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# A study of correlation of serum ferritin with glycated haemoglobin in diabetes mellitus type 2 patients: a case control study

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## ABSTRACT

**Context**: Diabetes mellitus (DM) is one of the leading causes of morbidity and mortality worldwide and it has dreadful complications. It is important to disclose every hidden aspect of the diseases to control it in better way. **Aim**: To find association of elevated serum ferritin level with Diabetes mellitus (DM type 2) with and its correlation with level of glycated hemoglobin (HbA1c).**Material and methods**- The study population consisted of 108 individuals, out of them 53 were type 2 diabetic patients (case) and 55 were age and sex matched healthy individuals (control). Comparison of serum ferritin level was done between cases and controls. Correlation of serum ferritin level was seen with duration and severity of diabetes mellitus (DM type 2) and glycated haemoglobin (HbA1c).**Results**: Serum ferritin level of case group was found significantly higher than the control group and there was significant positive correlation of serum ferritin level with duration and poor control of DM type 2 and HbA1c. **Conclusion**: There can be a role of ferritin level as an indicator of control of glycaemia as HbA1c and Serum ferritin level can also be used as a marker of insulin resistance and duration of the disease.

**Key words:** Diabetes mellitus, HbA1C, Serum ferritin

## Introduction

Approximately 5.1 million people in the age group 20-79 years died from diabetes which is equal to 8.4% of global mortality rate in the same age group [1]. As per data of 2010 in India 65.1 million people in the age group 20-79 years age group have diabetes which is expected to rise to 109 million by 2035[2]. Diabetes mellitus is one of the most common diseases of current era which is characterized by hyperglycemia either due to insulin deficiency or insulin resistance. DM type 2 is also leading cause of coronary artery disease, peripheral artery disease, end-stage renal disease (ESRD) and adult blindness. With an increasing incidence worldwide, DM will be a leading cause of mortality and morbidity [3]. So it is important to research over new useful aspects and disease entities. 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 [4-13]. Raised Serum Ferritin may possibly be related to the occurrence of long term complications of diabetes, both micro vascular and macro vascular [14-15].The level of glycated hemoglobin (HbA1c) reflects the mean blood glucose concentration over the preceding 6–8 weeks. Measurement of HbA1c therefore provides valuable information for management of diabetes mellitus[16] but HbA1c may be affected by a variety of genetic, haematologic and illness-related factors [17] like haemoglobinopathies (depending on the assay employed), certain types of anemia, and disorders associated with accelerated red cell turnover such as malaria [16,18] so it is important to have some useful alternative. Overall there is paucity of literature especially from India showing direct evidence of relation between Diabetes Mellitus and

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iron overload, this research was designed to enlighten this path and to find association of elevated serum ferritin level with Diabetes mellitus type 2 and its correlation with level of glycated hemoglobin .

**Material and Methods**

Study design- This was a case control study conducted at a tertiary care institute of western Rajasthan for duration of one year.

Inclusion criteria- 1) Cases- All patients of type 2 diabetes mellitus having hemoglobin level more than 10 gram percent in the age group 40 to 75 years with or without vascular complications and not on any kind of anti diabetic treatment from last 6 months or more. 2) Controls- This group consisted of age and sex matched healthy subjects (Non diabetic) coming to the hospital as patient`s attendant and also from medical or paramedical staff, persons attending OPD for routine checkup.

Exclusion criteria- 1) Type 1 diabetes mellitus, 2) Other states associated with altered serum ferritin levels like: Hemochromatosis, Chronic alcoholics, Chronic inflammatory conditions like SLE/ rheumatoid arthritis, Hepatitis, History of repeated blood transfusions, Iron deficiency anemia, Hypothyroidism, Chronic kidney disease.

Sampling and study participants- 53 diabetic patients were compared with 55 age and sex matched healthy controls according to inclusion and exclusion criteria. Each patient's written informed consent was taken to participate in the study. The data was collected using a pre structured and pre validated questionnaire in terms of detailed history, clinical examination and previous necessary investigations, along with age of onset and duration of diabetes. The following investigations were carried out on the study subjects like hemoglobin level, urine sugar, fasting blood glucose/ post-prandial blood glucose, HbA1c, serum ferritin, renal and liver function tests.Detailed history of all cases and controls along with examination was conducted and samples were sent for analysis. HbA1c was tested by BIO RAD D10 system which is based on the principle of High Performance Liquid Chromatography (HPLC). Diabetic patients tested for HbA1C were arranged into 3 groups-Well controlled: <6%, Moderately controlled:6%-8%, Poorly controlled:>8%. Serum ferritin was assayed by electrochemiluminiscence method. Normal range was taken 15-400 µg/L. Statistical analysis was done by using SPSS software to achieve aims and objective.

