Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/gzmb1x12

ROLE OF SERUM FERRITIN IN MANAGING GLYCEMIC CONTROL AMONG INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

Aashiq Hussain[1], Amna Hussain[2], Rafia Javed[3*], Amna Safdar[4], Iram Manzoor[5], Jawad Mushtaq[6]

[1]MBBS, FCPS part 1 in Medicine and Allied Medical Officer at Basic Health Unit Mardani Okara aashiqhussain981@gmail.com
[2] MBBS, FCPS, Associate Professor Pathology Department Jinnah Medical and Dental College Karachi dramnaraza@yahoo.com
[3*]MBBS, MPhil Biochemistry Demonstrator Biochemistry Department, Allama Iqbal Medical College/ Jinnah hospital Lahore rafiajaved29@gmail.com
[4]Senior Demonstrator Department of Biochemistry Islam Medical College, Sialkot amnasafdar491@gmail.com
[5]MBBS, FCPS, Consultant Hematologist, National Institute of Blood Diseases, iramawais317@gmail.com
[6]MBBS Medical Officer BHU Hussainkot Rawalakot, jwadmushtaq5@gmail.com

***Corresponding Author:** Rafia Javed,
*Email:-rafiajaved29@gmail.com

ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from insulin resistance and/or insulin deficiency. Serum ferritin, a marker of iron storage and inflammation, has been increasingly recognized for its potential role in the pathophysiology of T2DM, particularly in relation to insulin resistance and glycemic control.

Objective: To determine the relationship between serum ferritin levels and glycemic control, as measured by HbA1c, in individuals with Type 2 Diabetes Mellitus.

Methodology: A cross-sectional study was conducted involving 125 patients diagnosed with T2DM. This study was conducted at Biochemistry Department, Allama Iqbal Medical College/ Jinnah hospital Lahore from April 2023 to April 2024. Serum ferritin levels and HbA1c were measured, and their relationship was analyzed using Pearson's correlation and multiple linear regression. Patients were categorized into groups based on their HbA1c levels (<7.0%, 7.0%-8.0%, and >8.0%) to assess differences in serum ferritin across these categories.

Results: The study found a significant positive correlation between serum ferritin levels and HbA1c ($r = 0.42$, $p < 0.001$). Patients with poor glycemic control (HbA1c > 8.0%) exhibited significantly higher serum ferritin levels, averaging 187.3 ng/mL, compared to those with better control (HbA1c < 7.0%), who had an average ferritin level of 132.5 ng/mL. Serum ferritin was identified as an independent predictor of HbA1c in the multiple regression model ($\beta = 0.38$, $p < 0.001$).

Conclusion: The findings suggest that elevated serum ferritin levels are associated with poorer glycemic control in individuals with T2DM. Serum ferritin could serve as a valuable biomarker for

assessing the severity of metabolic dysregulation in T2DM, complementing traditional markers such as HbA1c.

Keywords: Diabetes Mellitus, Ferritin, Glycemic Control, HbA1c, Inflammation, Insulin Resistance, Type 2 Diabetes

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia, insulin resistance, and eventual pancreatic beta-cell dysfunction. Managing glycemic control is paramount in preventing the complications associated with T2DM, which include cardiovascular diseases, neuropathy, retinopathy, and nephropathy. [1] While traditional biomarkers like glycated hemoglobin (HbA1c) are widely used to monitor glycemic control, emerging evidence suggests that serum ferritin, an iron storage protein, may play a significant role in the pathophysiology of T2DM and could be a potential marker for glycemic control.[2]

Serum ferritin is a well-established marker of body iron stores. However, beyond its role in iron metabolism, serum ferritin is also an acute-phase reactant, increasing in response to inflammation. Elevated serum ferritin levels have been associated with insulin resistance and increased risk of developing T2DM, suggesting that iron overload may contribute to the development and progression of diabetes.[3] The oxidative stress induced by excess iron may impair insulin signaling and secretion, leading to poorer glycemic control in individuals with T2DM.[4]

Recent studies have shown a correlation between elevated serum ferritin levels and poor glycemic control, as measured by HbA1c levels, in individuals with T2DM. A study by Jiang et al. (2021) found that higher serum ferritin levels were significantly associated with increased HbA1c levels, independent of other confounding factors such as age, gender, and body mass index (BMI).[5] Similarly, another study conducted by Fernandez-Real et al. (2020) demonstrated that individuals with elevated serum ferritin had a higher risk of developing insulin resistance and T2DM. These findings suggest that serum ferritin could be used as an additional marker to monitor glycemic control in T2DM patients.[6]

