

A correlational Study of Serum Ferritin Levels with Glycemic Status in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Type 2 Diabetes Mellitus (DM) is the most common endocrine disease—a metabolic disorder of multiple etiologies. The relationship between iron metabolism and type 2 DM is bidirectional. Iron is a potent pro-oxidant that increases cell oxidative stress causing decreased insulin internalization and actions resulting in hyperinsulinemia and insulin resistance. The aim of this study is to estimate serum ferritin levels and to see for its correlation with good glycemic control.

Materials and methods: It was a case control study. Fifty (50) diagnosed cases of type 2 DM and fifty (50) age and sex matched healthy controls were included. Venous blood sample was analysed for serum fasting blood sugar (FBS), post prandial blood sugar (PPBS), serum ferritin, glycosylated haemoglobin (HbA1c) in both cases and controls. Statistical analysis was done using student 't' test. Pearson's correlation was performed to establish the relationship between study variables.

Results: The study showed statistically significant increase ($p < 0.05$) in serum ferritin levels in cases compared to controls. Our study showed a positive correlation between ferritin and blood sugar levels.

Conclusion: Type 2 Diabetes mellitus is associated with increased ferritin levels. Reliable and sensitive methods need to be developed to precisely measure catalytic iron that participates in oxidative injury.

Keywords: Type 2 Diabetes Mellitus, Ferritin, glycosylated haemoglobin

INTRODUCTION

Diabetes mellitus (DM) is a group of common metabolic disorders that share the phenotype of hyperglycemia. Type 2 diabetes mellitus (T2DM) is a predominant public health concern worldwide, accounting for 90% of the cases of diabetes globally.^{1,2,3}

It is caused by a complex interaction of genetics and environmental factors. In DM, lipid abnormalities, anaemia, alteration of liver and kidney functional indices have been implicated as major risk factors to the progression of Diabetic complications.⁴ The pathogenesis of type 2 diabetes mellitus (T2DM) is complex and involves the interaction of genetic and environmental factors.⁵ Individuals with type 2 DM show both insulin resistance and beta cell defects.⁶ Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance.⁷

Serum Ferritin, an acute phase reactant is a marker of iron stores in the body. Ferritin is an index of body iron stores and acts as an iron overload marker. Iron is a transition metal and a potential catalyst in cellular reaction that produces reactive oxygen species. Recent studies indicate that increased body iron stores has been associated with the development of glu-

cose intolerance, type 2 diabetes, metabolic syndrome and possibly the development of diabetic retinopathy, nephropathy and vascular dysfunction. The metabolic syndrome is closely linked to insulin resistance and numerous studies indicate a link to iron overload.

Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance, such as elevated blood glucose and insulin levels. Although the exact mechanism of iron-induced diabetes is uncertain, it is likely to be mediated by three key mechanisms:

- 1) insulin deficiency,
- 2) insulin resistance, and
- 3) hepatic dysfunction.

Several studies have shown that there is increased oxidative stress in Diabetic patients with Iron overload⁸ and also positive associations of serum ferritin concentrations with cardiovascular risk factors⁹, risk of insulin resistance syndrome, and risk of type 2 diabetes.¹⁰⁻¹² More recently the results from prospective studies from Caucasian populations suggested that Iron overload could predict the development of abnormal glucose metabolism.¹³ The aim of this study is to find the influence of body iron stores on type II diabetes mellitus and its correlation with HbA1c. We hypothesize that serum ferritin may be acting as a marker of oxidative stress in DM rather than just as a marker of increased iron overload

Although several epidemiological studies have reported a strong association between elevated serum ferritin and increased risk for type 2 diabetes; more so, a link between serum ferritin concentration and insulin resistance or type 2 diabetes has been established. However, it appears that little work on the relationship between iron status and type 2 diabetes mellitus has been done in our locality, hence, the need for this study.