**Results**

On comparison of serum ferritin levels between cases and controls it was found that the mean serum ferritin of diabetic population was 271.4µg/L (SD=47.755) and that of control group was 203.6 µg/L(SD=42.877). They were compared using Student's independent t test and p value< 0.05. Serum ferritin of case group is therefore significantly higher than the control group.

**Table 1: Comparison of serum ferritin levels between cases and controls**

| Group | N | Mean | Std. Deviation | t-Value | P-Value |
|---|---|---|---|---|---|
| **Case** | 53 | 271.40 | 47.755 | 7.337 | .000 |
| **Control** | 55 | 203.60 | 42.877 | | |
| **Total** | 108 | 240.27 | 56.654 | | |

Correlation between serum ferritin and HbA1c was also assessed. The mean HbA1c of case group was 6.849%.The correlation between glycated haemoglobin and serum ferritin was done by Pearson correlation test and it showed a significantly positive correlation (r=0.582) with serum ferritin [mean=271.40±47.755 µg/L].

**Table 2: Correlation between serum ferritin and HbA1c levels**

| Group | N | Mean ferritin | Std. Deviation | Pearson Correlation | P-Value |
|---|---|---|---|---|---|
| **S. Ferritin** | 53 | 271.40 | 47.755 | .582 | .000 |
| **HbA1c** | 53 | 6.849 | .8920 | | |

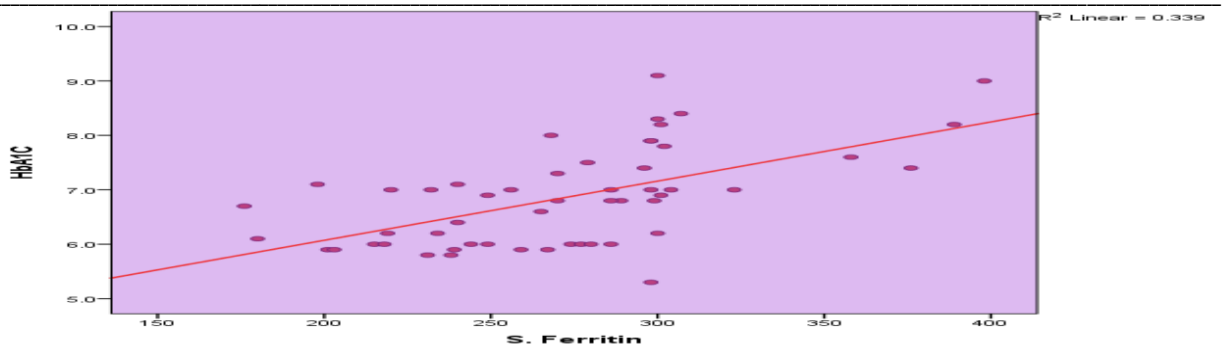


**Fig 1: Scatter diagram showing correlation between serum ferritin and glycated haemoglobin**

Serum ferritin level in different groups of HbA1c was observed. Mean ferritin of all three groups of glycated haemoglobin was calculated and highest mean ferritin is seen in the poorly controlled diabetic group [mean=332.5 µg/L ±47.408]. Mean ferritin of three groups were compared by F test, showing p value of 0.001($p<0.05$), showed significant difference between mean ferritin in 3 groups.

**Table 3: Comparison of mean ferritin amongst three groups**

| HbA1c Group | Mean serum ferritin | Std. Deviation | F-Value | P-Value |
|---|---|---|---|---|
| **Well Controlled** | 246.89 | 33.762 | 7.861 | .001 |
| **Moderately Controlled** | 267.55 | 43.453 | | |
| **Poorly Controlled** | 332.50 | 47.408 | | |
| **Total** | 271.40 | 47.755 | | |

Correlation between serum ferritin and duration of diabetes mellitus was observed. The duration of diabetes [mean=7.68 years±3.435] was showing a significant positive correlation (r=0.487) with serum ferritin [mean271.4±47.755 µg/L]. Analysis was done using Pearsons correlation test and p value <0.05.

**Table 4: Correlation between serum ferritin and duration of diabetes mellitus**

| Group | N | Mean | Std. Deviation | Pearson Correlation | P-Value |
|---|---|---|---|---|---|
| **S. Ferritin** | 53 | 271.40 | 47.755 | .487 | .000 |
| **DM Dur$^{n}$** | 53 | 7.68 | 3.435 | | |

