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Iron Profile in Patients with Type II Diabetes Mellitus in — A study in a Tertiary Care Hospital

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ABSTRACT

Background: The most prevalent metabolic condition, type 2 diabetes mellitus, is characterized by persistent hyperglycemia caused by abnormalities in insulin production, insulin action, or both. Iron, a transitional metal, has been demonstrated to play a key role in the pathophysiology of Type 2 Diabetes Mellitus, with a bidirectional link in which iron influences glucose metabolism, which in turn influences the iron metabolic pathways. The current study aimed to estimate the iron profile in Type 2 diabetes mellitus cases.

Methods: This cross-sectional study was done in the Department of Biochemistry, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. A total of n=100 cases of type II diabetes mellitus were included in the study and age and sex-matched healthy controls were also included in the study. Laboratory investigations included Fasting Blood glucose, Serum ferritin, Total iron-binding capacity, serum iron, and serum transferrin saturation.

Results: The fasting blood glucose was found to be significantly higher in the diabetes mellitus cases. The serum ferritin mean values were 105.32 μgm/dl. In the controls, the range of ferritin levels was 145 μgm/dl. The serum ferritin levels were found to be significantly reduced in the study cases as compared to the controls. Similarly, the total iron-binding capacity (TIBC) of the cases was found to be significantly increased as compared to the controls. The serum transferrin levels were also found to be elevated in the study cases as compared to the controls.

Conclusion: Iron is closely related to the development of diabetes mellitus. Elevated iron and ferritin levels are risk factors for diabetes and can lead to a variety of problems. Conversely in chronic diabetics, there is a tendency to develop iron deficiency anemia and other nutritional deficiency anemias as observed by the results of the current study. As a result, iron profile evaluation can be a valuable output of the expected investigations on diabetes and related problems.

KEYWORDS: Fasting Blood Sugar, Ferritin, Iron, Total Iron binding capacity, Transferrin, Type 2 Diabetes Mellitus

INTRODUCTION

The most prevalent metabolic condition is diabetes mellitus. [1, 2] It is characterized by chronic hyperglycemia caused by a disruption in carbohydrate, fat, and protein metabolism caused by defects in insulin secretion, insulin action, or both, as well as decreased glucose utilization and increased glucose production. [1, 3, 4] The etiology of diabetes mellitus appears to be multifactorial. The entire economic burden of type 2 diabetes is growing globally, as is the prevalence of any other metabolic illness. Type 2 Diabetes Mellitus (T2DM) has become more common in developing countries in recent years. In the Indian scenario, the escalation has shown a soaring tendency, owing to rising obesity, decreased daily exercise levels, and sedentary lifestyles because of industrialization and the aging of the population. [1] Multi-centric clinical studies undertaken by the Indian Council of Medical Research (ICMR) have revealed an increasing trend in diabetes incidence in both urban and rural India. In clinical practice, the prevalence has shown a comparable trend among men and women throughout most age groups (14 percent and 11 percent, respectively, in adults over the age of 20). [5] Most diabetics are between the ages of 40 and 59 years. The public health risks associated with Type II DM in the Indian context are undoubtedly concerning, since India presently ranks second in the world in terms of diabetic persons, with 65.1 million cases, trailing only China (98.4 million). [1, 5] The burden of diabetes is mostly supplied by Type II diabetes, which accounts for approximately 80% to 95% of the overall diabetic population. [2, 3] previous studies have evaluated the essential trace element Iron (Fe) and parameters related to it in diabetic patients, such as serum ferritin, serum transferrin, TIBC (Total Iron Binding Capacity), UIBC (Unsaturated Iron Binding Capacity), and Hb (Hemoglobin), as these are thought to be closely related to glucose metabolism. [6–8] Iron is a transitional metal and a possible catalyst in several cellular reactions that connect carbohydrate, protein, and lipid metabolisms, producing reactive oxygen species that have the potential to harm

pancreatic -cells due to oxidative stress. An increase in tissue iron corresponds to an increase in free radical generation, which in turn amplifies numerous pathways involved in inflammatory lesions, accelerating morbidity. [7–9] Although discrete attempts have been done with chosen metrics to understand the function of iron metabolism in Type II DM, further elaboration and reiteration are required to reach an optimal result when all iron index parameters are examined in a single research and population of Type II DM patients. Iron profile estimation in a TYPE II DM patient is frequently overlooked despite its importance, and significant research on iron profile in Type II DM is also lacking in recent years. The purpose of this study is to emphasize the function of iron metabolism in impaired glucose metabolism and to determine whether iron metabolism measures may also be used as predictors of Type II diabetes.

