e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(1); 589-592

Original Research Article

A Study to Assess Level of Serum Ferritin in Type 2 Diabetes Patients and the Correlation between Serum Free Iron Concentrations with Glycemic Control

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Received: 12-11-2023 / Revised: 15-12-2023 / Accepted: 22-01-2024
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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess level of serum ferritin in type 2 diabetes patients with good and poor glycemic control and also assessed the correlation between serum free iron concentrations with glycemic control.

Methods: This study was retrospective type was conducted in the Department of Medicine, Mata Gujari Memorial Medical College, Kishanganj, Bihar, India from May 2018 to April 2019. Our institute is a tertiary care hospital. Study population was patients of type 2 diabetes mellites visiting outpatient department of our hospital. This study comprises 50 patients with type 2 diabetes mellitus (treated with hypoglycemic drugs), as cases and 50 patients, age and sex matched apparently healthy adults as a control group.

Results: On comparison of serum ferritin levels between cases and controls it was found that the mean serum ferritin of diabetic population was 138.88± 64.95 ng/mL and that of control group was 60.92 ± 28.67 ng/mL (p value< 0.05). Serum ferritin of case group is therefore significantly higher than the control group. Similarly, BMI, fasting blood glucose (mg/dl) and glycated hemoglobin (HbA1C) values were significantly higher in diabetic group as compared to control group. We compared serum ferritin values with HbA1C values in diabetic patients. Increase in serum ferritin levels was noted with increasing values of HbA1C. The correlation between glycated hemoglobin and serum ferritin was done by Pearson correlation test and it showed a significantly positive correlation (r=0.507) with serum ferritin.

Conclusion: In present study, we noted a positive correlation between serum ferritin levels and increased HbA1c reflecting poor glycemic control. This highlights the need for strict glycemic control in these subjects. Further studies are needed to verify the importance of screening of hyper ferritin in type 2 diabetic patients and to define cut-off level of serum ferritin for possible early detection and subsequent prevention or delaying of impaired glucose tolerance and diabetes in those participants.

Keywords: Fasting blood glucose, HbA1c, Serum ferritin, Type 2 diabetes mellitus

Introduction

Diabetes mellitus is a serious health condition that progressively impacts various tissue and organ systems, significantly affecting the quality of life. The development of a vicious cycle involving increased insulin resistance and subsequent complications is a key characteristic of this disease. Increased serum ferritin and body iron reserves have emerged as possible contributions among the many risk variables and causes that have been discovered. The purpose of this investigation is to examine how elevated blood ferritin levels correlate with how long a person has had diabetes. Due to its redox nature, iron plays a crucial part in the pathophysiology of diabetes by being oxidized and reduced in a continuous cycle, which in turn generates reactive oxygen species via the Haber-Weiss reaction. Four pathways have been proposed by which iron affects diabetes: (a) insulin shortage since pancreatic islets are prone to oxidative damage from free radicals; (b) insulin resistance; (c) hepatic dysfunction; and (d) gathering of iron in the interstitial cells of the pancreas leading to the deposition of collagen and impaired microcirculation. [1]

Research findings indicate a direct and independent correlation between increased iron reserves in the body and the occurrence of metabolic disorders, raised fasting glucose levels, and dyslipidemia. [2,3] This is because free radical damage caused by elevated iron storage increases the risk of diabetes complications. Rajpathak et al. (2009) and De Sanctis et al. (2007) are only two of the many research groups that have established a correlation between high iron reserves and an increased chance of creating type 2 diabetes mellitus. [4,5] People with iron overload illnesses, such as hemochromatosis, or those who need regular transfusions, such as those with thalassemia, are also at an increased risk of developing diabetes. [5]

There is epidemiological data to show that consuming more heme, which is abundant in animal products like meat, increases one's chance of developing diabetes. [6] Oxidative stress may cause free radicals to form, and these radicals can damage pancreatic beta cells, resulting in less insulin being produced and secreted. [7] Reduced levels of cancer prevention agent catalysts, for example, superoxide dismutase, catalase, and glutathione peroxidase, make pancreatic islet cells more susceptible to oxidative injury. [8] In addition, studies have shown that phlebotomy, a process used to remove extra iron from the body, may boost insulin sensitivity. [9] In response to inflammatory stress, serum ferritin levels rise, which indicates an increase in iron reserves and may be used as a biomarker. [10]

The aim of the present study was to assess level of serum ferritin in type 2 diabetes patients with good and poor glycemic control and also assessed the correlation between serum free iron concentrations with glycemic control.

