



## ASSOCIATION OF SERUM FERRITIN LEVEL AND HbA1C LEVEL IN DIABETIC INDIVIDUALS

**Jyoti Tomar**

Demonstrator, SNMC, Agra

**Dr. Shreya Nigoshkar**

Professor and Head, Index Medical College, Indore (M.P)

**Kamini Savita\***

Demonstrator, SNMC, Agra \*Corresponding Author

### ABSTRACT

**Background:** The prevalence of diabetes mellitus, a group of metabolic disorders characterized by high blood sugar levels, is rapidly increasing worldwide. Serum Ferritin is an acute phase reactant, which is a marker of iron stores in the body. Many studies explain that raised body iron stores and subclinical hemochromatosis have been associated with the development of glucose intolerance, metabolic syndrome, and possibly the development of diabetic retinopathy, nephropathy, and vascular dysfunction. Glycemic control is closely associated with cardiovascular complications in diabetes. Changes in serum ferritin levels are associated with glucose intolerance. This study was conducted to know about the association between Serum Ferritin and HbA1C in Diabetic women and to study whether a correlation between S. ferritin and FBS, HbA1c exists. **Objectives:** The purpose of the study was to evaluate the Serum ferritin level and glycemic index in diabetic women and to investigate the relationship between in controls and diabetic women as well as between insulin, Serum ferritin, and glycated hemoglobin. **Materials and Methods:** In this study, 100 subjects were studied, and a case-control study was done with 50 outpatients and inpatients with diagnosed cases of Diabetes mellitus and 50 healthy individuals as controls from the Department of Medicine, S. N. Medical College, Agra. Serum levels of, ferritin, and blood glucose levels were measured by Chemiluminescence, and blood glycated hemoglobin (HbA1c) was measured by the HPLC method. The statistical analysis was carried out using the student's t-test. **Results:** There was a positive correlation between serum ferritin and HbA1c. **Discussion & Conclusion:** This study found that high levels of ferritin can predict future cardiovascular complications in individuals with diabetes. This study investigated its relationship with clinical and laboratory parameters of diabetes mellitus. It is observed that serum ferritin level is higher in participants with prediabetes with increments of HbA1c (%).

**KEYWORDS :** Diabetes Mellitus (DM), Serum Ferritin; Insulin Resistance, Glycated hemoglobin, Diabetic women

### INTRODUCTION

Diabetes mellitus (DM) is a syndrome of abnormal carbohydrate, fat, and protein metabolism. DM is caused by a lack of insulin and is a major public health concern. [1] Diabetes mellitus is diagnosed when there is an elevated level of glucose in the blood, known as hyperglycemia, that exceeds a specific threshold. This condition increases the risk of developing issues in the small blood vessels of various organs. Hyperglycaemia is the condition of various pathophysiological processes that develop gradually over a long period and ultimately lead to the pancreatic  $\beta$ -cells are not able to produce sufficient insulin to fulfill the needs of target tissues. [2] The presence of insulin deficiency can lead to the autoimmune destruction of  $\beta$ -cells in Diabetes Mellitus (DM), which accounts for around 10% of all diabetes cases [3]

According to the last International Diabetes Federation (IDF) report, the rate of diabetic patients will reach 438 million patients worldwide in 2030.[4] Since 1965 World Health Organization (WHO) has periodically updated and published guidance on how to classify diabetes mellitus.[5] This document provides an update on the guidance last published in 1999. The main feature of Diabetes Mellitus (DM) is chronic hyperglycemia resulting from either a defect in insulin secretion from the pancreas or resistance of the body cells to produce insulin or both. The characteristic symptoms of diabetes are polyuria, polydipsia, polyphagia, and unexpected weight loss. [6]

