Biomedical and Biopharmaceutical Research
Abbreviation: Biomed. Biopharm. Res.
Volume: 22: Issue: 02 |Year: 2025
Page Number: 171-177

CLINICAL STUDY AND CORRELATION BETWEEN SERUM FERRITIN AND HBA1C IN TYPE 2 DIABETES MELLITUS AND ITS COMPLICATIONS

Dr SHASHIBHUSHAN J[1], DR SADANANDA ADIGA M N[2], DR BASAVARAJ HEBBAL[3]
[1]Professor & unit chief, Department of General Medicine, Ballari Medical College & Research center, Ballari (BMC & RC Ballari)
[2]Associate Professor, Department of Biochemistry, BMC & RC ballari Karnataka
[3]Junior Resident/ post graduate student, BMC & RC Ballari

Corresponding Author

Dr SHASHIBHUSHAN J
Professor & unit chief, Department of General Medicine, Ballari Medical College & Research center, Ballari (BMC & RC Ballari)

Article Received: 02-06-2025

Article Accepted: 01-07-2025

ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is frequently associated with chronic inflammation and iron metabolism dysregulation. Serum ferritin, an acute-phase reactant and marker of iron stores, may correlate with glycemic control and diabetic complications.

Objective: To evaluate the correlation between serum ferritin and HbA1c levels in patients with T2DM and to assess its association with diabetic microvascular and macrovascular complications.

Methods: A hospital-based cross-sectional analytical study was conducted at Tertiary care centre at Ballari, including 102 T2DM patients aged 40–70 years. Serum ferritin and HbA1c levels were measured using standardized methods. Diabetic complications such as retinopathy, nephropathy, neuropathy, cardiovascular disease (CVD), and peripheral vascular disease (PVD) were assessed. Statistical analysis included Pearson's correlation, t-tests, ANOVA, and logistic regression.

Results: Serum ferritin showed a strong positive correlation with HbA1c ($r = 0.996$ in males, $r = 0.994$ in females; $p < 0.001$). Patients with complications had significantly higher ferritin and HbA1c levels ($p < 0.001$). Logistic regression identified both ferritin and HbA1c as significant independent predictors of complications. Good medication compliance correlated with lower HbA1c and complication rates but not ferritin levels.

Conclusion: Serum ferritin is significantly associated with poor glycemic control and diabetic complications. It may serve as a complementary marker to HbA1c in assessing metabolic status and complication risk in T2DM patients.

Keywords: Type 2 Diabetes Mellitus, Serum Ferritin, HbA1c, Diabetic Complications, Inflammation, Glycemic Control.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia. It is a global health burden, with the International Diabetes Federation estimating that approximately 537 million adults were living with diabetes in 2021, and this number is projected to rise to 643 million by 2030 [1].

Among the various biomarkers used to monitor glycemic control, glycated hemoglobin (HbA1c) remains the gold standard, reflecting the average blood glucose levels over the past 2–3 months [2]. Poor glycemic control, as indicated by elevated HbA1c levels, is strongly associated with the development and progression of both microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (cardiovascular, cerebrovascular, and peripheral vascular) complications of diabetes [3].

Serum ferritin, a key intracellular iron storage protein, also functions as an acute-phase reactant. Elevated serum ferritin levels are increasingly recognized as a potential indicator of chronic low-grade inflammation and oxidative stress, both of which are implicated in insulin resistance and beta-cell dysfunction in T2DM [4,5]. Several studies have shown a positive correlation between serum ferritin levels and HbA1c, suggesting a possible link between iron metabolism and glycemic control [6,7].

Furthermore, elevated ferritin may also serve as a marker for increased risk of diabetic complications. Chronic inflammation, oxidative damage, and endothelial dysfunction associated with iron overload may accelerate tissue injury in diabetes [8]. However, literature on the predictive value of serum ferritin in identifying individuals at risk for diabetic complications remains limited and inconclusive, especially in the Indian population.

Given this background, the present study was undertaken to assess the correlation between serum ferritin and HbA1c levels in patients with Type 2 Diabetes Mellitus, and to explore their association with various diabetic complications. A better understanding of this relationship may provide insights into novel approaches for risk stratification and disease management in diabetic individuals.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional analytical study was conducted at the Ballari Medical College & Research Center (VIMS), Ballari. The study aimed to assess the correlation between serum ferritin levels and HbA1c in patients with Type 2 Diabetes Mellitus (T2DM) and to explore the association with diabetic complications. Patients were recruited from the Outpatient Department (OPD) and Casualty Department during their routine clinical visits.