Materials and Methods

This study was retrospective type was conducted in the Department of Medicine, Mata Gujari Memorial Medical College, Kishanganj, Bihar, India from May 2018 to April 2019. Our institute is a tertiary care hospital. Study population was patients of type 2 diabetes mellites visiting outpatient department of our hospital. This study comprises 50 patients with type 2 diabetes mellitus (treated with hypoglycemic drugs), as cases and 50 patients, age and sex matched apparently healthy adults as a control group.

Inclusion Criteria

Diabetic patients (type 2, treated with hypoglycemic drugs), age more than 30 years of both the gender. Diabetic patients met the criteria American Diabetes Association.9 Exclusion Criteria

Patients with anemia (Hemoglobin levels less than 12g/dl in women and less than 13g/dl in males) or receiving treatment for anemia in the past three months, Patients receiving iron supplements, pregnant women. Patients with history of blood donation in the last three months, Patients with diagnosed type 1 diabetes mellitus, Patients with hepatic disorders, renal disorders, malignancies, acute infections, fever, myocardial infarction, bleeding disorders or Patients with history of drug or alcohol abuse. Patients on medication with possible influence on serum ferritin levels. Patients who do not give consent to the study

All participants after their written informed consent underwent detailed physical and clinical examination. BMI was calculated using standard formula. Under all aseptic and antiseptic conditions 5 ml of blood sample was collected from each subject (with overnight fasting) and divided into a sterile empty vial and an EDTA vial. EDTA vials are used for estimation of glycated hemoglobin and blood glucose. The rest of the sample was then allowed to stand for some time and then centrifuged for separation of serum. Blood glucose measurement by spectrometry Glucose oxidase per oxidase (GOD-POD) method which is enzymatic, specific, accurate and rapid method of measurement of true blood glucose. Estimation of serum ferritin was done by using automated Chemiluminescence Immunoassay system (CLIA).

Statistical analysis Arithmetic mean and standard deviation were calculated to assess the levels of various parameters in both groups using SPSS version 21

Results

Table 1: Comparison of means of the different anthropometric, clinical and biochemical characteristics

Parameters	Diabetic group	Control group	P value
Age (years)	51.03 ± 11.62	50.91+12.23	>0.05
Male / female	23 / 27	21 / 29	>0.05
Serum ferritin (ng/mL)	138.88 ± 64.95	60.92 ± 28.67	<0.01
BMI (Kg/m2)	26.31 ± 3.05	23.81 ± 2.69	<0.01
Fasting blood glucose (mg/dL)	161.28 ± 48.51	81.85 ± 14.24	<0.01
Glycated hemoglobin (HbA1C)	8.92 ± 2.21	5.39 ± 0.71	<0.01

On comparison of serum ferritin levels between cases and controls it was found that the mean serum ferritin of diabetic population was 138.88± 64.95 ng/mL and that of control group was 60.92 ± 28.67 ng/mL (p value< 0.05). Serum ferritin of case group is therefore significantly higher than the control

group. Similarly, BMI, fasting blood glucose (mg/dl) and glycated hemoglobin (HbA1C) values were significantly higher in diabetic group as compared to control group.

Table 2: Comparison of serum ferritin with HbA1C in diabetic patients

HbA1C	N	Mean ± SD HbA1C	Serum Ferritin
6 -7.5	16	6.84 ± 0.62	92.45 ± 38.55
7.51- 9	14	8.08 ± 0.82	118.22 ± 21.83
9.01-10.5	11	9.94 ± 0.45	155.60 ± 39.21
> 10.5	9	11.89 ± 1.13	228.12 ± 11.75

We compared serum ferritin values with HbA1C values in diabetic patients. Increase in serum ferritin levels was noted with increasing values of HbA1C.

