative prospective cross-sectional study was done in the Department of Hematology, Islamabad Medical Complex (IMC), Pakistan, between 1<sup>st</sup> July 2024 and 30<sup>th</sup> December 2024. A total of 108 participants were included. Participants were stratified into diabetic (HbA1c > 6.5%) and control (HbA1c ≤ 6.5%) groups.

**Results:** Diabetic patients exhibited significantly higher serum ferritin (SF) ( $172.8 \pm 54.6$  ng/mL vs.  $98.5 \pm 35.2$  ng/mL in controls and HbA1c levels ( $8.2 \pm 1.1$  vs.  $5.8 \pm 0.4$ ;  $p < 0.001$ ). Hemoglobin levels were lower in diabetics ( $13.0 \pm 1.3$  g/dl for males,  $11.2 \pm 1.1$  g/dl for females) compared to controls ( $14.2 \pm 1.1$  ng/mL for males,  $12.5 \pm 1.0$  ng/mL for females). Neither group had a significant correlation between serum ferritin and hemoglobin. The Chi-square test did not demonstrate a statistically significant association between serum ferritin levels and diabetes status (chi-square = 5.83,  $p = 0.054$ ). However, a descriptive trend was noted: patients with high SF levels had an Odds Ratio of 6.875 compared to those with low ferritin levels.

**Conclusion:** Elevated SF levels in diabetic patients may reflect systemic inflammation or metabolic dysregulation, while reduced hemoglobin levels may indicate anemia-related abnormalities or comorbid condition; however, anemia of chronic disease was not specifically investigated in the present study. Serum ferritin and hemoglobin levels are independently altered in diabetes and do not correlate statistically.

**Keywords:** Diabetes, Ferritin, Hemoglobin

This article can be cited as: Anwar S, Iftikhar M, Butt M, Naeem A, Mahboob M, Waqar A. Correlation of serum ferritin and hemoglobin levels between normal and type 2 diabetic mellitus (DM) individuals. Pak J Pathol. 2026; 37(2): 69-73. DOI: <https://doi.org/10.55629/pakjpathol.v37i2.967>

## INTRODUCTION

Diabetes mellitus (DM) is a common condition in which the body cannot make or use insulin properly, leading to high blood sugar levels. As it progresses, almost all systems, including cardiovascular, nervous, renal, etc., are involved, eventually manifesting as several health-related complications [1]. All the body systems work together, so problems like insulin resistance, abnormal fat metabolism (dyslipidemia), and long-term inflammation, as shown by increased inflammatory markers, are closely linked to each other. Diabetes mellitus (DM) is a group of common disorders of metabolism, sharing the phenotype of raised blood sugar levels. This results from defective secretion or action of insulin, or both. The underlying abnormalities

involved in the development of hyperglycemia vary widely. Type 2 diabetes is a prototypic multi-factorial complex disease [2]. Environmental factors like lack of physical activity and poor eating habits clearly play a role. Obesity and genetic factors also contribute to the development of the disease.

In mammals, ferritin mainly helps the cells in storing iron, not transporting it. In contrast, the serum ferritin (SF) level is widely used to assess iron status [3]. Additionally, serum ferritin (SF) levels can rise significantly in response to inflammation or various diseases. Ferritin not only serves as a marker for assessing iron levels but also plays an important role in disorders related to energy metabolism [4]. High ferritin levels are closely linked to chronic conditions like type 2 diabetes and heart disease [5]. Correlation analysis showed that serum ferritin level was negatively correlated with good cholesterol (HDL-C). In contrast, it was positively correlated with triglycerides (TG), total cholesterol (TC), and bad cholesterol (LDL-C) [6].

Ferritin is a common protein found inside cells that stores iron and releases it when needed. In humans, it helps to maintain a strict balance through preventing both the deficiency and overload of iron

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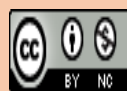
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Receiving Date: 04 Nov 2025

Revision Date: 15 Jun 2026

Acceptance Date: 20 Jun 2026

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[7]. Plasma ferritin indirectly indicates the total iron stored in the body. It keeps iron in a safe, non-toxic form, stores it safely, and delivers it where it's needed. Free iron can be harmful because it promotes the formation of free radicals through chemical reactions (Fenton and Haber–Weiss reactions). Too much iron in the body may contribute to diabetes through three main mechanisms: Insulin deficiency, insulin resistance, and liver dysfunction. Excess iron accumulates in the pancreas and liver, triggering severe oxidative stress that damages insulin-producing beta-cells and disrupts peripheral insulin signaling cascades. This pathological framework explains the significance of monitoring iron biomarkers like serum ferritin that relate to understanding tissue-level metabolic dysfunction and long-term glycemic complications in diabetic individuals. While studies elsewhere have firmly linked chronic inflammation to diabetes and insulin resistance, its direct impact on hematological and iron profiles requires closer examination. Chronic, low-grade metabolic inflammation triggers a cascade of cytokines that directly upregulates serum ferritin as an acute-phase reactant, irrespective of actual tissue iron stores. Concurrently, these same inflammatory pathways disrupt iron homeostasis by inducing functional iron sequestration, which restricts iron availability for red blood cell production and ultimately results in lower hemoglobin levels (anemia of chronic disease). The relationship between these two markers for Type 2 Diabetes is therefore crucial to understand systemic inflammation. [8]. Inflammation involves several body responses to harmful stimuli, including fever, higher cortisol levels, increased white blood cells and platelets, anemia, and loss of muscle mass [8] [9]. Inflammation is closely linked to insulin resistance, but it's still not clear whether treating inflammation can help reduce the risk of developing diabetes [1]. Consequently, this study aimed to investigate the correlation between serum ferritin and hemoglobin levels in Pakistani subjects, and to evaluate whether a statistical association exists between stratified serum ferritin categories and type 2 diabetes mellitus risk.

The associations of elevated serum ferritin or hematological parameters with metabolic syndrome have been studied. However, the direct clinical interplay between serum ferritin and hemoglobin levels within the unique genetic and dietary context of Pakistani T2DM patients has not been investigated. Chronic hyperglycemia induces a state of low-grade systemic inflammation. It considers

ferritin as an acute-phase reactant while simultaneously suppressing bone marrow responsiveness, potentially leading to anemia of chronic disorder. Investigating correlation of these two parameters or act as completely independent pathological indicators is crucial for refining diagnostic monitoring and therapeutic strategies for diabetes-associated complications. Therefore, this study was designed to evaluate the precise correlation between serum ferritin and hemoglobin levels in this high-risk population.

## MATERIAL AND METHODS

This comparative prospective cross-sectional study was conducted at Islamabad Medical Complex, Pakistan, from 1<sup>st</sup> July 2024 to 30<sup>th</sup> December 2024 after approval from the ethical committee vide reference number NESCOM-44(33)/2024-IMC dated 28<sup>th</sup> Jun 2024. A non-probability sequential sampling method was used to select participants. Exclusion criteria were applied objectively using patients' medical history, physician-documented diagnoses, hospital records, and laboratory findings available at the time of enrollment. Patients with a documented diagnosis of type 1 diabetes mellitus, evidence of active acute infection based on clinical assessment and laboratory parameters, chronic inflammatory disorders confirmed from medical records, known hematological disorders, or a history of blood transfusion within the preceding three months were excluded from the study. People who met the inclusion criteria were included after giving written informed consent. Complete blood count (CBC) was performed on the hematology analyzer Sysmex XN-1000. Serum ferritin levels were quantified via Chemiluminescent Microparticle Immunoassay (CMIA) using the Abbott ARCHITECT ci4100 analyzer. HbA1c concentrations were measured via an enzymatic assay on the Abbott ARCHITECT ci4100 system. The dataset contained variables such as age, gender, serum ferritin, hemoglobin (Hb), and HbA1c level. Results were shown as mean  $\pm$  standard deviation (SD). Data analysis and statistical analysis were performed using SPSS v20.0 software program. Results were considered statistically significant at  $p < 0.05$  (two-sided). To evaluate the association between stratified serum ferritin levels (Low, Normal, High) and diabetes risk, a Chi-square test was applied, and Odds Ratios (OR) with 95% confidence intervals were calculated.

## RESULTS

Data were classified based on age and gender to assess variations in ferritin and hemoglobin levels. A

total of 108 patients were included in the study, distributed across different age groups as shown in Figure-I and Table-I: The maximum number of both the control and diabetic categories was in the age range of 41- 60 years. The sample included both males and females, so that a comparison could be done based on gender [10].

The comparison table for Mean HbA1C, Serum Ferritin (SF), and Hemoglobin (Hb) levels in the Diabetic and Control Groups, including p-values, is given in Table-II.