Aims of the study were to measure the level of Serum Ferritin, Fasting and Postprandial Blood Sugar glycosylated hemoglobin in patient with Type-2 Diabetes mellitus and controls and to correlate serum ferritin levels with FBS, PPBS and HbA1c

MATERIAL AND METHODS

Study participants: This was a case control study. The

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study was carried out on 50 cases of clinically diagnosed type 2 diabetes mellitus in the age group 30-70 years attending the Medicine OPD at SNMC and HSK hospital, Navanagar, Bagalkot. Fifty (50) age and sex matched healthy subjects were taken as controls. Study duration was from June 2014 to August 2014. Ethical clearance was obtained from the institute's ethical clearance committee. Informed consent was taken from the cases and controls after explaining the procedure. Diabetes Mellitus was diagnosed as per the WHO diagnostic criteria.¹⁴

Exclusion criteria: The patients with type 1 diabetes mellitus, hemolytic anemia, hemoglobin variants, pregnancy, hepatic disease and infectious diseases like tuberculosis, sarcoidosis etc were excluded from this study. Patient with secondary diabetic complications—micro and macrovascular, those with h/o multiple transfusions, overt thyroid dysfunction, chronic kidney disease, chronic liver disease, those on corticosteroid therapy, those with pancreatitis, those not willing to participate in the study were also excluded.

Biochemical analysis: A sample of 3 ml venous blood was collected in both fasting and post prandial state under aseptic precautions. It was allowed to clot and serum was separated by centrifugation.

The following parameters were studied.

1. FBS and PPBS –Glucose oxidase peroxidase method.^{15,16} (kits supplied by Erba Diagnostics). The parameters were read using semi auto analyser (STAT FAX 3300).
2. HbA1c was estimated by Nycocard reader II.¹⁷
3. Serum ferritin was estimated by chemiluminescence immuno assay (CLIA) method using Maglumi Snibe 1000 hormone analyser

Statistical methodology: Data was expressed in terms of mean \pm SD. Chi-square test was applied to estimate the difference between the two groups of population. Unpaired 't'-test was used to study the changes in serum ferritin levels be-

Characteristics	Groups	Mean \pm SD	t	P
FBS (mg/dL)	Cases	204.5 \pm 54.4	11.1	0.001*
	Controls	90.1 \pm 12.3		
PPBS (mg/dL)	Cases	310.3 \pm 62.6	17.2	0.001*
	Controls	110.9 \pm 8.6		
HbA1c (%)	Cases	7.9 \pm 0.6	15.8	0.001*
	Controls	5.4 \pm 0.5		
Serum Ferritin (ng/dl)	Cases	336.9 \pm 46.3	18.5	0.001
	Controls	127.2 \pm 40.9		

*statistically highly significant, FBS- Fasting blood sugar, PPBS-Post prandial blood sugar, HbA1c –Glycosylated Hemoglobin

Table-1: Comparison of FBS, PPBS and HbA1c levels in both groups

Correlation between	Pearson's Correlation Coefficient(r)	Significance	
FBS and Ferritin	+ 0.47	p < 0.001	Highly significant positive correlation
PPBS and Ferritin	+0.60	p < 0.001	Highly significant positive correlation
HbA1c and Ferritin	+0.75	p<0.001	Highly significant positive correlation

FBS-fasting blood sugar, PPBS-post prandial blood sugar, HbA1c-glycosylated haemoglobin

Table-2: Correlation between study variables

tween the study groups. Pearson correlation was performed to establish the relationship between study variables. p value <0.05 was considered statistically significant.

RESULTS

This was a comparative case control study conducted on 50 cases of type 2 DM (n=50) and 50 age and sex matched healthy controls (n=50). Serum ferritin was estimated, analyzed and correlated with HbA1c, FBS and PPBS. The results were expressed as mean \pm standard deviation.

The mean age (in years) of cases was 49.5 \pm 11.7 years and that of controls was 46 \pm 10.3 years and was not significant. Table 1 shows comparison of serum ferritin, FBS, PPBS and HbA1c levels in both groups and was statistically significant (p<0.05). The mean serum ferritin levels (ng/dL) in cases was 336.9 \pm 46.3, and in controls was 127.2 \pm 40.9 and was highly significant (p <0.0001).

There was significant positive correlation between serum ferritin and fasting blood sugar (r=+0.47, p=0001) (Table 2, Figure 1).

Serum ferritin and HbA1c: There was positive correlation between serum ferritin and HbA1c, r = +0.75, p < 0.001 and was highly significant. (Table 2, Figure 2).

DISCUSSION

Serum ferritin, a reflector of body iron stores was significantly higher in diabetic patients when compared to controls and this significantly increased as the duration of diabetes increased. This possibly reflects the subclinical hemochromatosis developing in a long standing diabetic patient. Fernandez et al in their studies concluded that increased body

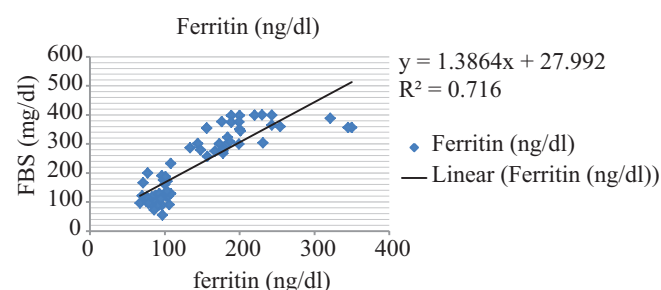


Figure-1: Correlation between Ferritin and FBS

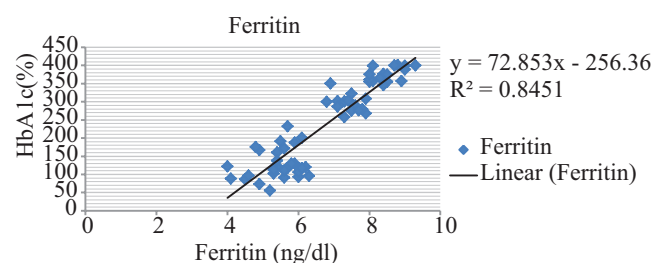


Figure-2: Correlation between Ferritin and HbA1c

iron stores are possibly associated with occurrence of glucose intolerance, type-2 DM.

Serum Ferritin had a positive correlation with FBS, PPBS and HbA1c. This reflected the relation between serum ferritin and glycaemic control, both short term and long term. Cantur KZ et al confirmed in their studies that poorly controlled diabetes patients had hyperferritinemia. Excess iron impairs pancreatic β cell function and causes β cell apoptosis.¹⁸ Iron serves as a potent pro-oxidant in human body and participates in the generation of reactive oxygen species (ROS) such as hydroxyl radical.¹⁹ The susceptibility of β -cells to iron-induced oxidative stress and the iron deposition in β -cells usually leads to apoptosis, and consequently, to insulin deficiency.¹⁵ Iron deposition also induces insulin resistance by inhibiting glucose uptake in fat and muscle tissues, and reducing the capacity of liver to extract insulin, which results in an abnormal increase in hepatic glucose production.²⁰

Limitations: It was conducted on a small sample of population. Further study on a large scale population is needed.

CONCLUSION

To conclude, the major issue arises whether to estimate S. ferritin routinely in all type 2 diabetes patients and whether to set a cut off value of serum ferritin for good glycaemic control. Though our study is a pointer in this direction, we would recommend further studies in this path for setting up specific guidelines. In summary, there is suggestive evidence that iron plays a pathogenic role in diabetes and its complications such as microangiopathy and atherosclerosis. Reliable and sensitive methods need to be developed to precisely measure the free/ catalytic iron that participates in oxidative injury. Iron chelation therapy may present a novel way to interrupt the cycle of catalytic iron-induced oxidative stress and tissue injury and consequent release of catalytic iron in diabetes and to prevent diabetes-related complications.

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