Serum ferritin is an acute-phase reactant and is a marker of iron stores in the body. [7] Iron overload may affect glucose metabolism and glucose metabolism affects several iron metabolic pathways [8] Serum ferritin levels are higher in people having abnormal glucose tolerance (AGT) [9]. Increased serum ferritin levels in diabetic men and women may cause mortality [10]. Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of

hepatic insulin extraction by the liver, and interference with insulin's ability to suppress hepatic glucose production. [11] Iron is a transitional metal that can easily become oxidized. [12] Excess iron damages  $\beta$ - cells of the pancreas due to oxidative stress which can contribute to the pathogenesis of diabetes mellitus. [13]

Excess iron damages  $\beta$ -cells of the pancreas due to oxidative stress which can contribute to the pathogenesis of diabetes mellitus. [14]

In diabetic patients, the HbA1c may not be only correlated with blood sugar level but also with iron status if the patient happens to be suffering from iron deficiency anemia.[15] Serum ferritin level had a relationship with hyperglycemia and its level decreased with the lowering of serum blood glucose.[16] Hemoglobin biomarker is utilized for estimating the average blood glucose levels over the previous two to three months. HbA1C is a biomarker where glucose molecule binds with hemoglobin. Hence more iron levels more glucose binds with Hb. In diabetic patients, the HbA1c may not be only correlated with blood sugar level but also with iron status if the patient happens to be suffering from iron deficiency anemia. [17] serum ferritin level had a relationship with hyperglycemia and its level decreased with the lowering of serum blood glucose.[18]

This study aims to know about the serum ferritin level in confirmed cases of diabetic women individuals

### MATERIAL AND METHOD

#### Subjects

Blood Sample was collected from a sample (n = 100), which consisted of T2DM patients (n=50) and controls(n=50). Blood samples should be collected in vacutainers. The samples were collected from outpatients of OPD MEDICINE in "S. N Medical College Agra from 25 December 2023 to 28 March 2024

**Inclusion Criteria**

1. Patients having diabetic symptoms (polydipsia, polyuria, and weight loss) and random blood glucose levels above 180 mg/dl, and fasting blood glucose levels above 150mg/dl.
2. Diagnosed type 2 diabetes mellitus patients on treatment
3. Control: Healthy controls in the age group 45-65 years

**Exclusion Criteria**

1. Children below 18, pregnant women, mentally challenged persons.
2. HIV-positive patients, cirrhotic patients.
3. Patients having anti-staphylococcal drug treatment that may be started within the last 10 days
4. Overt thyroid dysfunction, Chronic kidney disease, Chronic liver disease, On corticosteroid therapy

**Data Collection**

Performa of the patient was filled by each patient and by a relative of patients which includes age, sex, and history of cardiovascular disease and hypertension. Laboratory parameters including Serum ferritin, and glycosylated hemoglobin circumference. A fasting plasma glucose  $\geq 126$  mg/dl or previous history of diabetes mellitus was required for the diagnosis of diabetes. Blood was collected from patients after an overnight (8 hr).

**Diagnosis of Diabetes**

Diagnosis of diabetes was based on the criteria indicated by the American Diabetes Association (ADA), (2012) [12], fasting blood sugar level (FBS)  $\geq 126$  mg/dL. Subjects in healthy control groups have FBS below 110 mg/dl.

Venus blood 4 mL was collected in the early morning, and the heparin anticoagulant tube was placed at room temperature for 30 minutes. The serum was separated after centrifugation at the speed of 4000 r/min for 15 minutes. Fasting blood glucose was measured by an automatic biochemical Analyzer, and glycosylated hemoglobin level was measured by an automatic glycosylated hemoglobin Analyzer.

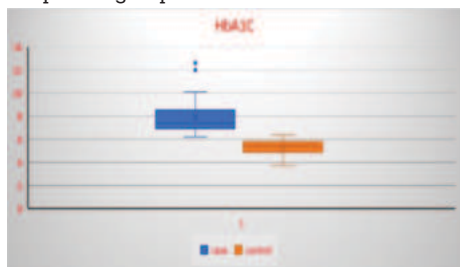
**Diagnosis Serum Ferritin**

Blood samples for Ferritin measurement were collected in Plain (red cap) vacutainers. Samples were collected from Confirmed diabetics or Symptomatic Diabetic patients. After centrifugation for 5 minutes at 5000 rpm, Serum separated from blood and then, serum concentrations for ferritin were measured in the laboratory by standard laboratory methods in Fully Automatic Biochemistry Analyzer. This Analyzer works on the principle of a spectrophotometer.