MATERIAL AND METHODS

The study was carried out in the Department of General Medicine and Department of Biochemistry, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the local language. The estimated sample size is 91 we included n=100 cases in the study

Method of collection of Data: N=100 cases of type II diabetes mellitus and age and sex-matched controls were included in the study. Patients and control baseline data, clinical findings, and basic investigation report were obtained on a pre-structured proforma after written informed consent from the patients duly signed by them without any kind of financial burden on the patients.

Inclusion criteria were patients diagnosed with diabetes mellitus type 2, visiting the OPD of Prathima Institute of Medical Sciences, aged from 40 – 65 years of both genders, age and sex-matched volunteers as controls.

Exclusion criteria were patients with cardiovascular diseases, patients with other endocrinal disorders Controls who have donated blood recently ,those on vitamin supplementation and not willing to participate in the study voluntarily

The T2DM patients in our study ranged from freshly diagnosed to those already on medications were included. A semi-structured questionnaire was used to obtain the demographic profile of the cases. For laboratory investigation 5ml of venous blood sample was collected under strict aseptic precaution in the fasting condition. All blood samples were collected in a vacutainer and kept at room temperature for 30-40 minutes to allow clotting to be completed and then centrifuged at 3000 revolutions per minute for 10 min to obtain clear serum samples. Serum samples were separated and aliquoted for the following investigations. Serum ferritin: By Chemiluminescent immunoassay (CLIA), Serum transferrin: By Turbidimetry (Nephelometry) method using Immunochemistry System. Serum iron: By Bathophenanthroline sulphonate method (manual method using spectrophotometer), Total Iron Binding Capacity (TIBC): By Ion Exchange Resin Ferrozine method.

Statistical analysis: The data was collected and uploaded on an MS Excel spreadsheet and analyzed by SPSS version 22 (Chicago, IL, USA). Quantitative variables were expressed on mean and standard deviations and qualitative variables were expressed in proportions and percentages. Fisher's exact test has been used to find the difference between two proportions.

RESULTS

In our study, a total of n=100 cases of type 2 diabetes mellitus and n=100 controls were included. In the cases, the age range of the patients was from 40 – 64 years and the mean age was 51.25 $\pm$ 10.5 years 69% of the cases were males and 31% of the cases were females. In the control group, the age range was from 40 – 60 years and the mean age was 46.85 $\pm$ 11.2 years. The total number of males included in the controls was 70% and females were 30%. There was no statistical difference between both groups based on the age and distribution of cases were concerned. The range of fasting blood glucose in the cases (n=100) was from 100 – 350 mg/dl and the mean values were 132.25 mg/dl. The mean duration of diabetes in the cases of the study was 3.5 $\pm$ 1.5 years. For the control group out of (n=100) the range of fasting blood glucose was 70 – 140 mg/dl and the mean values were 95.67 mg/dl. The fasting blood glucose was found to be significantly higher in the diabetes mellitus cases and the p values were (< 0.001) which is highly significant. The serum ferritin levels in the cases of the study ranged from the minimum values of 2.2 μgm/dl to 330 μgm/dl the mean values were 105.32 μgm/dl. In the controls, the range of ferritin levels was 5.2 μgm/dl to 350 μgm/dl the mean values were 145 μgm/dl. The serum ferritin values were found to be lower in cases and p-value analysis indicated (p=0.021) hence considered significant. The serum ferritin levels were found to be significantly reduced in the study cases as compared to the controls. Similarly, the total iron-binding capacity (TIBC) of the cases was found to be significantly increased as compared to the controls. The serum transferrin levels were also found to be elevated in the study cases as compared to the controls as depicted in Table 1

A multivariate logistic regression analysis was done with all the above parametersTable 2 to find out risk factor stratification and establish a direct association considering odd's ratio and 95% confidence interval of the difference. However, we couldn't comment on risk factor stratification from the corresponding odd's ratio for each variable to establish an association, as none of the corresponding 'P' values was statistically significant

