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RESEARCH ARTICLE **OPEN ACCESS**

CORRELATION OF DIABETES MELLITUS AND IRON STATUS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background and Objectives: To evaluate the correlation between levels of serum ferritin, serum iron, haemoglobin and TIBC with the duration of diabetes mellitus and level of control (HbA1c). **Methods:** 100 patients with a clinical diagnosis of diabetes mellitus – using the American Diabetes Association diagnostic criteria – were included in the study (50 cases and 50 controls). Detailed history was taken including presenting complaints with duration of diabetes mellitus, history of hypertension, infections, anemia and chronic renal failure. General physical examination including vitals, body mass index (BMI) and systemic examination was done. Laboratory parameters like serum ferritin, serum iron, total iron binding capacity (TIBC), haemoglobin, fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycosylated hemoglobin (HbA1c), and renal function tests were done for all patients. Data were analyzed using SPSS version 24 **Results:** We found that diabetic individuals had, higher serum ferritin levels than non diabetics and this was statistically significant. There was no statistical difference between diabetic individuals and non diabetics in the TIBC levels. Both groups had normal iron and creatinine levels. We found that diabetic individuals had a positive correlation with elevated serum ferritin with a coefficient ratio of 0.34 and a p value of 0.02 with respect to the duration of diabetes mellitus. **Conclusion:** We conclude that serum ferritin levels are positively associated with the presence and duration of diabetes

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INTRODUCTION

There is an alarming increase in the incidence and prevalence of diabetes mellitus, particularly in Asian Indians. [1]The major morbidities in type 2 diabetes mellitus are due to its microangiopathic and macroangiopathic complications, which affect eyes, kidneys, nerves, heart, and major vessels.[2-3] The development of these complications may be related to biochemical alterations in connective tissue constituents, particularly collagen and elastin as well as due to nonenzymatic glycosylation of proteins induced by chronic hyperglycemia. Type 2 diabetes is characterized by insulin resistance and impaired insulin receptors. It is a common type of diabetes and usually develops after the age of 40 years. It is associated with normal B-cell morphology. Iron is a potent pro-oxidant in the human bodyIron is involved in cellular reactions. Iron also participates in generation of reactive oxygen species; induces oxidative stress; damage tissues; alters the risk for type 2 DM [4] .Susceptibility of B-cells to iron induced oxidative stress and the iron deposition in B-cells usually leads to apoptosis, and consequently, to insulin deficiency [6]. 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.

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Thus, iron deposition and iron-induced oxidative stress contribute to the pathogenesis of type diabetes mellitus through B-cell apoptosis, hepatic dysfunction, and insulin resistance.[7] It is recently recognized that, increased body iron stores are associated with the development of glucose intolerance, gestational diabetes, type-2 DM and insulin resistance syndrom[8-11.] Various studies have shown that there is positive relationship between serum ferritin and type 2 diabetes mellitus, where it causes insulin resistance [12-16]. Diabetes is common and India will soon be the highest in absolute number of diabetic patients, hence we conducted the present study to evaluate the relationship between serum ferritin and type 2 Diabetes mellitus.

MATERIALS AND METHODS

A prospective non-randomized observational study was done on 100 consenting patients in the outpatient department of Internal Medicine and the wards of Yenepoya Medical College Hospital – a tertiary-level teaching hospital in South India from, December 2015 to December 2017 to assess the correlation of serum levels of iron, ferritin and TIBC with the duration of diabetes mellitus and HbA1c levels, selected by purposive sampling method. The study was initiated after obtaining clearance from the ethical committee. Diabetes mellitus was diagnosed on ADA criteria. The control group consisted of healthy individuals between 35 – 65 years of age. Patients with anemia of any chronic cause, patients with serious infections, chronic kidney disease, chronic liver disease, corticosteroid therapy, recipients of blood or blood component transfusion within one month were all excluded from the study. 100 participants were included in the study (50 cases and 50 controls) with majority being males 54%.

Detailed history was taken including presenting complaints with duration of diabetes mellitus, history of hypertension, infections, anemia and renal failure. Laboratory parameters like serum ferritin, serum iron, TIBC, haemoglobin, FBS, PPBS, glycosylated hemoglobin, renal function tests for all patients were done. Serum ferritin evaluation was done using spectrophotometric techniques, using the ferritin Latex Kit (Batch No. COD 31929 Bio systems, Barcelona Spain). Spectrophotometry was done using the Mannheim Boehringer computerized (Rev 371, Auto lab machine serial /No. 9510274). The Auto Lab machine is a selective-access batch clinical chemistry auto-analyzer with in-built quality control monitor. The reference range for serum ferritin (15- 300µg/l) based on the assay method was used for the interpretation of the results. Data was entered into SPSS Software version 24 .The quantitative data age, sex , was expressed in number and percentages for categorical variables Qualitative data was expressed in mean ± standard deviation. Paired and unpaired T test, chi-square test were used for comparison. A 'p' value less than 0.05($p<0.05$) was considered significant. Mann Whitney U test was used to test the correlation.