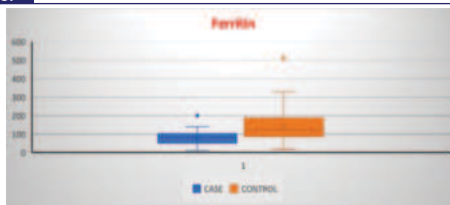
**Diagnosis of HbA1C**

A whole blood sample should be taken in EDTA vacutainers. The whole blood should run in an HbA1C Analyzer. This Analyzer works on Principal of HPLC techniques  
Result

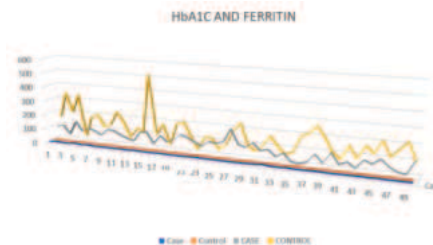
In total, 100 patients with DM were included in this study. The majority of the patients were male (66%) and their mean age was 52 years. Where 50 Patients are T2DM and 50 are controls, non-T2DM patient group.



**Fig.1 Graph Showing A Relation Between Case And Control Of HbA1C**



**Fig.2 Graph Showing The Relation Between Case And Control Of Ferritin**



**Fig.3 Graph Showing The Co-relation Between Case And Control Of Ferritin And HbA1C**

The Two-tailed P value of serum ferritin and HbA1c of controls and cases are less than 0.0001 by conventional criteria, this difference is considered to be extremely statistically

Serum ferritin was significantly higher in the cases ( $p < 0.01$ ) When compared to controls. Serum ferritin was significantly related to the duration of diabetes ( $p < 0.01$ ). As the duration of diabetes increased, serum ferritin also increased. There was a positive correlation between serum ferritin and HbA1c.

**Fig.4 Observation Table For Ferritin And HbA1C**

PARAMETER	CASE Mean + SD	CONTROL Mean + SD	p-Value
HbA1C	7.90+1.46	5.29 +0.65	<0.0001
FERRITIN	142.20+89.30	76.95+36.34	<0.0001

**DISCUSSION**

Our study discovered that diabetic patients have more ferritin levels as compared to non- diabetic patients. Serum ferritin level resembles body iron stores.[19] Which was significantly higher in diabetic patients when compared to controls and this significantly increased as the duration of diabetes increased. The study also revealed a significant correlation between HbA1c levels and serum ferritin, indicating that serum ferritin can be used as a routine screening tool for the early detection of diabetes. Therefore, serum ferritin levels are affected in hyperglycemic conditions. This study confirms the relation between serum ferritin and glycaemic control.

Cantur KZ et al[20] strongly confirms in their studies that poorly controlled diabetes patients had hyperferritinemia. it showed that serum ferritin was increased in diabetes as long as glycemic control was not achieved. They also found a correlation between ferritin levels and diabetic retinopathy.

In diabetics, a positive correlation between increased serum ferritin and poor glycemic control, reflected by higher HbA1c, has been suggested by Eschwege et al. [21] Our study showed no correlation between serum ferritin level Sumesh Raj et al.[22] Concluded in their studies that There was a positive correlation between serum ferritin and FBS, HbA1c.