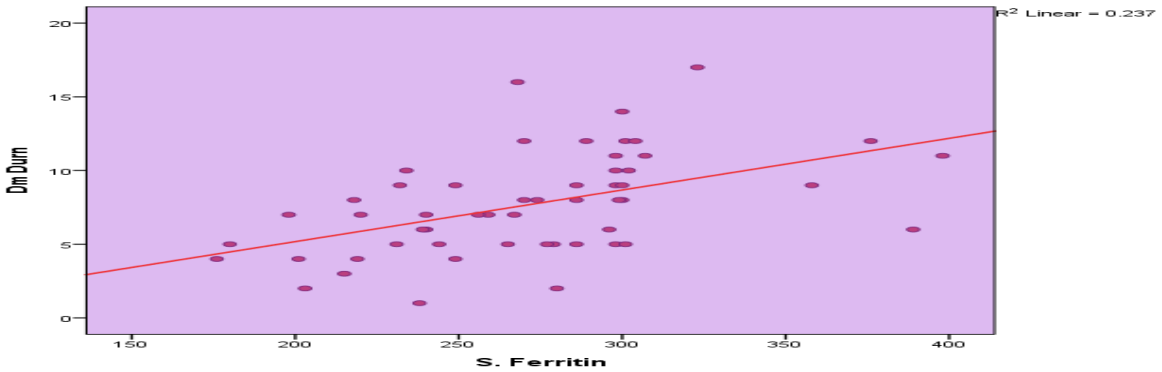


**Fig 2: Scatter diagram showing correlation between serum ferritin and duration of diabetes mellitus[r=0.487]**

**Discussion**

Evidence of systemic iron overload contributing to abnormal glucose metabolism was first derived from the observation that the frequency of diabetes is increased in classic hereditary hemochromatosis (HH). Improvement in insulin sensitivity and insulin secretion with frequent blood donation and decreased iron stores was also found [19,20].Transfusion iron overload is the most common cause of acquired iron overload. In a study of 80 transfusion-dependent β-thalassemic patients, diabetes was reported in 19.5% of patients and impaired glucose tolerance in 8.5% of patients. [21]. Loma Linda University's Adventist Health Study was the first to report the association between meat intake and type 2 diabetes risk [22] that has since been consistently observed by several other studies [23,24]. Numerous studies have confirmed that this association is related to the high heme content of meat and increased dietary heme intake [19,25 –27]. Similarly, high body iron stores have been linked to insulin resistance [28,29], metabolic syndrome [28,30–32], and gestational diabetes [33,34]. Recently, Jiang et al. [35] carried out a nested case-control study within the nurses cohort with similar results.In current study, mean serum ferritin of diabetic group was (271.4±47.755 µg/L ) differed significantly ($p<0.05$) from the control group (203.6±42.877 µg/L).Sumesh Raj et al.[36] support this study in manner that in their study serum ferritin was significantly higher in the cases ,when compared to controls ($p<0.01$) and serum ferritin was also significantly related to the duration of diabetes ($p<0.05$). Serum ferritin was significantly related to HbA1c (r-0.209, $p<0.05$ vs r- 0.582,$p<0.05$) as found in current study. Some other studies found similar results that the mean serum ferritin in diabetics was significantly higher than control group like Sharifi et al. [37] (101.5±73 µg/L vs.43.5±41.8 µg/L, $P<0.001$) and Sushma et al.(234.5 µg/L ±62.98 vs 126±45.6 µg/L)[38].In our study, there is a moderately positive correlation (r=0.582) between serum ferritin (mean271.4±47.755µg/L) and glycated haemoglobin (mean 6.849±0.892%) implying a role of ferritin in diabetic control but the study by Sharifi et al. [37] showed that there was no significant correlation between serum ferritin and HbA1c (r= 0.23) in diabetic patients. In the study by Sharifi et al., diabetic complications were exclusion criteria. But in our study, we included diabetic patients with complications also. So difference in observation between our study and Sharifi et al. could be attributed to this as one possibility. Further studies are required to establish this correlation and for better comparison between studies.Mean ferritin values in current study was significantly different in the three groups of glycated haemoglobin which again favours a role of ferritin in the long term control of diabetes mellitus. Poorly controlled group had the highest mean serum ferritin levels (332.5±47.408 µg/L).Cantur KZ et al [39] confirmed in their studies that poorly controlled diabetes patients had hyperferritinemia. They also found a correlation between ferritin level and diabetic retinopathy. In diabetic subjects, a positive correlation between increased serum ferritin and poor glycemic control, reflected by higher HbA1c, has been suggested by Eschwege et al[40].In current study, serum ferritin was showing a moderately positive correlation(r=0.487) with increasing duration of diabetes mellitus. Serum ferritin levels increased as the duration of diabetes increased as in Sumeshraj et al. [36] and this is correlated well with our study.Hence the current study concludes that present study showed positive correlation between serum ferritin and glycated haemoglobin which implies the role of ferritin as an indicator of control of glycemia and diabetic complications. There was a positive correlation between serum ferritin with duration of diabetes. So serum ferritin could be used as a marker of insulin resistance.

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