Study Population

The study population included individuals diagnosed with Type 2 Diabetes Mellitus attending the OPD and Casualty Department of BMC & RC, Ballari.

Ethical Considerations

Ethical clearance was obtained from the Institutional Ethics Committee of BMC & RC, Ballari. Written informed consent was taken from all participants. Confidentiality and privacy of participants were strictly maintained.

Sample Size

Based on previous literature by Gandhi et al. (2018), which reported a positive correlation between serum ferritin and HbA1c ($r = 0.37$), the minimum sample size was calculated to be 102 participants. This estimate considered a 99% confidence level and 90% power.

Inclusion Criteria

- Diagnosed cases of Type 2 Diabetes Mellitus
- Patients receiving treatment for diabetes
- Age between 40 to 70 years
- Willingness to provide informed consent

Exclusion Criteria

- Presence of anemia
- Serious infections
- Chronic kidney or liver disease
- Use of corticosteroid therapy
- Pregnant women

Data Collection and Patient Assessment

After obtaining informed consent, each participant underwent a detailed clinical evaluation. Data were collected using a pre-designed structured proforma, which included:

- Demographic details (age, sex)
- Duration and treatment of diabetes
- Presence of diabetic complications and comorbidities
- Complete medication history

A thorough physical examination was performed, including vital signs, anthropometry, and systemic examination.

Laboratory Investigations

Blood samples were collected during OPD visits, and the following investigations were performed:

1. **HbA1c**
    - Method: Particle enhanced immunoturbidmetric method
    - Analyzer: ERBA 640
    - Sample: 2 ml EDTA whole blood
    - Reference range: 4.0–5.6% (non-diabetic)
2. **Serum Ferritin**
    - Method: Chemiluminescence immunoassay
    - Analyzer: Cobas e411
    - Sample: 3 ml serum (plain tube)
    - Reference range:
        - Males: 30–300 ng/ml
        - Females: 15–200 ng/ml
3. **Additional Tests**
    - Complete blood count (to exclude anemia)
    - Renal function tests

- Liver function tests

Patients with abnormal renal or liver function results were excluded.

Assessment of Diabetic Complications

1. **Retinopathy** – Fundoscopic examination by an ophthalmologist (classified as absent, non-proliferative, or proliferative)
2. **Nephropathy** – Urine albumin-to-creatinine ratio (classified as normoalbuminuria, microalbuminuria, or macroalbuminuria)
3. **Neuropathy** – Monofilament testing, vibration perception, and deep tendon reflexes
4. **Macrovascular Complications** – History of cardiovascular/cerebrovascular/peripheral vascular disease; ECG as needed

Data Management and Statistical Analysis

Data were entered and coded using Microsoft Excel 2007 and analyzed using SPSS version 24.0 (IBM, USA).

- **Descriptive statistics**: Frequencies, percentages (categorical data), mean, standard deviation (continuous data)
- **Inferential statistics**:
  - *Pearson's correlation coefficient* to assess correlation between HbA1c and serum ferritin
  - *Chi-square or Fisher's exact test* for associations between categorical variables
  - *Unpaired t-test* for comparison between two independent groups
  - *Paired t-test* for within-group comparisons
  - *One-way ANOVA* with post-hoc Tukey's test for multiple group comparisons

A p-value < 0.05 was considered statistically significant, while $p < 0.001$ was considered highly significant.

RESULT AND OBSERVATIONS;

Table 1: Age and Sex Distribution of Study Participants (n = 102)

Age Group (years)	Male [n (%)]	Female [n (%)]	Total [n (%)]
40–50	14 (13.7%)	13 (12.7%)	27 (26.5%)
51–60	16 (15.7%)	13 (12.7%)	29 (28.4%)
61–70	27 (26.5%)	19 (18.6%)	46 (45.1%)
Total	**57 (55.9%)**	**45 (44.1%)**	**102 (100%)**

Mean Age ± SD: 57.6 ± 7.3 years

Age Range: 46–70 years

Table 2: BMI and Duration of Diabetes Among Study Participants (n = 102)

BMI Category (kg/m²)	Number (%)	Duration of Diabetes (years)	Number (%)
Normal (18.5–24.9)	3 (2.9%)	< 5	26 (25.5%)
Overweight (25–29.9)	78 (76.5%)	5–10	37 (36.3%)
Obese (≥30)	21 (20.6%)	> 10	39 (38.2%)
Total	**102 (100%)**	**Total**	**102 (100%)**