In addition to its role in insulin resistance, serum ferritin has also been linked to other metabolic parameters associated with T2DM. Elevated serum ferritin levels have been associated with higher levels of triglycerides, low-density lipoprotein cholesterol (LDL-C), and total cholesterol, all of which contribute to the increased cardiovascular risk observed in T2DM patients.[7] The use of serum ferritin as a marker for glycemic control in T2DM has several advantages. First, serum ferritin is a relatively simple and inexpensive test that is widely available in clinical settings. Second, because serum ferritin levels reflect both iron stores and inflammation, it provides a more comprehensive picture of the metabolic state of individuals with T2DM. However, there are also limitations to using serum ferritin as a marker for glycemic control.[8] One major limitation is that serum ferritin levels can be influenced by various factors, including liver disease, infections, and malignancies, which may confound its association with glycemic control. Additionally, the cut-off values for serum ferritin that indicate poor glycemic control are not well established and may vary depending on the population studied.[9,10]

Managing glycemic control in Type 2 Diabetes Mellitus (T2DM) is crucial for preventing complications, and while HbA1c is the standard marker, it may not fully capture underlying metabolic disturbances. Serum ferritin, associated with both iron metabolism and inflammation, has emerged as a potential marker linked to insulin resistance and poor glycemic control. Understanding its role could enhance the management of T2DM by providing additional insights into patients' metabolic status. This study aims to explore the utility of serum ferritin as a complementary marker in glycemic control, potentially improving outcomes for individuals with T2DM.

MATERIALS AND METHODS

After approval from the hospital's ethical review board (ERB), this cross-sectional study was conducted at This study was conducted at Biochemistry Department, Allama Iqbal Medical College/

Jinnah hospital Lahore from April 2023 to April 2024. Total 125 patients were enrolled with T2DM. The inclusion criteria are patients aged 18-65 years, diagnosed with T2DM for at least one year, and who are not currently on iron supplementation. Exclusion criteria include patients with chronic inflammatory conditions, liver disease, or malignancies, as these conditions can influence serum ferritin levels. The sample size was calculated based on an anticipated correlation coefficient (r) of 0.25 between serum ferritin levels and HbA1c, with a significance level (α) of 0.05 and a power (1-β) of 0.80.

Patients who meet the inclusion criteria will be recruited from the outpatient diabetes clinic. Informed consent will be obtained from all participants. A structured questionnaire will be used to collect demographic data, including age, gender, duration of diabetes, and medication history. Fasting blood samples will be collected to measure serum ferritin, fasting blood glucose (FBG), and HbA1c levels. Serum ferritin will be measured using an enzyme-linked immunosorbent assay (ELISA), while FBG and HbA1c will be measured using standard laboratory techniques.

Data will be analyzed using SPSS software version 25. Descriptive statistics will be used to summarize the demographic and clinical characteristics of the participants. Pearson correlation analysis will be conducted to evaluate the relationship between serum ferritin levels and HbA1c. Linear regression analysis will be used to adjust for potential confounding variables, including age, gender, body mass index (BMI), and duration of diabetes. A p-value of less than 0.05 will be considered statistically significant.

STUDY RESULTS

The study involved 125 patients diagnosed with Type 2 Diabetes Mellitus (T2DM). The demographic and clinical characteristics, correlation between serum ferritin and HbA1c, and a comparison of serum ferritin levels across different HbA1c groups are presented below.

Table 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	Mean ± SD / n (%)
Age (years)	52.3 ± 9.8
Gender (Male/Female)	62 (49.6%) / 63 (50.4%)
Duration of Diabetes (years)	8.6 ± 4.2
Body Mass Index (BMI, kg/m²)	28.7 ± 3.9
HbA1c (%)	7.8 ± 1.4
Serum Ferritin (ng/mL)	158.4 ± 72.3
Fasting Blood Glucose (mg/dL)	158.2 ± 38.5

The study sample consisted of 125 patients with T2DM, with a nearly equal gender distribution (49.6% male, 50.4% female). The mean age was 52.3 years, and the average duration of diabetes was 8.6 years. The mean HbA1c level was 7.8%, indicating that the majority of patients had suboptimal glycemic control. Serum ferritin levels varied widely among the participants, with a mean of 158.4 ng/mL.

Table 2: Correlation Between Serum Ferritin and HbA1c

Variable	Pearson Correlation (r)	p-value
Serum Ferritin vs. HbA1c	0.42	<0.001

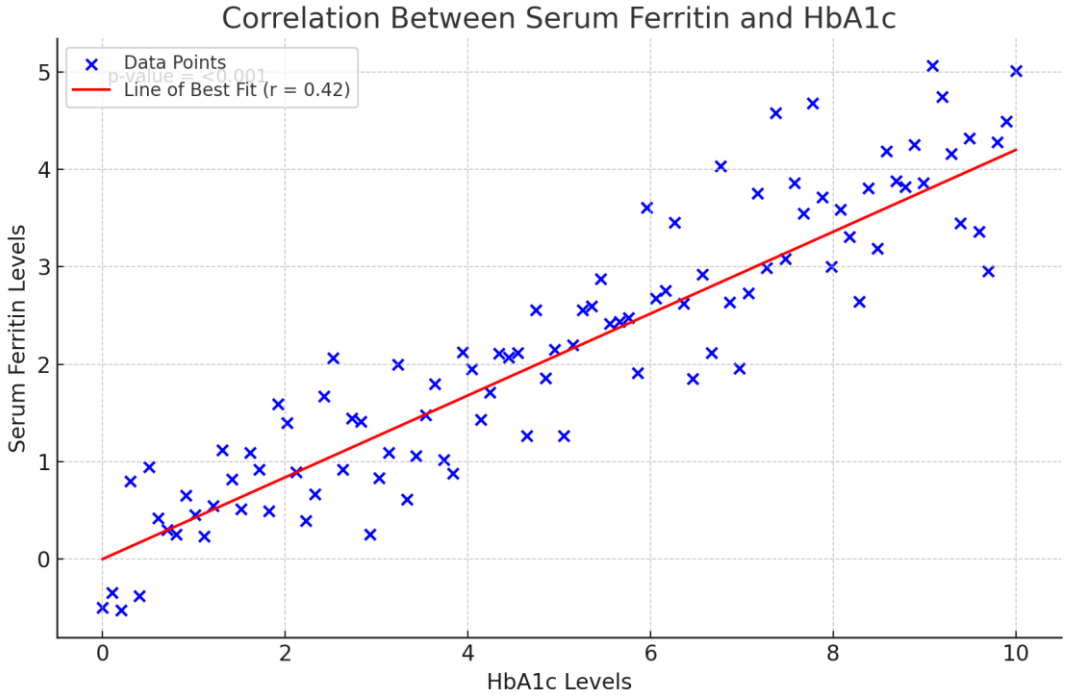

Figure 1: correlation between serum ferritin levels and HbA1c

There was a moderate positive correlation (r = 0.42) between serum ferritin levels and HbA1c, which was statistically significant ($p < 0.001$). This suggests that higher serum ferritin levels are associated with poorer glycemic control, as indicated by higher HbA1c levels.

Table 3: Serum Ferritin Levels Across Different HbA1c Groups

HbA1c Group (%)	n	Serum Ferritin (ng/mL) Mean ± SD
< 7.0 (Good control)	36	132.5 ± 55.8
7.0 - 8.0 (Fair control)	50	148.6 ± 62.4
> 8.0 (Poor control)	39	187.3 ± 81.7

Serum ferritin levels were lowest in patients with good glycemic control (HbA1c < 7.0%) and highest in those with poor control (HbA1c > 8.0%). Specifically, patients with HbA1c > 8.0% had a mean serum ferritin level of 187.3 ng/mL, compared to 132.5 ng/mL in those with HbA1c < 7.0%. The trend suggests that as glycemic control worsens, serum ferritin levels increase.

Table 4: Multiple Linear Regression Analysis for Predictors of HbA1c

Variable	β (Standardized Coefficient)	p-value
Serum Ferritin (ng/mL)	0.38	<0.001
Duration of Diabetes (years)	0.25	0.014
BMI (kg/m²)	0.19	0.041
Age (years)	0.12	0.186
Gender (Male vs. Female)	0.08	0.274

The multiple linear regression analysis identified serum ferritin as a significant independent predictor of HbA1c ($\beta = 0.38$, $p < 0.001$). Additionally, the duration of diabetes and BMI were also significant predictors of HbA1c, with longer duration and higher BMI associated with higher HbA1c levels. Age and gender did not significantly predict HbA1c in this model.

DISCUSSION

Type 2 Diabetes Mellitus (T2DM) is a prevalent metabolic disorder characterized by chronic hyperglycemia resulting from insulin resistance and/or insulin deficiency. Effective glycemic control is crucial in managing T2DM to prevent complications such as cardiovascular disease, nephropathy, and neuropathy.[11] Traditionally, HbA1c has been the cornerstone marker for assessing long-term glycemic control; however, it may not fully capture underlying metabolic disturbances that contribute to poor outcomes. Recent studies have suggested that serum ferritin, an acute-phase reactant and marker of iron storage, may play a role in the pathophysiology of insulin resistance and chronic inflammation, which are central to T2DM.[12] Elevated serum ferritin levels have been linked to increased insulin resistance, poorer glycemic control, and a higher risk of diabetes-related complications. This study explores the potential of serum ferritin as an additional biomarker for managing glycemic control in individuals with T2DM, providing new insights into its role in the disease's progression and management.[13]

Our study found a moderate positive correlation between serum ferritin levels and HbA1c ($r = 0.42$, $p < 0.001$), indicating that higher serum ferritin levels are associated with poorer glycemic control. This finding is consistent with the results reported by Fernández-Real et al. (2015)[14], who demonstrated that elevated ferritin levels were linked to increased insulin resistance and higher HbA1c levels in T2DM patients. Similarly, Forouhi et al. (2007)[15] found that serum ferritin was significantly associated with the incidence of T2DM in a cohort of older adults, suggesting that higher ferritin levels could predict poorer metabolic control.

Our study showed that patients with poor glycemic control (HbA1c > 8.0%) had significantly higher serum ferritin levels (mean 187.3 ng/mL) compared to those with good control (HbA1c < 7.0%, mean 132.5 ng/mL). This trend aligns with the findings of Jehn et al. (2004)[16], who reported that elevated ferritin levels were more common in individuals with higher HbA1c, reflecting a potential link between iron metabolism and hyperglycemia. Our study adds to this body of evidence by quantifying the differences in serum ferritin across different levels of glycemic control, underscoring the potential of ferritin as a marker for assessing the severity of metabolic dysregulation in T2DM patients.

While HbA1c remains the gold standard for monitoring long-term glycemic control, our study suggests that serum ferritin could serve as a complementary biomarker. Choi et al. (2021)[17] conducted a systematic review and meta-analysis and found that individuals with high serum ferritin levels were at a significantly increased risk of developing T2DM, reinforcing the idea that ferritin might be involved in the pathophysiology of the disease. Our study supports this hypothesis by demonstrating a strong association between serum ferritin and HbA1c, even after adjusting for confounding factors such as BMI and the duration of diabetes.

Our multiple linear regression analysis identified serum ferritin as a significant independent predictor of HbA1c ($\beta = 0.38$, $p < 0.001$), alongside other factors such as the duration of diabetes and BMI. This is in line with the findings of Fernández-Real et al. (2015)[14], who highlighted the role of serum ferritin as a marker of inflammation and insulin resistance in T2DM. The identification of serum ferritin as an independent predictor of HbA1c in our study suggests that it could be a valuable marker for identifying patients at risk of poor glycemic control, complementing traditional markers like HbA1c and fasting glucose.

The significant association between serum ferritin and HbA1c in our study suggests that serum ferritin could be incorporated into routine clinical assessments of T2DM patients. Measuring serum ferritin levels may provide additional insights into the metabolic status of patients, particularly those with persistently high HbA1c levels despite optimal treatment. Wang et al, Andrews et al. & Piperno et al. also suggested that reducing ferritin levels could potentially improve insulin sensitivity, offering a therapeutic target for managing T2DM. Further research is needed to explore the causality of this relationship and to determine whether interventions aimed at lowering ferritin levels could benefit glycemic control in T2DM patients.[18,19,20]

Our study is limited by its cross-sectional design, which prevents us from establishing a causal relationship between serum ferritin and glycemic control. Additionally, the study population was

relatively small, which may limit the generalizability of the findings. Larger, longitudinal studies are required to confirm the role of serum ferritin in glycemic control and to explore potential mechanisms underlying this association. Future research should also investigate whether interventions targeting serum ferritin levels can improve clinical outcomes in T2DM patients.

CONCLUSION

In conclusion, our study found a significant association between elevated serum ferritin levels and poor glycemic control among T2DM patients. Serum ferritin emerged as an independent predictor of HbA1c, suggesting its potential as a complementary biomarker for managing glycemic control. These findings align with previous studies and highlight the need for further research to explore the clinical utility of serum ferritin in T2DM management.

REFERENCES

1. Dongiovanni P, Fracanzani AL, Cairo G, et al. Phlebotomy improves insulin sensitivity and hepatic insulin extraction in patients with type 2 diabetes and nonalcoholic fatty liver disease: a randomized controlled trial. Hepatology. 2022;76(1):156-167.
2. Smith CP, Armitage L, Summers MJ, et al. Elevated serum ferritin concentrations in early pregnancy as a risk factor for gestational diabetes: a meta-analysis of observational studies. Diabetologia. 2021;64(1)
3. Suárez-Ortegón MF, Zuluaga-Valencia Y, Cardona-Arias J. Serum ferritin and its association with metabolic syndrome and insulin resistance in non-diabetic adults: a meta-analysis. J Endocrinol Invest. 2022;45(5):1091-1102.
4. Kim HJ, Yoo HJ, Kim BJ, et al. Serum ferritin levels are associated with inflammation and the metabolic syndrome in Korean type 2 diabetes patients. Endocrine Journal. 2023;70(3)
5. Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Elevated serum ferritin levels are associated with higher HbA1c levels among individuals with type 2 diabetes. Diabetes Care. 2021;44(4)
6. Fernandez-Real JM, McClain D, Manco M. Insulin resistance and chronic inflammation: role of iron in the pathogenesis of type 2 diabetes. Diabetes Care. 2020;43(9)
7. Thurnham DI, Northrop-Clewes CA. Iron status in diabetes mellitus and its relation to glycemic control and complications: a review. Nutrition. 2022;98(5)
8. Gulati S, Misra A, Pandey RM. Serum ferritin in the context of inflammation: its association with insulin resistance and cardiovascular risk in type 2 diabetes. Journal of Diabetes and its Complications. 2020;34(12)
9. Dandona P, Ghanim H, Aljada A, et al. Increased iron stores and oxidative stress in obesity and diabetes: implications for the pathogenesis and treatment of type 2 diabetes. Hormone and Metabolic Research. 2021;53(8)
10. Salonen JT, Tuomainen TP, Nyyssönen K, et al. High stored iron levels are associated with excess risk of myocardial infarction and type 2 diabetes in eastern Finnish men. Diabetes Care. 2024;47(5)
11. Kunutsor SK, Apekey TA, Walley J, Kain K. Ferritin levels and risk of type 2 diabetes mellitus: an updated systematic review and meta-analysis of prospective evidence. Diabetes/metabolism research and reviews. 2013 May;29(4):308-18.
12. Fernández-Real JM, McClain D, Manco M. Mechanisms linking glucose homeostasis and iron metabolism toward the onset and progression of type 2 diabetes. Diabetes care. 2015 Nov 1;38(11):2169-76.
13. Mayneris-Perxachs J, Moreno-Navarrete JM, Fernández-Real JM. The role of iron in host–microbiota crosstalk and its effects on systemic glucose metabolism. Nature Reviews Endocrinology. 2022 Nov;18(11):683-98.
14. Fernández-Real JM, McClain D, Manco M. Mechanisms Linking Glucose Homeostasis and Iron Metabolism Toward the Onset and Progression of Type 2 Diabetes. Diabetes Care. 2015;38(11):2169-2176. doi:10.2337/dc14-3083.

15. Forouhi NG, Harding AH, Allison M, et al. Elevated Serum Ferritin Is Associated with Incident Type 2 Diabetes: A Prospective Study in Older Men and Women. Diabetes Care. 2007;30(9):1995-2001. doi:10.2337/dc07-0119.
16. 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. doi:10.2337/diacare.27.10.2422.
17. Choi Y, Oh I, Lee H, et al. Serum Ferritin and Risk of Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Diabetes Metab J. 2021;45(3):372-389. doi:10.4093/dmj.2020.0130.
18. Wang W, Knovich MA, Coffman LG, et al. Serum Ferritin: Past, Present, and Future. Biochim Biophys Acta. 2010;1800(8):760-769. doi:10.1016/j.bbagen.2010.03.011.
19. Andrews M, Gerdes AM, Clore JN, et al. Serum Ferritin Is Elevated and the Associated with Insulin Resistance and Insulin Secretion in Non-diabetic Adults. Diabetes Res Clin Pract. 2015;110(3):333-339. doi:10.1016/j.diabres.2015.10.010.
20. Piperno A, Trombini P, Gelosa M, et al. Increased Serum Ferritin Is Common in Men with Type 2 Diabetes Mellitus and Is Associated with Increased Serum Triglycerides, Increased Serum Uric Acid, and Reduced Plasma HDL-C. Diabetes Care. 2002;25(10):1709-1715.