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Original Research Article

# To Investigate the Correlation between Glycated Hemoglobin and Serum Ferritin Levels in Individuals with Type 2 Diabetes

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**Conflict of interest: Nil**

**Abstract**

**Aim:** To investigate the correlation between glycated hemoglobin and serum ferritin levels in individuals with type 2 diabetes.

**Materials and Methods:** This study was conducted in the Department of Biochemistry, Homi Bhabha Cancer Hospital (HBCH), Lahartara and Mahamana Pandit Madan Mohan Malaviya Cancer Centre (MPMMCC), Sundarbagiya, BHU Campus, Varanasi, Uttar Pradesh, India for one year. The study consists of total 100 subjects out of which 50 were diabetic patients compared with 50 ages and sex matched normal healthy controls. Blood samples were analyzed for Ferritin, HBA1C and fasting plasma glucose. A written informed consent was taken from the subjects. Clinically diagnose type 2 diabetes mellitus patients on treatment in the age group of 35-70 years. For the diagnosis of diabetes mellitus, FPG ≥126 mg/dl or previous history of diabetes mellitus was required. Controls: Healthy controls in the age group of 35-70 years with no history of any medical disorder. They had fasting plasma glucose levels of <110 mg/dl and hemoglobin levels of more than 12 g/dl.

**Results:** In the present study we recruited total 100 subjects, out of which 50 subjects were in the cases group (29 males & 21 females) and 50 subjects were in the control group (26 males & 24 females). All the subjects belong to the age groups of 35-70 years. The mean age of the case group and the control group were 50.16 ± 7.0 years and 49.58 ± 6.70 years, respectively (Table 1). Both the groups were statistically similar in the age with the p-value of 0.76. There was no statistical significant difference between the mean hemoglobin level in diabetics (13.65 ± 1.3 g/dl) and normal controls (13.5 ± 1.3 g/dl). The mean BMI in diabetics was 27.5 ± 4.2 kg/m2 and for control group was 23.4 ± 2.8 kg/m2 ($p < 0.001$). The mean FPG, HbA1c and serum ferritin levels were significantly higher with P<0.001 in diabetic group compared to controls (Table 2). In addition, there was a positive correlation between serum ferritin and FPG, HbA1c. Serum ferritin is significantly correlated with FPG (r-0.20, P< 0.05) in diabetic patients. Serum ferritin is also positively related to HbA1c (r-0.9, P<0.01).

**Conclusion:** Serum ferritin and HBA1c level were elevated in patients with type 2 diabetes mellitus when compared to healthy individuals and it indicates that serum ferritin can be used as a marker.

**Keywords:** glycated hemoglobin, serum ferritin, type 2 diabetes



## Introduction

Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder characterized by chronic hyperglycemia due to insulin resistance and β-cell dysfunction. Glycated hemoglobin (HbA1c) is the most widely used biomarker for assessing long-term glycemic control in diabetic patients, as it reflects average blood glucose levels over the preceding 2-3 months. However, various factors can influence HbA1c levels independently of glycemia, including iron status, which is measured by serum ferritin levels. The relationship between HbA1c and serum ferritin levels in T2DM has garnered significant research interest due to its potential implications for the accuracy of HbA1c as a marker of glycemic control and its broader metabolic consequences. [1-4] Serum ferritin is a marker of iron storage and is often elevated in individuals with iron overload conditions. In T2DM, elevated serum ferritin levels can indicate not only increased iron stores but also inflammation, as ferritin is an acute-phase reactant. The dual role of ferritin complicates the interpretation of its association with HbA1c. Several studies have reported a positive correlation between serum ferritin and HbA1c levels in T2DM patients, suggesting that higher iron stores or inflammatory states may contribute to increased HbA1c levels, independent of glucose control . [5,6] Iron overload has been implicated in the pathogenesis of insulin resistance and T2DM. Excessive iron deposition in tissues can lead to oxidative stress and damage to

pancreatic β-cells, thereby impairing insulin secretion and action. This iron-mediated β-cell dysfunction may contribute to hyperglycemia and elevated HbA1c levels. Conversely, iron deficiency anemia can also affect HbA1c levels by altering red blood cell turnover and lifespan, leading to falsely elevated HbA1c readings. Thus, both iron overload and deficiency can influence HbA1c measurements, complicating the assessment of glycemic control in T2DM patients . [7-10] Inflammation, commonly present in T2DM, can also elevate serum ferritin levels. Chronic low-grade inflammation is a hallmark of T2DM and is associated with insulin resistance. Inflammatory cytokines can increase hepatic ferritin synthesis, leading to elevated serum ferritin levels. This inflammation-induced hyperferritinemia may be associated with higher HbA1c levels, reflecting both poor glycemic control and the inflammatory state. Understanding the interplay between inflammation, iron metabolism, and HbA1c is crucial for accurately interpreting HbA1c levels in T2DM patients . [11] The clinical significance of the association between HbA1c and serum ferritin in T2DM extends beyond glycemic monitoring. Elevated serum ferritin has been associated with an increased risk of diabetes-related complications, including cardiovascular disease and nephropathy. Ferritin may serve as a marker for identifying T2DM patients at higher risk of complications, prompting more aggressive management strategies. Moreover, understanding this association can guide the development of therapeutic interventions targeting iron metabolism and inflammation to improve glycemic control and reduce the risk of complications in T2DM . [12-14]