Table-II showed that the diabetic group had significantly higher mean HbA1C and serum ferritin levels than the control group. Pearson correlation coefficient ( $r$ ) between serum ferritin and haemoglobin levels for diabetic and control groups was computed separately to see if any linear correlation exists (Table-III).

Table-III indicates that serum ferritin and hemoglobin levels were not significantly correlated in either the

diabetic or control groups. The diabetic group shows a near-zero negative correlation, indicating no meaningful relationship. The control group has a weak positive correlation, but the p-value suggests that it is not statistically significant. This indicates that there is no strong direct relation between serum ferritin and hemoglobin levels.

Table-IV shows that the Chi-square Test (5.83,  $p = 0.054$ ) suggests a marginal association between serum ferritin levels and diabetes, but it is not statistically significant at  $p < 0.05$ . Moreover, Odds Ratio (6.875): Patients with high serum ferritin levels are 6.875 times more likely to be diabetic than those with low ferritin. The Chi-square test did not demonstrate a statistically significant association between serum ferritin levels and diabetes status (chi-square = 5.83,  $p = 0.054$ ). However, a descriptive trend was noted: patients with high serum ferritin levels had an Odds Ratio of 6.875 compared to those with low ferritin levels.

**Table-I. Demographic features among both groups.**

| Age Group | Frequency in Control Group | Frequency in Diabetic Group | Male: Female (Control) | Male: Female (Diabetic) | p value |
|-----------|----------------------------|-----------------------------|------------------------|-------------------------|---------|
| 0-20      | 3                          | 0                           | 2:1                    | 0:0                     | -       |
| 21-40     | 12                         | 10                          | 7:5                    | 6:4                     | 0.65    |
| 41-60     | 28                         | 37                          | 15:13                  | 20:17                   | 0.42    |
| 61-80     | 7                          | 7                           | 4:3                    | 5:2                     | 0.78    |
| 81-100    | 1                          | 3                           | 1:0                    | 2:1                     | 0.29    |

**Table-II. Laboratory findings.**

| Parameter | Control Group (Mean $\pm$ SD)                     | Diabetic Group (Mean $\pm$ SD)                    | p-value |
|-----------|---------------------------------------------------|---------------------------------------------------|---------|
| HbA1C     | 5.8 $\pm$ 0.4                                     | 8.2 $\pm$ 1.1                                     | <0.001  |
| SF        | 98.5 $\pm$ 35.2                                   | 172.8 $\pm$ 54.6                                  | <0.01   |
| Hb        | 14.2 $\pm$ 1.1 (Males) / 12.5 $\pm$ 1.0 (Females) | 13.0 $\pm$ 1.3 (Males) / 11.2 $\pm$ 1.1 (Females) | 0.03    |

**Table-III: Correlation Analysis between Serum Ferritin and Hemoglobin**

| Parameter                       | Control Group | Diabetic Group |
|---------------------------------|---------------|----------------|
| Correlation Coefficient ( $r$ ) | 0.1790        | -0.0095        |
| p-value                         | 0.2757        | 0.9480         |

**Table-IV: Difference of serum ferritin levels among diabetic and non-diabetic.**

| Variables      | Low SF | Normal SF | High SF | Chi-square | P-Value | Odds Ratio |
|----------------|--------|-----------|---------|------------|---------|------------|
| Diabetic Group | 12     | 31        | 11      | 5.83       | 0.054   | 6.875      |
| Control Group  | 15     | 26        | 2       |            |         |            |

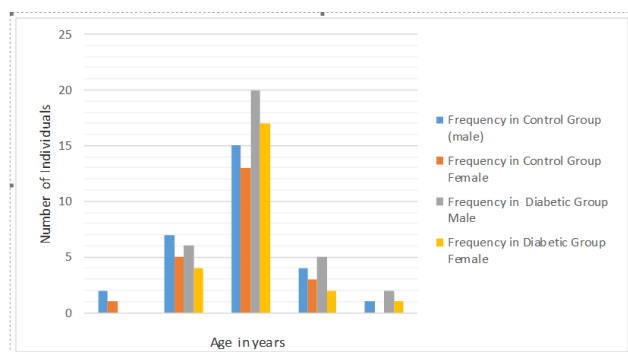


**Figure-I: Age-wise distribution of subjects.**

## DISCUSSION

Diabetes Mellitus (DM) is a significant and global public health problem due to the related comorbidities. Many studies have looked at how the body's iron levels are related to the risk of developing type 2 diabetes and how inflammation affects blood sugar control in these patients. The results of these studies are not consistent, but most of them show a positive association between elevated iron-level which stores indirectly measured via serum ferritin levels and the development of type 2 diabetes. When

intracellular iron storage capacity is exceeded, excess free iron triggers oxidative stress, impairing both insulin secretion and peripheral insulin sensitivity. Positive correlation was found in studies conducted in Western Turkey, Ethiopia, India, and China [1] [7].