Variable	Cases		Controls		P-value
	Mean	SD	Mean	SD	
Serum Iron (μgm/dl)	65.23	20.25	145.74	30.19	0.032*
Serum Ferritin (μgm/dl)	105.32	35.25	145.0	40.37	0.021*
Serum TIBC (μgm/dl)	470.95	45.71	350.27	35.63	0.041*
Serum Transferrin (mg/dl)	355.62	35.72	295.26	30.44	0.033*
Fasting blood sugar levels (mg/dl)	132.25	70.35	95.67	32.65	0.001*

* Significant

Table 1: Bivariate analysis of theIron parameters included in the study

Variable	95% CI		Odds Ratio
Fasting blood sugar (mg/dl)	0.125	8.25	1.32
Serum Iron (μgm/dl)	0.885	5.12	1.85
Serum Ferritin (μgm/dl)	0.994	2.19	0.86
Serum TIBC (μgm/dl)	0.025	1.41	0.23
Serum Transferrin (mg/dl)	0.81	1.71	1.49

Table 2: Multivariate logistic regression analysis of the parameters

DISCUSSION

Iron measures such as serum ferritin, serum transferrin, serum iron (Fe), serum TIBC (Total Iron Binding Capacity), and transferrin saturation are changed in T2DM patients, according to most studies and recent literature. These characteristics are now known to be intimately connected to glucose metabolism and may potentially be etiological factors in T2DM. [10, 11] Because changing glucose metabolism impacted the iron profile, there is a tight link between the iron profile and T2DM. The changed iron profile or free iron increases oxidative stress and creates inflammatory cytokines, resulting in this reciprocal interaction. [12–14] The fasting blood glucose was found to be significantly higher in the diabetes mellitus cases and was highly significant ($p<0.001$). The serum ferritin levels in the cases of the study mean values were 105.32 μgm/dl. In the controls, the mean values were 145 μgm/dl. The serum ferritin values were found to be significantly lower in cases. The serum ferritin levels were found to be significantly reduced in the study cases as compared to the controls. Similarly, the total iron-binding capacity (TIBC) of the cases was found to be significantly increased as compared to the controls. The serum transferrin levels were also found to be elevated in the study cases as compared to the controls. All these effects show that Diabetics are more prone to develop low iron stores as compared to the normal controls. Several other studies were done in this regard and also point out the same observations made in the patients with type 2 diabetes mellitus. [15–19] Huang J et al., [20] discovered that serum ferritin concentration was adversely related to insulin sensitivity, indicating a tight relationship between insulin resistance and total body iron reserves. A similar study done in Brazil by Monteiro SCM et al., [21] discovered a link between prediabetes, insulin resistance, and serum ferritin. Manikandan et al., [8] found that mean serum iron levels were lower in patients than in controls. Free iron, as a potent prooxidant, increases cell oxidative stress by participating in the Haber Weiss & Fenton reaction, which produces highly toxic free radicals or reactive oxygen species, namely hydroxyl radical (OH) and hydroperoxyl radical (HOO^{-}), capable of inducing lipid peroxidation [22] as well as further causes oxidative stress and tissue damage, altering the risk for T2DM. [23] Obesity is a problem and risk factor for T2DM. Fat accumulates in fat cells, and these fat cells create substances that cause inflammation. [11] Hyperglycemia has a deleterious impact on numerous metabolic processes, including iron metabolism, in T2DM patients. The maximum level of iron that may be bound to iron-binding proteins, such as transferrin, is referred to as serum TIBC. Transferrin provides for the majority of serum's total iron-binding capacity (TIBC). However, in healthy individuals, approximately one-third (around 30%) of this capacity of transferrin is saturated with iron, leaving a considerable percentage as a reserve known as unsaturated iron-binding capacity (UIBC). TIBC levels are higher in people with iron deficiency and lower in people with chronic inflammatory illnesses such as diabetes and cancer. [24–26]

CONCLUSION

Iron is closely related to the development of diabetes mellitus. Elevated iron and ferritin levels are risk factors for diabetes and can lead to a variety of problems. Conversely, in chronic diabetics, there is a tendency to develop iron deficiency anemia and other nutritional deficiency anemias as observed by the results of the current study. As a result, iron profile evaluation can be a valuable output of the expected investigations on diabetes and related problems.

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