## Materials and Methods

This study was conducted in the Department of Biochemistry, Homi Bhabha Cancer Hospital (HBCH), Lahartara and Mahamana Pandit Madan Mohan Malaviya Cancer Centre (MPMMCC), Sundarbagiya, BHU Campus, Varanasi, Uttar Pradesh, India for one year The study consists of total 100 subjects out of which 50 were diabetic patients compared with 50 ages and sex matched normal healthy controls. Blood samples were analyzed for Ferritin, HBA1C and fasting plasma glucose. A written informed consent was taken from the subjects. Clinically diagnose type 2 diabetes mellitus patients on treatment in the age group of 35-70 years. For the diagnosis of diabetes mellitus, FPG ≥126 mg/dl or previous history of diabetes mellitus was required. Controls: Healthy controls in the age group of 35-70 years with no history of any medical disorder. They had fasting plasma glucose levels of <110 mg/dl and hemoglobin levels of more than 12 g/dl. They did not have a history of medication use, and were matched with the diabetic group regarding age and sex. Chronic Infections, Chronic Liver Disease, Chronic Renal Disease, Overt Thyroid Dysfunction Patients on Corticosteroids Therapy Anemia (Hb<10 gm/dL) 5 mL of fasting blood sample was collected and centrifuged for serum/plasma separation.

## Data Analysis

Sample were analyzed for the measurement of plasma glucose by glucose oxidase-peroxidase method, whole blood taken in EDTA vial for HbA1c by Immuno-turbidimetric method and serum ferritin was assessed by ELFA method by commercially available kit provided by Roche Cobas Integra. Results were analyzed with SPSS software and student t-test was done for quantitative variables and Pearson's regression for correlation between variables. P-value

<0.05 was considered as a significant.

## Results

In the present study we recruited total 100 subjects, out of which 50 subjects were in the cases group (29 males & 21 females) and 50 subjects were in the control group (26 males & 24 females). All the subjects belong to the age groups of 35-70 years. The mean age of the case group and the control group were 50.16 ± 7.0 years and 49.58 ± 6.70 years, respectively (Table 1). Both the groups were statistically similar in the age with the p-value of 0.76. There was no statistical significant difference between the mean hemoglobin level in diabetics (13.65 ± 1.3 g/dl) and normal controls (13.5 ± 1.3 g/dl). The mean BMI in diabetics was 27.5 ± 4.2 kg/m2 and for control group was 23.4 ± 2.8 kg/m2 ($p < 0.001$). The mean FPG, HbA1c and serum ferritin levels were significantly higher with P<0.001 in diabetic group compared to controls (Table 2). In addition, there was a positive correlation between serum ferritin and FPG, HbA1c. Serum ferritin is significantly correlated with FPG (r-0.20, P< 0.05) in diabetic patients. Serum ferritin is also positively related to HbA1c (r-0.9, P<0.01).

**Table 1: Baseline characteristics of Cases and Control.**

| S. No. | Parameters | Controls | Cases |
|---|---|---|---|
| 1 | No. of Individuals | 50 | 50 |
| 2 | Age (Years) | 49.58 ± 6.70 | 50.16 ± 7.0 |
| 3 | BMI (Kg/m2) | 23.4 ± 2.8 | 27.5 ± 4.2 |
| 4 | Hemoglobin (g/dL) | 13.5 ±1.3 | 13.65 ± 1.3 |

**Table 2: Mean values of different variables among Controls and Cases.**

| Variables | Controls | Cases p-Value | Variables |
|---|---|---|---|
| Serum Ferritin (ng/mL) | 64.12 ± 30.38 | 155.58 ± 48.12 | <0.001 |
| Fasting Plasma Glucose (mg/dL) | 94.08 ± 10.2 | 164.5 ± 30.02 | <0.001 |
| HBA1C (%) | 5.13 ± 0.82 | 7.98 ± 1.13 | <0.001 |

The mean FPG, HbA1c and serum ferritin levels were significantly higher with P<0.001 in diabetic group.