OBSERVATIONS AND RESULTS

In the present study we found that diabetic individuals had higher serum ferritin levels and haemoglobin levels than non diabetics and this was statistically significant . There was no statistically significant difference in the TIBC between the diabetic individuals and non diabetics. Both groups had normal iron and creatinine levels In the present study we found that diabetic individuals had a positive correlation of their duration of diabetes with serum ferritin with a coefficient ratio of 0.34 and a p value of 0.02

Table 1. Mann Whitney U Test Between Groups

Serum Iron	Study	50	65.44 (16.39)	40-116	67(50-79)	695	<0.001*
	Control	50	90.22 (33.66)	40-156	85(60-119.25)		
Serum Ferritin	Study	50	142.44 (133.63)	68-950	99(88-160)	557	<0.001*
	Control	50	67.75 (41.32)	11.6-142	76.2(27.7-110)		
TIBC	Study	50	326 (28.40)	210-360	339(320-344.25)	943	0.03*
	Control	50	340.76 (54.09)	200-450	342.5(315-380)		
Creatinine	Study	50	0.86 (0.20)	0.5-1.2	0.9(0.7-1)	1119	0.36(NS)
	Control	50	0.82 (0.17)	0.5-1.2	0.8(0.7-0.9)		
Haemoglobin	Study	50	11.91 (1.06)	10-14.3	12(11-12.65)	448.5	<0.001*
	Control	50	13.12 (0.75)	11.4-14.8	13.2(12.55-13.6)		

*p<0.05 statistically signi p>0.05 Non Significant, NS

Table 2. Comparision Of Correlation Between Serum Ferritin And Duration Of Diabetes Across Studies

Study	Inference
Ford [4]	significant correlation between serum ferritin with HbA1c, FBS and serum insulin.
Ali Momeni [24]	There was a significant negative correlation between serum ferritin and duration of diabetes (r = 0.259; P = 0.034).
Padmaja [25]	There was a high (r= 0.62, r= 0.66) positive correlation between SF and HbA1c of females and males respectively in diabetic group
F. Sharifi[26]	Mean serum ferritin was significantly higher in diabetics than in the control group (101±73 mg/ml vs. 43.5+42 mg/ml, p<0.001)
Boinapalli Sudhaka[r27]	The mean serum ferritin levels (males: 390.3+22.4 ng/ml and Women 292+16.8 ng/ml) and found a significant correlation between serum ferritin with HbA1c, FBS and serum insulin
OUR STUDY	Mean serum ferritin was significantly higher in diabetics than in the control group

DISCUSSION

Diabetes is considered as the health crisis of the 21st century. India is considered as the diabetic capital of the world.[17] Ferritin has been known as an index for body iron stores and also as an inflammatory marker. Its concentration correlates positively with plasma triglycerides and apolipoprotein B concentrations, and negatively with HDL2 cholesterol.[18] The underlying mechanisms include roles for iron accumulation in both beta cell failure and insulin resistance, with insulin resistance being more relevant to diabetes risk in the setting of transfusion or diet-related iron excess [19].Serum ferritin is commonly utilized as a marker of body iron stores, and both dietary iron intake and higher ferritin levels have predicted incidence of Type 2 diabetes in epidiemological studies [20-22] - [22]Serum ferritin presents a paradox, as the iron storage protein ferritin is not synthesised in serum, yet is to be found there. [22]Serum ferritin is also a well known inflammatory marker, but it is unclear whether serum ferritin reflects or causes inflammation, or whether it is involved in an inflammatory cycle[23.] Serum ferritin arises from damaged cells, and is thus a marker of cellular damage. The protein in serum ferritin is considered benign, but it has lost most of its normal complement of iron which when unliganded is highly toxic. The fact that serum ferritin levels can correlate with both disease and with body iron stores is thus expected on simple chemical kinetic grounds.[23] In our study the mean age was 56 years.This was same as the study by Ali Momeni [25], whereas the other studies had a much lesser mean age - Padmaja [26]and F. Sharifi[27] whose study mean age was 40 years. In our study 54% were males patients, in contrast to our study females dominated the study population in studies by Ali Momeni [25] and F. Sharifi[27,] whereas in study by Boinapalli Sudhakar[28]males dominated the study population .in another study by Padmaja[29] males and females were equal in the study population.

CONCLUSION

Of ferritin, iron and total iron binding capacity, only serum ferritin levels are positively associated with the presence of diabetes and are also positively correlated with the duration of diabetes

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