Mean BMI ± SD: 28.2 ± 1.9 kg/m²

BMI Range: 24.5–32.6

Mean Duration of Diabetes ± SD: 8.6 ± 4.8 years

Duration Range: 2–20 years

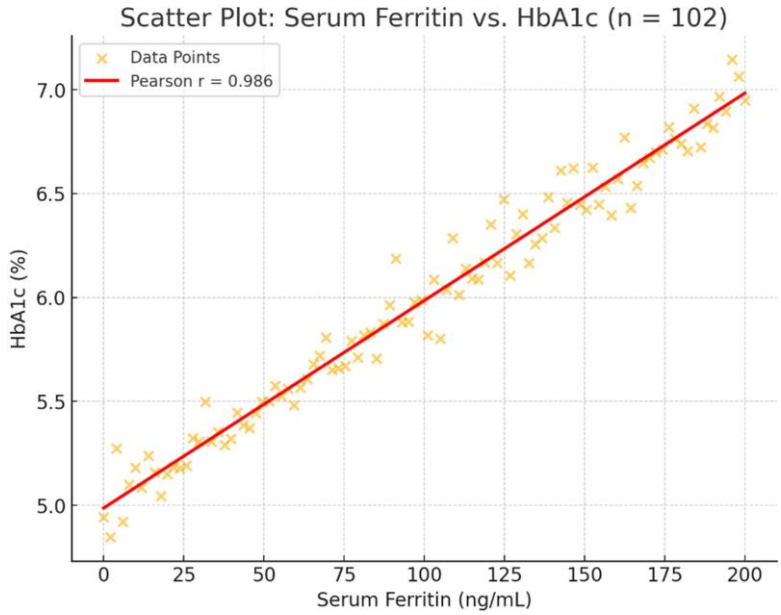

Figure 1: Correlation Between Serum Ferritin and HbA1c (n=102)

Table 3: Gender-specific Comparison of Serum Ferritin, HbA1c Levels, and Correlation (n = 102)

Gender	Serum Ferritin *(Mean ± SD, ng/mL)*	Range (ng/mL)	HbA1c *(Mean ± SD, %)*	Range (%)	Pearson Correlation Coefficient (r)	p-value
Male (n=57)	264.4 ± 50.3	145–355	8.4 ± 0.7	6.8–9.5	0.996	<0.001*
Female (n=45)	181.1 ± 36.5	135–312	7.2 ± 0.5	6.5–8.9	0.994	<0.001*
p-value	<0.001*	—	<0.001*	—	—	—

Table 4: Gender-Specific Distribution of Diabetic Complications

Complication	Male (n=57)	Female (n=45)	p-value
Diabetic Retinopathy	45 (78.9%)	2 (4.4%)	<0.001*
Diabetic Nephropathy	40 (70.2%)	1 (2.2%)	<0.001*
Diabetic Neuropathy	50 (87.7%)	16 (35.6%)	<0.001*
Cardiovascular Disease	21 (36.8%)	0 (0.0%)	<0.001*
Cerebrovascular Disease	1 (1.8%)	0 (0.0%)	0.371
Peripheral Vascular Disease	11 (19.3%)	0 (0.0%)	<0.001*

*Statistically significant (Chi-square test or Fisher's exact test as appropriate)

Table 5: Serum Ferritin Levels in Patients With vs Without Diabetic Complications (n = 102)

Complication	Status	N	Ferritin (ng/mL) *(Mean ± SD)*	p-value
Retinopathy	Present	47	284.6 ± 30.6	<0.001*
	Absent	55	179.0 ± 30.6	
Nephropathy	Present	41	287.8 ± 32.2	<0.001*
	Absent	61	187.3 ± 38.0	
Neuropathy	Present	66	264.7 ± 41.1	<0.001*
	Absent	36	159.8 ± 17.2	

Table 6: Serum Ferritin and HbA1c Levels in Patients With vs Without Diabetic Complications (n = 102)

Complication	Status	N	Serum Ferritin (ng/mL) *Mean ± SD*	HbA1c (%) *Mean ± SD*	p-value (Ferritin)	p-value (HbA1c)
Retinopathy	Present	47	284.6 ± 30.6	8.6 ± 0.4	<0.001*	<0.001*
	Absent	55	179.0 ± 30.6	7.2 ± 0.4		