Table 3: Correlation between serum ferritin and HbA1c levels Group

	Mean ±SD	Pearson Correlation
Serum Ferritin (ng/mL)	138.88 ± 64.95	.507
Glycated hemoglobin (HbA1C)	8.92 ± 2.21	

The correlation between glycated hemoglobin and serum ferritin was done by Pearson correlation test and it showed a significantly positive correlation (r=0.507) with serum ferritin.

Discussion

Diabetes Mellitus is a noncommunicable disease having predominant public health concern, affecting millions of people worldwide. According to International Diabetes Federation report, 415 million people worldwide have this disease and India harbors 69.1 million, the second highest number of diabetics in the world. [11] Type 2 Diabetes mellitus (T2DM) is the most prevalent form of diabetes. It is expected that type 2 diabetes rise to 9.3% by year 2030, particularly in Indian population, the reasons might include migration of human beings from rural to urban areas with change in dietary habits, and the shift to an increasingly sedentary lifestyle. [12] Recent data show that about one third of the urban population in India's major cities has metabolic syndrome, major precursor of Type 2 Diabetes mellitus. [13]

On comparison of serum ferritin levels between cases and controls it was found that the mean serum ferritin of diabetic population was 138.88± 64.95 ng/mL and that of control group was 60.92 ± 28.67 ng/mL (p value< 0.05). Serum ferritin of case group is therefore significantly higher than the control group. Similarly, BMI, fasting blood glucose (mg/dl) and glycated hemoglobin (HbA1C) values were significantly higher in diabetic group as compared to control group. We compared serum ferritin values with HbA1C values in diabetic patients. Increase in serum ferritin levels was noted with increasing values of HbA1C. Scientific studies has revealed unsuspecting influences between iron metabolism and type 2 diabetes. The relationship is bi-directional; iron affects glucose metabolism, and glucose metabolism impinges on several iron metabolic pathways. It is increasingly recognized that iron influences glucose metabolism, even in the absence of significant iron overload. [14] Other mechanisms related to serum ferritin are, potent hydroxyl radicals from iron by Heber–Weiss and Fenton reactions impair mechanism of vasodilatation, disrupt endothelium, accelerate development of atherosclerosis, diabetic nephropathy, and other microvascular complic ations associated with type II diabetes within 7 years. [15] Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by liver, and interference with insulin's ability to suppress hepatic glucose production. [16] In present study levels of BMI, fasting blood glucose, HbA1c and serum ferritin were significantly higher in diabetic patients as compared to controls. Similar findings were noted by Chandrashekhar et al [17] and Kundu et al. [18]

The correlation between glycated hemoglobin and serum ferritin was done by Pearson correlation test and it showed a significantly positive correlation (r=0.507) with serum ferritin. A significant increase in serum ferritin levels was observed in diabetic patients with raised HbA1c compared to well controlled ones, findings are consistent with the study of Chandrashekhar et al. [17] They also observed that serum ferritin was increased in type 2 diabetic patients as long as glycemic control was not achieved. Others have also studied and found that serum ferritin, a reflector of body iron stores, was significantly higher in diabetic patients when compared to controls and is significantly increased with the duration of diabetes and HbA1c values. [19,20]

Pramiladevi et al.. noted a significant correlation in diabetics compared with individuals with normal blood sugar regarding increased serum ferritin, and

hyper ferritin may be one of the causes for development of insulin resistance before overt diabetes. [21] Contrary to present study, Thilip Kumar G et al. reported that patients with type 2 diabetes had significantly higher serum ferritin level when compared to healthy controls but there is no correlation between serum ferritin with mean blood glucose and HbA1c. [22]

Conclusion

In present study, we noted a positive correlation between serum ferritin levels and increased HbA1c reflecting poor glycemic control. This highlights the need for strict glycemic control in these subjects. Further studies are needed to verify the importance of screening of hyper ferritin in type 2 diabetic patients and to define cut-off level of serum ferritin for possible early detection and subsequent prevention or delaying of impaired glucose tolerance and diabetes in those participants.

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