Notably, 17.5% of our diabetic cohort fell within the 21-40 age bracket. This observation aligns with contemporary epidemiological trends in Pakistan and South Asia, which demonstrate a distinct shift toward early-onset T2DM driven by high genetic susceptibility, lifestyle transitions, and visceral adiposity in younger populations. Prevalence of type 2 diabetic mellitus continues to rise in Pakistan, a densely populated South Asian nation. From 2000 to 2021, the number of adults with diabetes in Pakistan increased sharply from about 5.2 million to 33 million. The rate of diabetes also varies between different age groups and between genders. The results of our study demonstrated statistically significant differences in both serum ferritin and hemoglobin levels between the diabetic and non-diabetic groups ( $p < 0.01$  and  $p = 0.03$ , respectively). Specifically, serum ferritin was markedly elevated in diabetic patients, while hemoglobin levels were significantly lower compared to healthy controls. This may be explained by innate biological differences in serum ferritin levels between races. In addition, the body composition of different races has different effects on the levels of serum ferritin [2] [11].

Lower hemoglobin levels in diabetics suggest anemia of chronic disease or iron deficiency as potential comorbidities [6] [12].

Despite these differences, the lack of a statistically significant correlation between serum ferritin and hemoglobin levels suggests that these markers independently contribute to the health status of diabetic patients rather than having a direct relationship [13] [14]. The insignificant association of high serum ferritin with diabetes risk highlights its potential as a biomarker for metabolic dysfunction but requires further investigation to establish etiology [5] [15] [16].

While our data show that individuals with high serum ferritin have a substantially higher likelihood of being diabetic, the causal relationship remains inherently bidirectional [17]. Elevated iron can actively drive pancreatic and hepatic insulin resistance via oxidative stress; conversely, the chronic inflammation of established diabetes upregulates ferritin as an acute-phase protein [18]. Due to the cross-sectional nature of this study, we cannot definitively decouple whether elevated ferritin acts as an upstream cause

or a downstream consequence of diabetes. It highlights the need for future longitudinal trials.

## CONCLUSION

This study investigates the correlation between serum ferritin and hemoglobin levels in Pakistani subjects, with a focus on their association with diabetes mellitus. While serum ferritin and hemoglobin levels were found to vary significantly between diabetic and non-diabetic individuals, correlation analysis revealed no statistically significant relationship between these markers in either group. Elevated serum ferritin levels in diabetic patients may reflect metabolic dysregulation or underlying inflammatory processes, whereas reduced hemoglobin levels may indicate anemia-related abnormalities commonly associated with type 2 diabetes mellitus. However, the etiology of anemia was not specifically investigated in this study and warrants further evaluation using comprehensive iron and inflammatory markers. These findings highlight the independent roles of serum ferritin and hemoglobin as health markers rather than interrelated factors influencing diabetes. In future work, we plan to focus on longitudinal studies assessing inflammatory markers along with iron metabolism parameters to better understand their combined impact on glycemic control and progression of diabetes.

## CONFLICT OF INTEREST

None

## GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

## AUTHORS CONTRIBUTION

**Shazia Anwar:** Substantial contribution to study design, acquisition of data, manuscript writing, critical reviews, final approval, responsible for every aspect of the research

**Madeeha Iftikhar:** Substantial contribution to acquisition of data, critical reviews, final approval, responsible for every aspect of the research

**Madiha Butt:** Substantial contribution to analysis and interpretation of data, manuscript writing, critical reviews, final approval, responsible for every aspect of the research

**Abdul Naeem:** Substantial contribution to study design, critical review, manuscript writing, final approval, responsible for every aspect of the research

**Maryam Mahboob:** Substantial contribution to acquisition of data, critical reviews, final approval, responsible for every aspect of the research

**Ayesha Waqar:** Substantial contribution to study design, acquisition of data, manuscript writing, critical reviews, final approval, responsible for every aspect of the research

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