

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

Key Words: serum ferritin, diabetes, iron profile, transferrin saturation

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I. Introduction

There is an alarming increase in the incidence and prevalence of diabetes mellitus, particularly in Asian Indians. ¹The 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 body Iron 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 the liver to extract insulin, which results in an abnormal increase in hepatic glucose production. 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 syndrome ⁸⁻¹¹.

Various studies have shown that there is a 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.

II. 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 the 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.

III. 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

IV. 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 excess¹⁹. 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

epidemiological studies²⁰⁻²² 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 cycle²³

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 Momeni²⁵, whereas the other studies had a much lesser mean age - Padmaja²⁶ and F. Sharifi²⁷ 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 Momeni²⁵ and F. Sharifi²⁷, whereas in study by Boinapalli Sudhakar²⁸ males dominated the study population .In another study by Padmaja²⁹ males and females were equal in the study population .

Table 2: Comparison 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 ²⁷ | 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 |

V. 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.

Bibliography

- [1]. Ramachandran A, Snehalatha C, Shetty AS, Nanditha A. Trends in prevalence of diabetes in Asian countries. World journal of diabetes. 2012 Jun 15;3(6):110.
- [2]. Kim KS, Son HG, Hong NS, Lee DH. Associations of serum ferritin and transferrin% saturation with all-cause, cancer, and cardiovascular disease mortality: Third National Health and Nutrition Examination Survey follow-up study. Journal of Preventive Medicine and Public Health. 2012 May;45(3):196.
- [3]. Sen S, Chakraborty R, De B. Complications of diabetes mellitus. In Diabetes Mellitus in 21st Century 2016 (pp. 69-100). Springer Singapore.
- [4]. Bharadwaj D, Singh A. Genetic Basis for Increased Risk for Vascular Diseases in Diabetes. In Mechanisms of Vascular Defects in Diabetes Mellitus 2017 (pp. 27-71). Springer, Cham.
- [5]. Fang YZ, Yang S, Wu G. Free radicals, antioxidants, and nutrition. Nutrition. 2002 Oct 31;18(10):872-9.
- [6]. Olejnicka BT, Andersson A, Tyrberg B, Dalen H, Brunk UT. β -cells, oxidative stress, lysosomal stability, and apoptotic/necrotic c
- [7]. Fernández-Real JM, López-Bermejo A, Ricart W. Cross-talk between iron metabolism and diabetes. Diabetes. 2002 Aug 1;51(8):2348-54.
- [8]. Dmochowski K, Finegood DT, Francombe W, Tyler B, Zinman B. Factors determining glucose tolerance in patients with thalassemia major. J Clin Endocrinol Metab 1993; 77:478-83.
- [9]. Cavallo-Perin P, Pacini G, Cerutti F, Bessone A, Condo C, Sacchetti L, et al. Insulin resistance and hyperinsulinemia in homozygous β -thalassemia. Metabolism 1995; 44: 281–86.
- [10]. Wrede CE, Buettner R, Bollheimer LC, Scholmerich J, Palitzsch KD, Hellerbrand C. Association between serum ferritin and the insulin resistance syndrome in a representative population. Eur J Endocrinol 2006;154:333-40.
- [11]. Dymock IW, Cassar J, Pyke DA, Oakley WG.. Observations on the pathogenesis, complications and treatment of diabetes in 115 cases of haemochromatosis. Am J Med 1972; 52:203-10
- [12]. Mellitus TI, Bansal P. Is serum ferritin associated with type II diabetes mellitus: A clinical study in a representative Indian population. The presentation of Medical Science & Research. 2011;2(1).
- [13]. Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. International The present of Research in Medical Sciences. 2017 Jan 26;1(1):12-5.

- [14]. Abou-Shousha S, Abd EM, Sultan HK. Interleukin-8, ferritin and soluble transferrin receptors in type II diabetes mellitus. The Egyptian presentation of immunology. 2006;13(1):19-25.
- [15]. Khan DA, Qayyum S. Evaluation of cardiac risk by oxidative stress and inflammatory markers in diabetic patients. Pak J Med Sci. 2009 Oct 1;25(5):776-81.
- [16]. Joshi, Shashank R., and Rakesh M. Parikh. "India: The Diabetes Capital of the World: Now heading Towards Hypertension." The present al-Association Of Physicians Of India 55.Y (2007): 323.
- [17]. Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine. 2014 Dec 31;42(12):698-702.
- [18]. Zimmet PZ. The pathogenesis and prevention of diabetes in adults: genes, autoimmunity, and demography. Diabetes care. 1995 Jul 1;18(7):1050-64.
- [19]. Tuomi T. Type 1 and type 2 diabetes. Diabetes. 2005 Dec 1;54(suppl 2):S40-5.
- [20]. John WG. Use of HbA1c in the diagnosis of diabetes mellitus in the UK. The implementation of World Health Organization guidance 2011. Diabetic medicine. 2012 Nov 1;29(11):1350-7.
- [21]. Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum?. Indian journal of endocrinology and metabolism. 2016 Jul;20(4):546.
- [22]. Momeni A, Behradmanesh MS, Kheiri S, Abasi F. Serum ferritin has correlation with HbA1c in type 2 diabetic patients. Advanced biomedical research. 2015;4.
- [23]. Wilson JG, Maher JF, Lindquist JH, Grambow SC, Crook ED. Potential role of increased iron stores in diabetes. The American journal of the medical sciences. 2003 Jun 1;325(6):332-9.
- [24]. Sekine N, Cirulli V, Regazzi R, Brown LJ, Gine E, Tamarit-Rodriguez J, Girotti M, Marie S, MacDonald MJ, Wollheim CB. Low lactate dehydrogenase and high mitochondrial glycerol phosphate dehydrogenase in pancreatic beta-cells. Potential role in nutrient sensing. Journal of Biological Chemistry. 1994 Feb 18;269(7):4895-902.
- [25]. Momeni A, Behradmanesh MS, Kheiri S, Abasi F. Serum ferritin has correlation with HbA1c in type 2 diabetic patients. Advanced biomedical research. 2015;4.
- [26]. Padmaja P, Shabana S, Shariq M. Serum Ferritin and HbA1c levels in type 2 Diabetes Mellitus. Int J Clin and Biomed Res 2015; 1 (3):30-
- [27]. Sharifi F, Sazandeh SH. Serum ferritin in type 2 diabetes mellitus and its relationship with HbA1c. ACTA MEDICA IRANICA 2004. 42;(2) 142 To 145.
- [28]. Sudhakar B, Rita MS, Yadav YC (2015) Correlation of Serum Ferritin with Components of Metabolic Syndrome and its Relationship with the Insulin Resistance in Men and Women. Clin Med Biochemistry Open Access 2:109. doi:10.4172/2471-2663.1000109

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