

# Correlation Between Serum Ferritin Levels and Glycemic Control in Type 2 Diabetes Mellitus: A Case-Control Study

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## Abstract

**Background:** Diabetes mellitus is a global health crisis affecting major population. There are various prognostic factors related to the disease. This study was done to assess the correlation between serum ferritin levels and fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) in T2DM patients compared to normal control.

**Methods:** A case-control study involving 100 participants (50 T2DM patients and 50 healthy controls) was conducted. Serum ferritin, fasting blood sugar (FBS), and glycated hemoglobin (HbA1c) levels were measured. Statistical analysis included t-tests for group comparisons and Pearson's correlation to assess associations between variables. Data were analyzed using SPSS v17. Continuous variables were expressed as mean  $\pm$  standard deviation (SD). Statistical significance was set at  $p < 0.05$ .

**Results:** Serum ferritin levels were significantly higher in T2DM patients ( $113.13 \pm 44.29$  ng/mL) compared to controls ( $24.38 \pm 11.04$  ng/mL,  $p < 0.001$ ). A strong positive correlation was observed between serum ferritin and HbA1c ( $r = 0.971$ ,  $p < 0.001$ ).

**Conclusion:** Elevated serum ferritin levels are strongly associated with poor glycemic control in T2DM. These findings suggest ferritin's potential as a biomarker for diabetes management and progression.

**Keywords:** HbA1c; ferritin; diabetes mellitus; glycemic control

## Introduction

Diabetes mellitus is a global health crisis affecting an estimated 537 million adults worldwide as of 2021, with type 2 diabetes mellitus (T2DM) accounting for approximately 90

## Materials and Methods

This case-control study was conducted for a period of one year from March 2024 to Feb 2025 in two tertiary care centres at IMS & SUM Bhubaneswar. The study received approval from the Institutional Ethics Committee. Participants Cases: 50 diagnosed T2DM patients with a disease duration  $\geq 6$  months. Controls: 50 age- and sex-matched healthy individuals with no history of diabetes or chronic illness (FBS  $< 100$  mg/dl, HBA1C  $< 5.7\%$ ).

**Inclusion Criteria:** Adults aged 30–60 years; T2DM patients with HbA1c  $\geq 6.5\%$  and FBS  $\geq 126$  mg/dL.

**Exclusion Criteria:** Patients with anemia, any other chronic disease, recent surgery, inflammatory conditions, or those taking iron supplements.

**Data Collection:** Venous blood samples were collected after an 8-hour overnight fast in specific vials. Serum ferritin was measured using chemiluminescent immunoassays (Abbott Architect). FBS was measured by the glucose oxidase method, and HbA1c was assessed using high-performance liquid chromatography (HPLC). Anthropometric measurements, including weight, height, and waist circumference, were recorded to calculate body mass index (BMI).

**Statistical Analysis:** Data were analyzed using SPSS v17 which was the validated and licensed statistical software available at our institution during the study period. Continuous variables were expressed as mean ± standard deviation (SD). One-way ANOVA was used where applicable. Independent t-tests compared serum ferritin levels between groups. Pearson’s correlation was used to evaluate relationships between ferritin and glycemic markers. Statistical significance was set at p-value<0.05.

**Results**

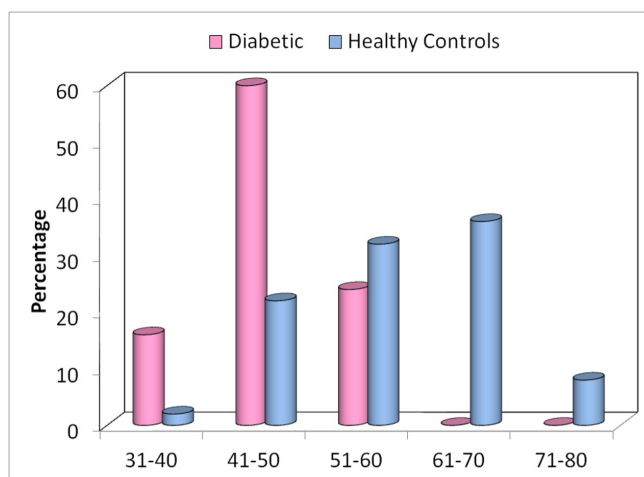
Out of 100 subjects enrolled in the study, a total of 50 (50%) were known patients of type 2 diabetes mellitus and comprised the case group of study while remaining 50 (50%) were healthy individuals who comprised the control group of the study.