## Discussion

The present study concludes positive correlation between serum ferritin and glycated hemoglobin, which implies the role of ferritin as an indicator of glycemia control and diabetic complications. So serum ferritin can be used as a marker for screening of insulin resistance & type 2 diabetes mellitus. From this study, we recommend that more studies should be performed to confirm the implications of serum ferritin as a marker for type 2 diabetes mellitus and its role in pathogenesis of T2DM. High body iron stores that are serum ferritin have been linked to insulin resistance [10,11], metabolic syndrome [10,12,13] and gestational diabetes [14,15]. In diabetic patient, the HbA1c not only correlates with blood sugar level but also with the iron status if the patient happens to be suffering from iron deficiency anaemia. [16] Serum ferritin level had a relationship with hyperglycemia and its level decreased with lowering of serum blood glucose. [17] Type 2 diabetes mellitus is a chronic metabolic disorder resulting from insufficient or ineffective insulin to control blood glucose concentration. [18] The prevalence of DM-type 2 has been increasing steadily all over the world. People living with type 2 diabetes mellitus are more vulnerable to short and long term complications, which often lead to their premature death. [19] T2D is primarily attributable to poor lifestyles and excess body weight. Promotion of healthy lifestyles and weight management, unfortunately, has been unsuccessful in curbing the increasing public health burden of T2D. Oxidative stress plays an important role in the pathogenesis of the complications seen in T2DM. [20] Superoxide and hydrogen peroxide appear to be the primary generated species. These reactive oxygen species play a role in the generation of additional and more reactive oxidants, including the highly reactive hydroxyl radical in which iron salts play a catalytic role in a reaction. This reaction is referred to as the metal catalyzed Haber-Weiss reaction. [21] The role of iron in the pathogenesis of diabetes is suggested by an increased incidence of type 2 diabetes in diverse causes of iron overload and reversal or improvement in diabetes (glycemic control) with a reduction in iron load achieved using either phlebotomy or iron chelation therapy. [22] The importance of protein glycation is well known in the pathogenesis of diabetic vascular complications. Transition metals also play a role in protein glycation induced by hyperglycemia. It has been shown that glycated proteins have a substantial affinity for the transition metals, and the bound metal retains redox activity and participates in catalytic oxidation. [23] Ferritin has been referred as a marker for insulin resistance possibly due to iron deposition in the liver leading to hepatic insulin resistance and increased hepatic glucose production. [24,25] Pancreatic damage due to some degree of subclinical hemochromatosis has been considered in some cases of diabetes. [26] Studies done by Ford ES et al. [27] & Tuomainen TP et al. [28] reported a strong association between elevated serum ferritin concentration and increased risk for diabetes. In present study a statistical significant increase in fasting plasma glucose, glycated hemoglobin and serum ferritin levels were observed in patients of T2DM as compared to healthy controls. This finding is supported by various studies Thanna RC et al. [29], Momeni A et al. [30], Rawat N et al. [31], Pramiladevi R et al. [32], Raj Set al.[ 33], Thilip Kumar G et al. 3, Kimet al. [34.] Cantur K Z et al. [35] in their studies confirmed that poorly controlled diabetes patients had hyperferritinemia. This showed that serum ferritin was increased in diabetes as long as glycemic control was not achieved. They also found a correlation between ferritin level and diabetic retinopathy.

## Conclusion

Serum ferritin and HBA1c level were elevated in patients with type 2 diabetes mellitus when compared to healthy individuals and it indicates that serum ferritin can be used as a marker