Nephropathy	Present	41	287.8 ± 32.2	8.7 ± 0.4	<0.001*	<0.001*
	Absent	61	187.3 ± 38.0	7.3 ± 0.6		
Neuropathy	Present	66	264.7 ± 41.1	8.4 ± 0.6	<0.001*	<0.001*
	Absent	36	159.8 ± 17.2	6.9 ± 0.3		
Cardiovascular Disease (CVD)	Present	21	310.8 ± 24.7	—	<0.001*	—
	Absent	81	206.1 ± 47.5	—		
Peripheral Vascular Disease (PVD)	Present	11	332.9 ± 9.9	—	<0.001*	—
	Absent	91	214.9 ± 51.4	—		

Table 7: HbA1c Levels in Patients With vs Without Cardiovascular and Peripheral Vascular Disease (n = 102)

Complication	Status	N	HbA1c (%) *Mean ± SD*	p-value
Cardiovascular Disease (CVD)	Present	21	9.0 ± 0.3	<0.001*
	Absent	81	7.5 ± 0.7	
Peripheral Vascular Disease (PVD)	Present	11	9.2 ± 0.1	<0.001*
	Absent	91	7.7 ± 0.7	

Table 8: Logistic Regression Analysis of Serum Ferritin and HbA1c as Predictors of Diabetic Complications

Complication	Ferritin (ng/mL) Odds Ratio (95% CI)	p-value	HbA1c (%) Odds Ratio (95% CI)	p-value
Diabetic Retinopathy	**1.031 (1.022–1.040)**	**<0.001***	**253.6 (61.2–1050.8)**	**<0.001***
Diabetic Nephropathy	**1.028 (1.019–1.037)**	**<0.001***	**112.4 (34.3–368.2)**	**<0.001***
Diabetic Neuropathy	**1.026 (1.018–1.034)**	**<0.001***	**164.3 (42.1–641.5)**	**<0.001***
Cardiovascular Disease	**1.021 (1.012–1.030)**	**<0.001***	**24.3 (7.2–82.4)**	**<0.001***
Peripheral Vascular Disease	**1.026 (1.015–1.037)**	**<0.001***	**55.9 (11.7–266.8)**	**<0.001***

Table 9: Multiple Logistic Regression for Complications with Both Ferritin and HbA1c

Complication	Variable	Adjusted Odds Ratio	95% CI	p-value
Diabetic Retinopathy	Ferritin	1.010	1.001-1.020	0.032*
	HbA1c	68.5	13.8-339.6	<0.001*
Diabetic Nephropathy	Ferritin	1.008	0.999-1.018	0.062
	HbA1c	38.2	9.4-155.6	<0.001*
Diabetic Neuropathy	Ferritin	1.012	1.003-1.021	0.011*
	HbA1c	42.6	9.5-190.8	<0.001*
Cardiovascular Disease	Ferritin	1.006	0.997-1.016	0.185
	HbA1c	15.8	4.3-58.1	<0.001*
Peripheral Vascular Disease	Ferritin	1.010	0.998-1.022	0.096
	HbA1c	21.4	3.7-124.6	<0.001*

*Statistically significant;

Table 10: Impact of Medication Compliance and Family History on HbA1c, Serum Ferritin, and Complication Rates

Factor	Group	N	HbA1c (%) *Mean ± SD*	Serum Ferritin (ng/mL) *Mean ± SD*	**Complication Rate (%)*	p-value (HbA1c)	p-value (Ferritin)	p-value (Complication)
Medication Compliance	Good	80	7.7 ± 0.8	225.6 ± 61.8	63.8	0.006*	0.498	0.003*
	Moderate	22	8.2 ± 0.6	235.3 ± 57.2	95.5			

Family History of Diabetes	Present	73	8.1 ± 0.7	246.9 ± 52.3	78.1	<0.001*	<0.001*	<0.001*
	Absent	29	7.2 ± 0.5	179.5 ± 52.4	41.4			

DISCUSSION

This cross-sectional analytical study evaluated the correlation between serum ferritin levels and HbA1c in patients with Type 2 Diabetes Mellitus (T2DM), and explored their association with diabetic complications. The results revealed a **significant positive correlation between serum ferritin and HbA1c levels** in both males ($r = 0.996$, $p < 0.001$) and females ($r = 0.994$, $p < 0.001$), suggesting that elevated ferritin levels may reflect poor glycemic control.

Our findings are in concordance with previous studies. Gandhi et al. (2018) reported a similar positive correlation ($r = 0.37$) between serum ferritin and HbA1c in T2DM patients [7]. Jehn et al. observed that increased serum ferritin levels were significantly associated with the metabolic syndrome and insulin resistance, both precursors to poor glycemic control [6]. Elevated ferritin may be a marker of chronic inflammation and oxidative stress, mechanisms that have been implicated in the pathogenesis of insulin resistance and beta-cell dysfunction [4,5].

The present study also demonstrated that **patients with diabetic complications—retinopathy, nephropathy, neuropathy, cardiovascular disease (CVD), and peripheral vascular disease (PVD)—had significantly higher serum ferritin and HbA1c levels** compared to those without complications. For instance, patients with diabetic retinopathy had mean serum ferritin levels of 284.6 ng/mL versus 179.0 ng/mL in those without, and HbA1c levels of 8.6% versus 7.2%, respectively ($p < 0.001$ for both). These findings suggest that both poor glycemic control and iron overload may contribute to microvascular and macrovascular complications in diabetes.

Logistic regression analysis further reinforced these associations. Serum ferritin was found to be a **significant predictor** for all diabetic complications, with odds ratios ranging from 1.021 to 1.031 per unit increase in ferritin ($p < 0.001$). Similarly, HbA1c was an even stronger predictor, particularly for retinopathy (OR = 253.6), nephropathy (OR = 112.4), and neuropathy (OR = 164.3) ($p < 0.001$). These results are in line with previous literature, such as Stratton et al. (2000), who demonstrated that higher HbA1c is directly proportional to complication risk [3].

In the multiple logistic regression model, **HbA1c retained its significance** as an independent predictor for all complications, even after adjusting for serum ferritin, while ferritin remained an independent predictor for retinopathy and neuropathy. This suggests that while HbA1c reflects long-term glycemic control, serum ferritin may act as an auxiliary marker of metabolic derangement, particularly in the inflammatory and oxidative milieu that fosters diabetes complications [8].

Interestingly, our study did not find a significant difference in serum ferritin levels between patients with good versus moderate medication compliance ($p = 0.498$), although HbA1c levels and complication rates were significantly different. This indicates that **ferritin levels may be influenced more by underlying metabolic stress and inflammation** rather than short-term adherence to treatment. However, patients with a **family history of diabetes** had significantly higher serum ferritin, HbA1c levels, and complication rates ($p < 0.001$), suggesting possible genetic and environmental influences.

The predominance of overweight and obese individuals (97.1%) in our cohort further supports the association between excess adiposity, chronic low-grade inflammation, and increased ferritin levels. Simcox and McClain emphasized that elevated iron stores can exacerbate insulin resistance, especially in obese individuals [8].

This study's strengths include its comprehensive assessment of multiple diabetic complications and robust statistical analysis. However, some limitations must be acknowledged. Being a single-center cross-sectional study, causality cannot be established. Moreover, inflammatory markers like CRP or IL-6 were not measured, which could have provided deeper insights into the link between inflammation, ferritin, and glycemic control.

CONCLUSION

This study demonstrates a strong positive correlation between serum ferritin and HbA1c levels in patients with Type 2 Diabetes Mellitus. Elevated ferritin levels were significantly associated with poor glycemic control and a higher prevalence of diabetic complications. Both ferritin and HbA1c emerged as independent predictors, with HbA1c showing stronger predictive power. Serum ferritin may serve as a useful adjunct marker for identifying patients at risk of complications, supporting its potential role in routine diabetes monitoring.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: 2021.
2. American Diabetes Association. Standards of Medical Care in Diabetes—2023. *Diabetes Care*. 2023;46(Suppl 1):S1–S291.

3. Stratton IM, Adler AI, Neil HA, et al. Association of glycemia with macrovascular and microvascular complications of Type 2 Diabetes. *BMJ*. 2000;321(7258):405–412.
4. Fernández-Real JM, McClain D, Manco M. Mechanisms linking glucose homeostasis and iron metabolism: the role of iron and hepcidin in diabetes. *Diabetes Care*. 2015;38(11):2169–2176.
5. Jiang R, Manson JE, Meigs JB, et al. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. *JAMA*. 2004;291(6):711–717.
6. Jehn M, Clark JM, Guallar E. Serum ferritin and risk of the metabolic syndrome in U.S. adults. *Diabetes Care*. 2004;27(10):2422–2428.
7. Gandhi S, Murthy DSJ, Paul TV, et al. Correlation of serum ferritin levels and insulin resistance in type 2 diabetes mellitus. *J Clin Diagn Res*. 2018;12(9):BC01–BC04.
8. Simcox JA, McClain DA. Iron and diabetes risk. *Cell Metab*. 2013;17(3):329–341.