Original Research Article

Serum ferritin in pre-diabetes and diabetes mellitus in relationship with glycemic status

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Abstract

Background: Iron has been suggested to play a role in the etiology of type 2 diabetes mellitus (T2DM). Evidence are sparse for other markers of iron metabolism that are regulated differently and might act through independent pathways. **Aims:** To analyze the serum ferritin levels in individuals having diabetes and to study its association Glycated hemoglobin (HbA1c%). **Materials and Methods:** The present crosssectional study was conducted for a period of 15 months in 150 individuals: Group-1: 75 healthy subjects, and group-2: 75 patients diagnosed with type 2 Diabetes Mellitus Number of age and gender matched controls selected randomly. All the relevant demographic data were collected and anthropometric measurements including height and weight were measured to calculate BMI. Serum Ferritin levels in Type 2 diabetes mellitus and correlation between Serum ferritin and HbA1c% is done. **Results:** The highest prevalence was found in the age group 41-50 years (38%) followed by the age group of 51-60 (27%). It was observed that male female ratio of 1.2:1. Serum ferritin was significantly higher in the cases ($p<0.01$) when compared to controls. Serum ferritin was significantly related to the duration of diabetes ($p<0.05$). As the duration of diabetes increased, serum ferritin also increased. There was a positive correlation between serum ferritin and HbA1c. Serum ferritin is also significantly related to HbA1c (r- 0.21, $p<0.05$). **Conclusion:** serum ferritin was increased with HbA1c which is positively correlated in diabetes. Thus, routine screening for serum ferritin concentration in diabetic patients can be done to assess the body iron stores.

Key Words: Glycated Hemoglobin, Ferritin, Insulin resistance.

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INTRODUCTION

Diabetes mellitus (DM), one of the most prevalent endocrine disorders in the India now reached the proportions of a global pandemic. India, has a very high number of diabetics and has earned rank of being the diabetes capital of the world. The earliest evidence that systemic iron overload could contribute to abnormal glucose metabolism was that patients with classic hereditary hemochromatosis (HH) had increased frequency of diabetes mellitus. [1] Iron is an essential micronutrient for humans, primarily responsible for oxygen transport, electron transfer reactions and DNA synthesis. However, iron is also known to take part in the formation of highly reactive free radicals that can induce oxidative modification of various molecules (1). Since patients suffering from hereditary hemochromatosis – a disease characterized by massive iron overload – have been described to be more likely to develop type 2 diabetes mellitus (T2DM), iron overload is suspected to play a role in its etiology. Subsequent studies also suggested that elevated body iron stores, mainly measured by circulating ferritin levels, are associated with a higher T2DM risk in the general population. There is evidence that high body iron may have detrimental effects on both insulin secretion and sensitivity. However, more recent studies on diabetes in hereditary hemochromatosis have been inconclusive and ferritin levels may be influenced by reverse causation or confounding by inflammation, as ferritin is an acute-phase protein .[2,3] Studies examined the relationship between ferritin and hyperglycemia or insulin resistance in humans . These studies in general found positive associations, although transferrin is inversely related to

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body iron stores and ferritin. In addition, while increased ferritin is quite consistently associated with hyperglycemia or insulin resistance.[4] To analyze the serum ferritin levels in individuals having diabetes and to study its association Glycated hemoglobin (HbA1c%).

MATERIALS AND METHODS

The present crosssectional study was conducted for a period of 15 months in the Department of Biochemistry. Out of a total of 150 individuals:

Group-1: 75 healthy subjects, and group-2: 75 patients diagnosed with type 2 Diabetes Mellitus Number of age and gender matched controls selected randomly. All the relevant demographic data were collected and anthropometric measurements including height and weight were measured to calculate BMI. Under all aseptic and antiseptic conditions 5 ml of blood sample was collected from each subject from a suitable peripheral vein (preferably antecubital vein) by venipuncture using a sterile disposable syringe and divided into a sterile empty vial and an EDTA vial. EDTA vials are used for estimation of glycated hemoglobin. The rest of the sample was then allowed to stand for some time and then centrifuged for separation of serum. This serum was used for estimation of the other parameters. Serum ferritin was measured by immunoradiometric assay kit of the sandwich type based on two monoclonal antiferritin antibodies: one 125I- labelled anti-ferritin antibody in liquid phase and other monoclonal antiferritin antibody is coupled to magnetizable cellulose. Blood glucose was determined by the Hexokinase method and glycosylated hemoglobin by D 10 by HPLC method. Patients were evaluated with detailed history, meticulous examination and laboratory investigations. Since serum ferritin is an acute phase reactant and may be elevated in presence of inflammation, an attempt was made to minimize this potential source of confounding by excluding those patients with suspected infection, inflammation and liver disease and with positive CRP levels. Most of the patients were selected when they had come for treatment for diabetes.

Statistical analysis

Statistical analysis was performed using the software SPSS. Means of the different parameters were compared using one way analysis of variance (ANOV A). Pearson's Correlations between serum ferritin, blood glucose and BMI were evaluated using Pearson Co-relation Co-efficient. All tests were considered statistically significant if the p-value was <0.05.

RESULTS

In the present study carried out in diagnosed cases of type 2 diabetic mellitus, the youngest case study was found to be 33 years of age, and the oldest to be 75 years. The highest prevalence was found in the age group 41-50 years (38%) followed by the age group of 51-60 (27%). It was observed that male female ratio of 1.2:1.