## References

1. Iwasaki T, Nakajima A, Yoneda M, Yamada Y, Mukasa K, Fujita K, et al. Serum ferritin is associated with visceral fat area and subcutaneous fat area. Diabetes Care. 2005 Mar;28(3):2486-91.
2. Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. JAMA. 2004 Feb 11;291(6):711-7.
3. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. Diabetes Care. 1999 Dec;22(12):1978-83.
4. Eschwege E, Paternotte S, Brulhart-Meynet MC, Pi-Sunyer FX, Galan P, Giral P, et al. Serum ferritin and subsequent occurrence of type 2 diabetes in men and women: the French cohort. Diabetologia. 2008 May;51(5):897-90 4.
5. 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 Oct;38(10):2169-76.
6. Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: past, present and future. Biochim Biophys Acta. 2010 Nov;1800 (8):760-9.
7. Canturk Z, Cetinarslan B, Tarkun I, Canturk NZ. Serum ferritin levels in poorly- and well-controlled diabetes mellitus. Endocr Res. 2003 May;29(3):299-306.
8. Basuli D, Stevens RG, Torti FM, Torti SV. Epidemiological associations between iron and cardiovascular disease and diabetes. Front Pharmacol. 2014 Nov 12;5:117.
9. Padmaja P, Shabana S and Shariq Mas. Serum ferritin and HbA1c in type 2 diabetes mellitus. Int J Clin Biomed Res. 2015; 1:30-37.
10. Sheu WH, Chen YT, Lee WJ, Wang CW, Lin LY. A relationship between serum ferritin and the insulin resistance syndrome is present in non-diabetic women but not in non-diabetic men. Clin Endocrinol (Oxf). 2003; 58:380-383.
11. Tuomainen TP, Nyyssonen K, Salonen R, Tervahauta A, Korpela H, Lakka T. Body iron stores are associated with serum insulin and blood glucose concentrations: population study in 1,013 eastern Finnish men. Diab Care. 1997; 20:426-428.
12. Jehn MCJ, Guallar E. Serum ferritin and risk of the metabolic syndrome in U.S. adults. Diab Care. 2004; 27:2422-2428.
13. Bozzini C, Girelli D, Olivieri O, Martinelli N, Bassi A, De Matteis G. Prevalence of body iron excess in the metabolic syndrome. Diabetes Care. 2005; 28:2061-2063.
14. Lao TT, Tam KF. Maternal serum ferritin and gestational impaired glucose tolerance. Diab Care. 1997; 20:1368-1369.
15. Chen X, Scholl TO, Stein TP. Association of elevated serum ferritin levels and the risk of gestational diabetes mellitus in pregnant women: the Camden study. Diab Care. 2006; 29:1077-1082.
16. Zhuana T, Han H, Yang Z. Iron, oxidative stress and gestational diabetes, Nutrients. 2014; 5:3971-3974.
17. Momeni A, Behradmanesh S. Serum ferritin has correlation with HbA1c in type 2 diabetic patients. Adv Biomed Res. 2015; 4:74.h t t p : //ap p s . w h o. i nt /i r i s /bi t s t r eam /10665/2 04 871/1/9789241565257_eng.pdf
18. Padmaja P, Shabana S, Shariq M. Serum ferritin and HbA1c in type 2 diabetes mellitus. Int J Clin Biomed Res. 2015; 1:30-37.
19. Radoi V, Lixandru D, Mohara M, Virgolici B. Advanced glycation end products in diabetes mellitus: Mechanism of action and focused treatment. Proc Rom Acad Series B. 2012; 1:9-19.
20. Halliwell B, Gutteridge JMC. Role of free radicals and catalytic metal ions in human disease: an overview. Meth Enzymol. 1990; 18 6:1-85.
21. Swaminathan S, Fonseca VA, Alam MG, Shah SV. The role of iron in diabetes and its compli-cations. Diab Care. 2007; 30:1926-19 33.
22. Qian M, Liu M, Eaton JW. Transition metals bind to glycated proteins forming redox active glycochelates: implications for the pathogenesis of certain diabetic complications. Biochem Biophys Res Comm. 1998; 250:385-389.
23. Forouhi NG, Harding AH, Allison M, Sandhu MS, Welch A, Luben RE. Elevated serum ferritin levels predict new-onset type 2diabetes: results from the EPIC-Norfolk prospective study. Diabetologia. 2007; 50: 949 -956.
24. Fernandez-Real JM, Richard- Engel W, Arroyo E, Balanca R, Casamitjana-Abella R. Serum ferritin as a component of the insulin resistance syndrome. Diab Care 1998; 21:62-68.
25. Sharifi F, Sazandeh Sh. Serum ferritin in type2 diabetes mellitus and its relationship with HbA1c. Acta Med Iranica. 2004; 42:142-145.
26. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. Diab Care. 1999; 22:1978-1983.
27. Tuomainen TP, Nyyssonen K, Salonen R, Tervahuta A, Korpela H, Lakka T. Body iron stores are associated with serum insulin and blood glucose concentration: Population study in 1,013 eastern Finnish Men. Diab Care. 19 97; 20:426-428.
28. Thanna RC, Nigosker S. Level of serum ferritin and glycated haemoglobin in type 2 diabetes mellitus. Int J Med and Health Sci. 20 16; 2:49-51.
29. Momeni A, Behradmanesh MS, Khieri S, Abasi F. Serum ferritin has correlation with HbA1c in type 2 diabetic patients. Adv Biomed Res. 2015; 4:74.
30. Rawat N, Mathur N, Harikrishnan R, Choudhary J, Rawat K, Mathur M. A study of correlation of serum ferritin with glycated haemoglobin in diabetes mellitus type 2 patients: a case control study. Asian Pac J Health Sci. 2016; 3:83-88.
31. Pramiladevi R, Boke U, Kora S. Serum ferritin levels in type II diabetes mellitus. Sch J App Med Sci. 2013; 1:472-475.
32. Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. Int J Res Med Sci. 2013; 1:12-15.
33. Kim NH. Serum ferritin in healthy subjects and type 2 diabetes mellitus. Med Korea. 2000; 41:387-392.
34. Cantur KZ, Cetinarslay B, Tarkun I, Canturk NZ. Serum ferritin levels in poorly- and wellcontrolled diabetes mellitus. Endocr Res. 2003; 29:299-306.