Age of diabetic patients ranged from 33 to 59 years, majority were aged between 41–50 years (60%) followed by those aged 51–60 years (24%) and 31–40 years (16%). None of the diabetic patients were aged above 60 years. Mean age of diabetic patients was 47.34±5.61 years.

**Table 1:** Age wise distribution of subjects in two groups.

SN	Age (Years)	Group	Total (n=100) No.	Total (n=100) %	Diabetic (n=50) No.	Diabetic (n=50) %	Healthy (n=50) No.	
Healthy (n=50) %								
1.	31–40		9	9.0	8	16.0	1	
2.0								
2.	41–50		41	41.0	30	60.0	11	
22.0								
3.	51–60		28	28.0	12	24.0	16	
32.0								
4.	61–70		18	18.0	0	0.0	18	
36.0								
5.	71–80		4	4.0	0	0.0	4	
8.0								
Mean Age±SD (Range) in years			53.11±9.46 (33–78)		47.34±5.61 (33–59)		58.88±9.01 (40–78)	

$\chi^2=36.821$ ;  $p<0.001$ , SD- Standard Deviation



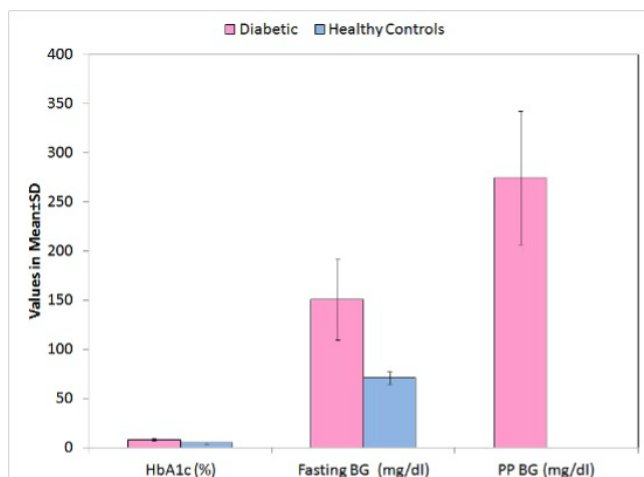
**Figure 1:** Bar diagram depicting age wise distribution of subjects in two groups.

Mean HbA1c and FBS levels of diabetic patients were significantly higher as compared to healthy controls ( $p<0.001$ ).

**Table 2:** Comparison of two groups for FBS and HbA1c levels.

SN	Parameter	Diabetic Mean (n=50)	Diabetic SD (n=50)	Healthy Mean (n=50)	Healthy SD (n=50)	t
P						
1.	HbA1c (%)	8.19	1.46	4.69	0.45	16.198
<0.001						
2.	FBS (mg/dl)	150.72	40.89	70.94	6.21	13.642
<0.001						
3.	PPBS (mg/dl)	274.44	67.57	–	–	–
–						

FBS- Fasting blood sugar, PPBS- Post-prandial blood sugar



**Figure 2:** Mean HbA1c and FBS levels of diabetic patients compared to controls.

A significant increasing trend in serum ferritin levels was observed with increasing HbA1c levels (p<0.001). Mean S. ferritin level of patients with HbA1c level <6% was 24.38±11.04 units which reached at 96.03±34.40 for patients with HbA1c level ranging from 6–10% and 218.14±52.58 units for patients with HbA1c levels >10%.