**REFERENCES**

1. Chouhan S, Kallianpur S, Tijare M, Prabhu T, Sowmya K, Gupta S, Estimation of salivary glucose levels as a Diagnostic aid for Diabetes Mellitus. Biology, Engineering, Medicine, and Science Reports. 2015;
2. Buse JB, Polonsky KS, Burant CE. Type 2 Diabetes mellitus. In: Larsen PR, Krokenberg HM, Melmed S, Polonsky KS. Williams Text Book of Endocrinology. Philadelphia: Saunders; 2003; pp 1427-42.
3. G.P Fadini et al. Characteristics and outcomes of the hyperglycemic \hyperosmolar non- ketotic syndrome in a cohort of 51 consecutive cases at a single center Diabetes Res Clin Pract (2011).

4. Steele C, Hagopian WA, Gitelman S, et al. Insulin secretion in type 1 diabetes. *Diabetes*. 2004;53:426-433.
5. E.S. Ford et al. Pre-diabetes and the risk for cardiovascular disease: a systematic review of the evidence *J Am Coll Cardiol* (2010)
6. Kundu D, Roy A, Mandal T, Bandyopadhyay U, Ghosh E, Ray D. Relation of iron stores to oxidative stress in type 2 diabetes. *Nigerian journal of clinical practice*. 2013 Mar 12;16(1):100-103.
7. Fernández-Real JM, Ricart-Engel W, Arroyo E, Balançá R, Casamitjana-Abella R, Cabrero D, Fernández-Castañer M, Soler J. Serum ferritin as a component of the insulin resistance syndrome. *Diabetes care*. 1998 Jan 1;21(1):62-8..
8. Roberts WL, De BK, Brown D, et al. Effects of hemoglobin C and S traits on eight glycohemoglobin methods. *Clin Chem*. 2002;48:383-385.
9. Koorts AM, Viljoen M. Acute phase proteins: Ferritin and ferritin isoforms. University of Petoria, South Africa. 2011;154-84.
10. Herbert V, Spencer S, Jayatilleke E, Kasadan T. Most free radical injury is iron-related: It is promoted by iron, heme, holoferritin and vitamin C and inhibited by desferoxamine and apoferritin. *Stem Cells*. 1994;12:289-303.
11. Padmaja P, Shabana S and Shariq Mas. Serum ferritin and HbA1c in type 2 diabetes mellitus. *Int J Clin an*
12. Cheung CL, Cheung TT, Lam KS, Cheung BM. High ferritin and low transferrin saturation are associated with pre-diabetes among a national representative sample of US adults. *Clinical nutrition*. 2013 Dec 1;32(6):1055-60
13. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. *Diabetes Care* 1999;22:1978-83.
14. Balasubramanian S. Effect of iron deficiency on glycation of hemoglobin in nondiabetics. [www.jdcn.net/JDCR/2012/4881;2421](http://www.jdcn.net/JDCR/2012/4881;2421).
15. Taifena Zhuanca, Huijun Han and Zhenyu Yang. Iron, oxidative stress and gestational diabetes, *Nutrients*. 2014;3971-74.
16. Ali Momeni, Mohammad Saeed Behradmanesh. Serum ferritin has a correlation with HbA1c in type 2 diabetic patients. *Adv Biomed Res*. 2015;4:74.
17. N.W Tietz, *Textbook of Clinical Chemistry and Molecular diagnostics*, 4th edition Elsevier P 1186-1191
18. Kaye TB, Guay AT, Simonson DC. Non-insulin-dependent diabetes mellitus and elevated serum ferritin level. *J Diabetes Complications* 1993;7:246-9
19. Gallou G, Guilhem I, Poirier JY, Ruelland A, Legras B, Cloarec L. Increased serum ferritin in insulin-dependent diabetes mellitus: relation to glycemic control. *Clin Chem* 1994;40:947-8.
20. Cantur K Z, Cetinarslay B, Tarkun I, Canturk NZ. Serum ferritin levels in poorly- and well-controlled diabetes mellitus. *Endocr Res* 2003;29:299-306.
21. Eschwege E, Saddi R, Wacjman H, Levy R, Thibult N, Duchateau A. Haemoglobin A1c in patients on venesection therapy for hemochromatosis. *Diabete Metab* 1982;8:137-40.
22. Sumesh Raj1,\* , G. V. Rajan2 Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus