

Original Article

Correlation between serum ferritin, serum iron and blood glucose level in patients of type 2 diabetes mellitus

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Abstract

Background: Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Ferritin is a ubiquitous intracellular protein complex that reflects the iron stores of the body. Many cross-sectional studies indicate that increased body iron stores have been associated with the development of glucose intolerance, type 2 diabetes, metabolic syndrome. This study was carried out to find out the relationship between serum ferritin, serum iron and type 2 diabetes and to see the influence of body iron stores and blood glucose.

Methods: This study includes 81 patients suffering from type 2 diabetes and compared with controls at BIRDEM General Hospital. Serum ferritin, serum iron and Fasting Blood Sugar (FBS) were measured.

Results: Serum ferritin was significantly higher ($p < 0.0001$) in the patients suffering from type 2 diabetes. The levels of serum ferritin were positively correlated with values of FBS.

Conclusions: There is a positive association between elevated iron stores measured by serum ferritin levels, serum iron and type 2 diabetes mellitus. The association of age category of study groups with serum ferritin were also seen.

Keywords: Type 2 diabetes mellitus, serum ferritin, serum iron and FBS.

Introduction

Diabetes Mellitus (DM) is a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of diabetes mellitus, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.¹ It has been suggested that in the diabetic patients a positive correlation between increased serum ferritin and glycaemic level.²

Increased ferritin 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.³

It's also observed that ferritin levels correlated with individual components of the metabolic syndrome particularly serum triglycerides and plasma glucose as well as markers of insulin resistance.⁴

Thus present study is designed to evaluate the correlation between serum ferritin and glycaemic control in patients of type 2 diabetes mellitus which will help to understand the significance of ferritin for the

better management of type 2 diabetes mellitus.

Methods

The study was designed as a case control study. The study was conducted over a period of January 2018 to January 2019. In the present study 81 cases of known type 2 diabetes mellitus, they were primarily diagnosed by clinical examination and further evaluated by biochemical investigations and 82 apparently healthy subjects as a control group were studied.

All cases were selected from the patients attending Out Patient Departments of BIRDEM General Hospital and the control subjects were selected randomly. Consent was taken from all the participants.

To find out the influence of body iron stores on biochemical parameters diabetics underwent the following investigations: Serum Ferritin, serum iron and blood glucose among the age groups ranging from 20 to 50 years old type 2 diabetic patients.

Data collection

A detailed proforma was filled up for each patient which included age, sex, past history of coronary artery disease, cerebrovascular accident, history of hypertension.

The age of onset and duration of diabetes was recorded. Also recorded was treatment history of patient whether on oral hypoglycemic agents, insulin or diet control alone.

Serum ferritin was done by Enzyme-Immunoassay (EIA) for the quantitative determination. For this ferritin estimation in human serum store at 20° C to 80° C. (Ref white, D., Kramer, D., Johndon, G., Dick, F and Hamilton, H. Am. J. Clin. Path. 72-346;1986). Normal reference range for serum ferritin is for male 16.4-323.0 ng/ml and for female 6.9 – 282.55 ng/ml. Serum iron was done by reagent kit which containing guanidinium hydrochloride and hydroxylamine (cat. No 1-419-0150). Reference of normal range serum iron is for men 59 - 158µg/dl and female 37-145µg/dl.

Serum fasting glucose were estimated by glucose oxidase (GOD) enzymatic method (Ref Kaplan L.A. Glucose Kaplan A et al. ClinChem The C.V Mosby Co. St Lois Toronto. Princeton 1984; 1032-1036.). Blood sample was collected from patients after an overnight (8-12hr) fasting.

Statistical analysis was done using SPSS software.

In data analysis, comparison of all parameters between control and study group was carried out by applying unpaired t-test and correlation with serum ferritin, serum iron and FBS. In the present study the Mean \pm SD of age in study group was 44.68 \pm 6.68 years as compared to 34.71 \pm 7.86 in control group.

Result

Table-1: Comparison of biochemical parameters between case and control groups

Case Control	N	Mean	Std. Deviation	Std. Error Mean	t	p
Age(yr)						
Case	81	44.68	6.68	.742	8.72	.000
Control	82	34.71	7.86	.868		
Serum ferritin (ng/ml)						
Case	81	300.07	244.68	27.19	1.98	.050
Control	82	221.49	261.85	28.92		
Serum iron (µgm/ml)						
Case	81	223.26	225.19	25.02	4.08	.000
Control	82	116.47	73.97	8.17		
FBS (mmol/l)						
Case	81	9.26	5.98	.66	6.71	.000
Control	82	4.73	1.27	.14		

Note: *p<0.05 – significant; **p<0.001 – highly significant; #p≥0.05 – not significant

Table-2: correlation of serum ferritin with other biochemical parameters in study groups

Name of parameter	Mean value	Two tailed P value	Pearson coefficient (r)
Serum ferritin	300.07	P<0.00001	0.600
Case	221.49		
Control			
Serum iron	223.26	P<0.0001	0.526
Case	116.47		
Control			
FBS	9.26	P<0.0001	0.701
Case	4.73		
Control			

Serum ferritin (r=0.600, p<0.0001), serum iron (r=0.526, p<0.0001), FBS (r=0.701, p<0.0001).

Above table shows the positive correlation between Ferritin, serum iron and FBS respectively.

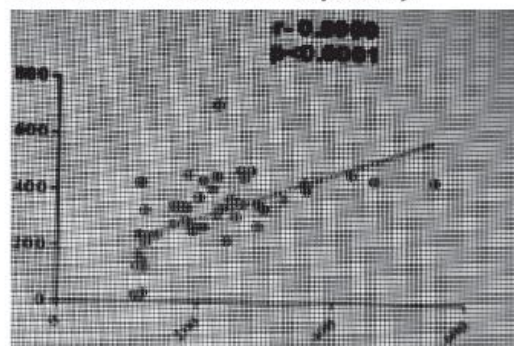


Fig: Shows correlation of serum ferritin blood sugar level with fasting

Discussion

It's obvious evident from the study that increased body iron stores reflected by Serum Ferritin levels had a statistically significant directly proportional correlation with FBS.

There is an increasing concern about the relationship between iron stores and type 2 diabetes with the evidence that elevated serum ferritin levels were independently predicted incident of type 2 diabetes in studies among apparently healthy men and women.⁴

Ferritin is an iron-phosphorus-protein complex that is a biomarker for evaluating body iron contents. Tissue and organ damage occurs when iron concentrations are elevated.⁵ Increased accumulation of iron affects insulin synthesis and its secretion from the pancreas and interferes with the insulin-extracting capacity of the liver. Iron deposition in muscle decreases glucose uptake because of muscle damage.

Conversely, insulin stimulates cellular iron uptake through increased transferring receptor externalization. Thus, insulin and iron can mutually potentiate their effects leading after a vicious cycle to insulin resistance and diabetes.⁶ Our findings are in agreement to by Rui Jiang among type 2 DM cases who reported the mean concentration of Ferritin were significantly higher in study group as compared to control subjects.⁷

It's evident from the study that ferritin levels were positively correlated with FBS. Similar study conducted by Sumeet Smotra et al.⁸ and Jeevan K. Shetty et al.⁹ found increased levels of Serum Ferritin and also reported that diabetics with increased level of Serum Ferritin had significantly poor glycaemic control reflected as compared to diabetes cases under good glycaemic control and healthy controls.

Positive correlation between FBS with serum ferritin and serum iron indicate hyperglycemia causing increased glycation of hemoglobin and increased release of free iron from glycated proteins like hemoglobin. This makes a vicious cycle of hyperglycemia, glycation of hemoglobin and increase in levels of free iron and ferritin. This increased presence of iron pool will enhance oxidant generation leading damage to biomolecules.⁹

In the present study, ferritin levels were significantly higher in patients of type 2 DM (300.07 ± 244.68 vs. 221.49 ± 261.85 ng/ml, $p < 0.0001$) as compared to controls (Table 1) which were consistent with the reports published by F. Sharifi and colleagues. They concluded that the ferritin (101 ± 73 mg/ml vs. 43.5 ± 42 mg/ml, $p < 0.001$) were significantly higher in patients of type 2 diabetes as compared to control subjects.⁷

Our findings are in agreement to by Rui Jiang among type 2 DM cases who reported the mean concentration of Ferritin were significantly higher in study group as compared to control subjects.⁷

Conclusion

Our findings suggest that iron overload reflected by increased serum ferritin and serum iron levels has the potential role in the development of type 2 diabetes. Therefore, in agreement with previous studies we suggest that serum ferritin and serum iron should be included in standard screening protocol to identify patients who are at risk of developing type 2 DM and also to assess the glycaemic control in patients who have already developed the disease.

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References

1. Alvin C. Powers. Diabetes mellitus. In: Dennis L. Kasper, Eugene Braunwald, Anthony S. Fauci, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, eds. Harrison's Principles of Internal Medicine. 17th ed. New York, NY: McGraw-Hill; 2005: 2275.
2. Eschwege E, Saddi R, Wacjman H, Levy R, Thibault N, Duchateau A. HaemoglobinA1c in patients on venesection on therapy for haemochromatosis. *DiabetMetab.* 1982;8(2):137-40.
3. Sumesh Raj, G. V. Rajan. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. *Int J Res Med Sci.* 2013;1(1):125.
4. Megan Jehn, Jeanne M. Clark, EliseoGuallar. Serum ferritin and risk of the metabolic syndrome in U.S. adults. *Diabetes Care.* 2004;27(10):2422-8.
5. SejongBae, Tuan D. Le, Karen P. Singh, Steven N. Blair, Jame R. Morrow. Association between serum ferritin, cardiorespiratory fitness and risk of type 2 diabetes. 18th World IMACS / MODSIM Congress. 2009;(07):103-16.
6. Jose´ Manuel Ferna´ndez-Real, Georgina Pen´arroja, Antoni Castro, Fernando Garcı´a-Bragado, Ildefonso Herna´ndez-Aguado, Wı´fredoRicart. Blood-letting in high-ferritin type 2 diabetes. *Diabetes.* 2002;51(04):1000-4.
7. Rui Jiang, JoAnn E. Manson, James B. Meigs, Jing Ma, Nader Rifai, Frank B. Hu. Body iron stores in relation to risk of type 2. *JAMA.* 2004;291(6):7117.
8. Liang Sun, Oscar H. Franco, Frank B. Hu, Lu Cai, Zhijie Yu, Huaixing Li, et al. Ferritin Concentrations, metabolic syndrome, and type 2 diabetes in middle-aged and elderly Chinese. *J ClinEndocrinol Metab.* 2008;93(12):4690-6.
9. Jeevan K. Shetty, MungliPrakash, Mohammad S. Ibrahim. Relationship between free iron and glycated hemoglobin in uncontrolled type 2 diabetes patients associated with complications. *Indian J ClinBiochem.* 2008;23(1):67-70.