**Table 3:** Association between HbA1c levels and serum ferritin (overall = cases + controls).

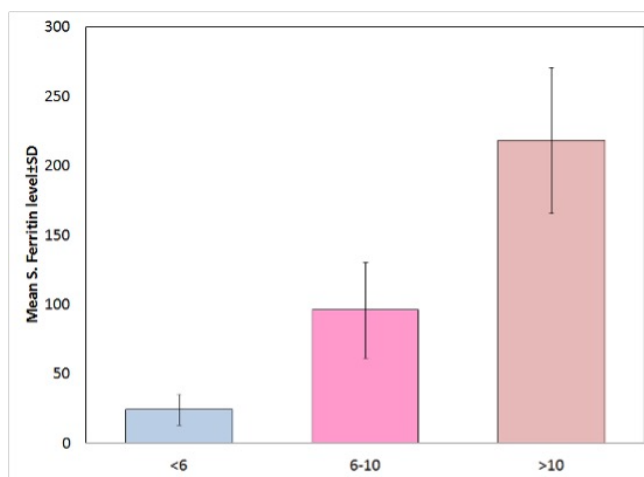
SN	HbA1c Levels (%)	No. of cases	Mean ferritin (ng/ml)
SD			
1.	<6	50	24.38
11.04			
2.	6–10	43	96.03
34.40			
3.	>10	7	218.14
52.58			

F=192.426 ng/ml; p<0.001 (ANOVA)

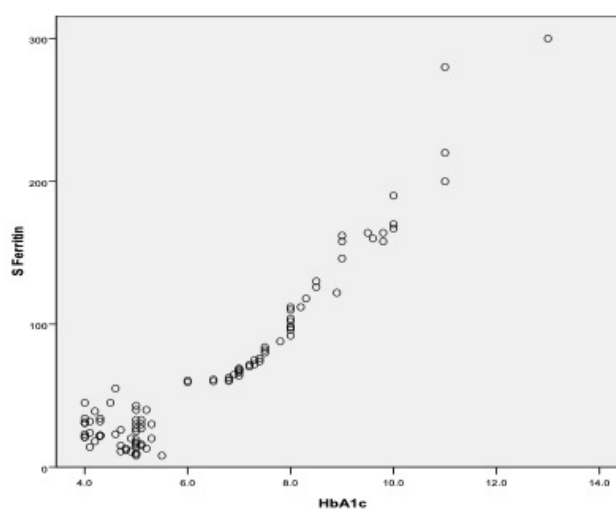
**Table 4:** Correlation between HbA1c levels and serum ferritin levels (Pearson correlation coefficient).

SN	Variable	No. of cases	r
P			
1.	Overall	100	0.946
<0.001			
2.	Cases	50	0.971
<0.001			
3.	Controls	50	-0.258
0.071			

Though serum ferritin levels of patients having diabetes for 6–10 years were higher (127.57±72.51) as compared to those having diabetes for <5 years (105.00±44.29) yet this difference was not significant statistically (p=0.177).



**Figure 3:** Association between HbA1c levels and serum ferritin.



**Figure 4:** Correlation between HbA1c levels and serum ferritin levels (Pearson correlation coefficient).

**Table 5:** Association between duration of diabetes and serum ferritin.

SN	Duration of Diabetes	No. of cases	Mean S. Ferritin
1.	<5 years	32	105.00
44.29			
2.	6–10 Years	18	127.57
72.51			

t=1.369; p=0.177 (NS)

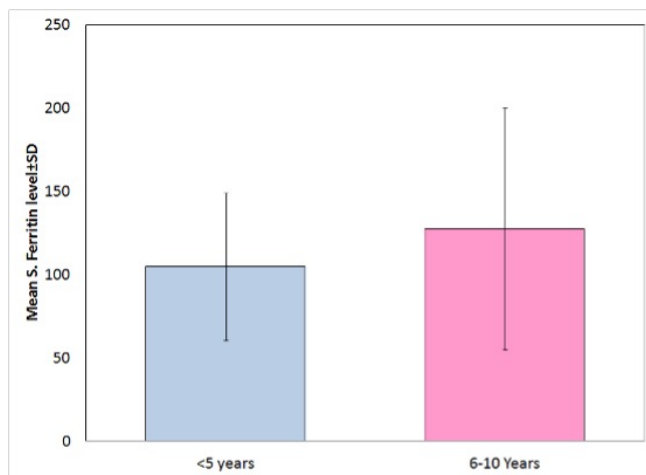
Overall a strong positive and significant correlation between fasting blood glucose levels and serum ferritin levels was observed (r=0.721; p<0.001). However, on evaluating the same for the two groups independently – only a mild and significant correlation was observed for cases (r=0.322; p=0.023). For controls the correlation was weak negative and statistically not significant (r=-0.160; p=0.266).

**Participant Demographics:** The mean age of participants was 53.6 ± 5.8 years, with a male-to-female ratio of 1.4:1. Most T2DM patients (70%) were aged between 41–60 years.

**Biochemical Findings Summary:**

Serum Ferritin: T2DM patients: 113.13 ± 44.29 ng/mL; Controls: 24.38 ± 11.04 ng/mL (p<0.001).

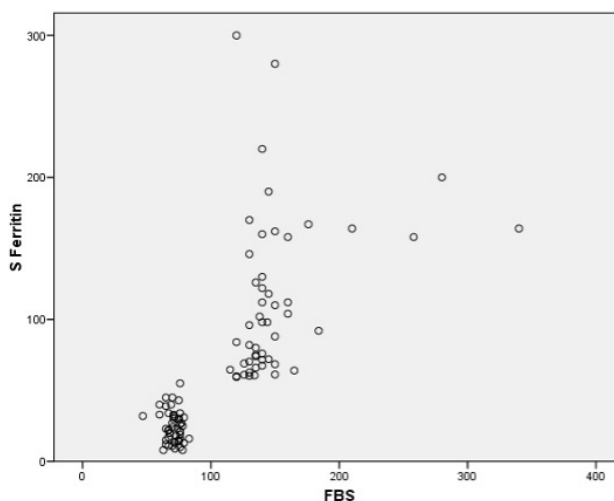
HbA1c: T2DM patients: 8.5 ± 1.2%; Controls: 5.4 ± 0.3% (p<0.001). This strong correlation may be attributable to the relatively homogeneous case group, a wide range of HbA1c values, and the exclusion of major confounding conditions such as anemia, acute inflammation, and iron supplementation. Additionally, ferritin acts as both an iron-storage protein and



**Figure 5:** Bar diagram depicting association between duration of diabetes and serum ferritin.

**Table 6:** Correlation between fasting blood glucose and serum ferritin levels (Pearson correlation coefficient).

SN	Variable	No. of cases	r
1.	Overall	100	0.721
<0.001			
2.	Cases	50	0.322
0.023			
3.	Controls	50	-0.160
0.266			



**Figure 6:** Correlation between fasting blood glucose and serum ferritin levels.

an acute-phase reactant, potentially amplifying its association with glycemic dysregulation. Nevertheless, we recognize that such a high correlation may also reflect sample size limitations and possible overestimation inherent to cross-sectional analyses.

FBS: T2DM patients:  $162 \pm 34$  mg/dL; Controls:  $89 \pm 12$  mg/dL ( $p < 0.001$ ).

**Correlation Analysis:** Ferritin and HbA1c: Strong positive correlation ( $r=0.971$ ,  $p < 0.001$ ). Ferritin and FBS: Moderate positive correlation ( $r=0.322$ ,  $p=0.023$ ). Overall a strong positive and significant correlation between fasting blood glucose levels and serum ferritin levels was observed ( $r=0.721$ ;  $p < 0.001$ ). However, on evaluating the same for the two groups independently – only a mild and significant positive correlation was observed for cases ( $r=0.322$ ;  $p=0.023$ ). For controls the correlation was weak negative and statistically not significant ( $r=-0.160$ ;  $p=0.266$ ).

## Discussion

This study highlights the significant elevation of serum ferritin levels in patients with type 2 diabetes mellitus (T2DM) compared to healthy controls. Raj *et al.* and Ganz *et al.* emphasized the role of such interventions in reducing oxidative stress and improving insulin sensitivity. Consistent with prior research, a strong positive correlation was observed between serum ferritin levels and glycemic markers such as glycated hemoglobin (HbA1c).[10, 11] These findings reinforce the potential of ferritin as a biomarker for glycemic control in T2DM. Jiang *et al.* demonstrated that elevated ferritin levels are associated with insulin resistance through mechanisms involving oxidative stress and  $\beta$ -cell dysfunction.[12] Similarly, Ma *et al.* identified a dose-dependent relationship between iron overload and impaired glucose metabolism, mediated by reactive oxygen species (ROS) and chronic inflammation.[13, 14] In line with these findings, our study supports the hypothesis that iron overload exacerbates hyperglycemia through oxidative damage and systemic inflammation. Like previous studies,[15] our findings highlighted the role of ferritin as an acute-phase reactant that reflects underlying chronic inflammation in metabolic diseases. Furthermore, Bao *et al.*[16] reported that high serum ferritin predicts an increased risk of developing T2DM, suggesting a bidirectional relationship between iron metabolism and diabetes progression.

**Clinical Implications:** Our findings have important clinical implications. Serum ferritin is a non-invasive, cost-effective biomarker that could aid in the early identification of T2DM patients at risk of poor glycemic control. Interventions targeting iron metabolism, such as dietary modifications, therapeutic phlebotomy, or iron chelation therapy, may offer potential benefits in improving glycemic outcomes.[17, 18, 19]

**Limitations and Future Directions:** Despite the strength of our findings, this study has limitations. The cross-sectional design limits our ability to establish causality between elevated serum ferritin levels and poor glycemic control. Additionally, the sample size was relatively small, and the study was conducted at a single center, which may limit the generalizability of the results. The use of predefined diagnostic cut-off values for HbA1c and fasting blood glucose to define cases (HbA1c  $\geq 6.5\%$ , FBS  $\geq 126$  mg/dL) and controls (HbA1c  $< 5.7\%$ , FBS  $< 100$  mg/dL), although necessary for accurate disease classification, inherently created distinctly separated groups. This methodological approach may have amplified between-group differences and strengthened observed associations between serum ferritin and glycemic parameters. Future longitudinal studies with larger cohorts are necessary to validate these findings.[20, 21] Emerging evidence suggests that genetic variations in iron metabolism may influence ferritin levels and their impact on glycemic control.[22, 23] Studies by Clara *et al.* and Hilton *et al.* explored the role of hepcidin and other regulatory molecules in this context. Additionally, the interplay between iron metabolism and gut microbiota warrants exploration, as recent research suggests a bidirectional relationship between dysbiosis and metabolic diseases.[24, 25] In conclusion, this study confirms that elevated serum ferritin levels are strongly associated with poor glycemic control in T2DM. By shedding light on the interplay between iron metabolism, inflammation, and oxidative stress, our findings provide a foundation for future research and potential therapeutic interventions. The widespread availability, standardized methodology, and relatively low cost of ferritin testing facilitate implementation across diverse healthcare settings. Future research should focus on longitudinal studies, large-scale randomized controlled trials of iron reduction therapies, validation across diverse populations, and economic evaluations of ferritin-based screening strategies.[26] Within the past decade, a complementary, novel set of T2DM biomarkers has largely been generated by metabolomic studies, which systematically analyse metabolites (low molecular weight biochemicals) in a biological sample.[27]

## Conclusion

This study highlights the significant relationship between elevated serum ferritin levels and poor glycemic control in patients with type 2 diabetes mellitus (T2DM). By demonstrating a strong positive correlation between serum ferritin and glycated hemoglobin (HbA1c), our findings underscore the potential utility of ferritin as a reliable biomarker for assessing glycemic status and identifying high-risk patients. HbA1c reflects average glycemic exposure but does not indicate underlying inflammatory or iron-related metabolic stress that may contribute to disease progression. Measurement of serum ferritin can provide additional information by identifying patients with iron overload or chronic low-grade inflammation, both of which are implicated in insulin resistance and  $\beta$ -cell dysfunction. Elevated serum ferritin not only reflects iron overload but also indicates systemic inflammation, oxidative stress, and  $\beta$ -cell dysfunction, which collectively contribute to the pathophysiology of T2DM. These findings hold important clinical implications. First, routine measurement of serum ferritin could become an integral part of diabetes management, providing valuable insights into the patient's metabolic and inflammatory state. Second, interventions targeting iron homeostasis, such as dietary modifications, therapeutic phlebotomy, and iron chelation therapy, may offer promising avenues for mitigating the deleterious effects of iron overload and improving glycemic outcomes. Third, incorporating serum ferritin assessments into routine diabetes care protocols could aid in stratifying patients based on their risk of complications, allowing for personalized and proactive management strategies.

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**Competing Interests:** None.

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