Table 1: Comparison of Demographic details

Variable	Controls group	Diabetic group	P- Value
Age in years	54+9	53+10	>0.05
BMI	24+1.5	26+2.1	<0.05
FBG	85+12	171+67	<0.05
PLBG	119+15	283+99	<0.05
Blood urea mg/dL	25+8.1	26.2+8.3	>0.05
Sr. Creatinine mg/dL	1.0+0.19	1.02+0.21	>0.05

Age, blood urea and serum creatinine are not significant on comparison in 2 groups. BMI, fasting blood glucose and post prandial blood glucose are significant in between the groups.

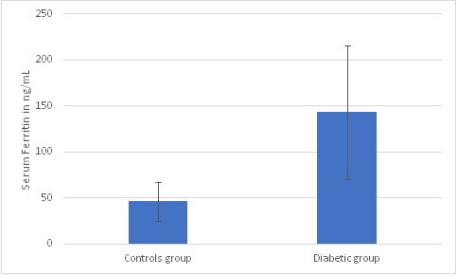

Figure 1

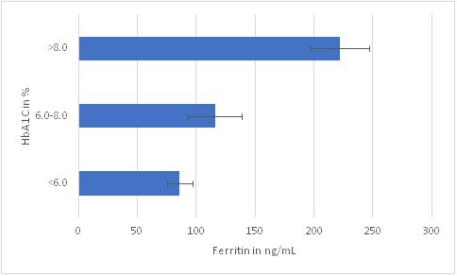

Figure 2

Figure 1: Serum ferritin in diabetic patients when compared to controls; **Figure 2:** Correlation between serum ferritin and HbA1c

Figure 1, Serum ferritin was significantly higher in the cases ($p<0.01$) when compared to controls. Serum ferritin was significantly related to the duration of diabetes ($p<0.05$). Figure 2, As the duration of diabetes increased, serum ferritin also increased. There was a positive correlation between serum ferritin and HbA1c. Serum ferritin is also significantly related to HbA1c (r- 0.21, $p<0.05$).

DISCUSSION

In the present study in diagnosed cases of type 2 diabetic mellitus, the highest prevalence was found in the age group 41-50 years (38%) .Similar findings were also observed Borah M, Scott and Fischer, Mc Nair *et al*, and Yoon.[5-8] They found the highest prevalence of type 2 DM in 41-50 years of age. present study has male predominance with male female ratio of 1.2:1. Borah M study showed 1.27:1. Caixas *et al* in their study has observed a male to female ratio of 1.14:1. Shah S.K *et al* reported the similar findings in the state of Assam. Khalid A *et al* also revealed a male preponderance of diabetes mellitus.[9-11] In present study Serum ferritin was significantly higher in the cases ($p<0.01$) when compared to controls. (Figure-2)Serum ferritin was significantly related to the duration of diabetes ($p<0.05$). Serum ferritin, a reflector of body iron stores was significantly higher in diabetic patients increased as duration of diabetes increased. This possibly reflects the subclinical hemochromatosis developing in a long standing diabetic patient.[12] Fernandez *et al*[13] in their studies concluded that increased body iron stores are possibly associated with occurrence of glucose intolerance, type-2 diabetes and gestational diabetes. Similar findings were obtained by Ford *et al*.[14] They had examined the cross-sectional associations among ferritin concentration, glucose tolerance status, and concentrations of insulin, glucose, and glycosylated hemoglobin for 20 years from the third national health and nutrition examination survey. There was a positive correlation between serum ferritin and HbA1c. Serum ferritin is also significantly related to HbA1c (r- 0.21, $p<0.05$). Serum Ferritin had a positive correlation with FBS and HbA1c. This reflected the relation between serum ferritin and glycaemic control, both short term and long term. Cantur KZ *et al*[15] confirmed in their studies that poorly controlled diabetes patients had hyperferritinemia. This showed that serum ferritin was increased in diabetes as long as glycemic control was not achieved. They also found a correlation between ferritin level and diabetic retinopathy. In diabetic subjects, a positive correlation between increased serum ferritin and poor glycemic control, reflected by higher HbAIc, has been suggested by Eschwege *et al*.[16] In a study carried out by Smotra S, *et al* in a tertiary care hospital in North India found that in those with increased level of Serum Ferritin, more number of patients had poor glycemic control reflected by higher levels of HbA1c % as compared to those with normal levels and was found to be statistically significant ($p<0.05$).[17] A study carried out by Jiang *et al* found that the mean ferritin concentration was significantly higher ($P<0.001$) in the cases than in the healthy controls.[18] Although the exact mechanism for association of elevated serum ferritin with type 2 diabetes mellitus is yet to be established, there are a number of prevailing theories. Iron overload is believed to be associated with insulin resistance. Iron deposition in the liver may cause insulin resistance by interfering with the ability of insulin to suppress hepatic glucose production. Pancreatic damage due to some degree of subclinical hemochromatosis has been considered at least in some cases of diabetes.[13] It is surmised that this increase may contribute to the pathogenesis of this disease as well as in the development of complications. In summary, there is suggestive evidence that iron plays a pathogenic role in diabetes and its complications such as microangiopathy and atherosclerosis. Reliable and sensitive methods need to be developed to precisely measure the free/catalytic iron that participates in oxidative injury. Iron chelation therapy may present a novel way to interrupt the cycle of catalytic iron–induced oxidative stress and tissue injury and consequent release of catalytic iron in diabetes and to prevent diabetes-related complications.

CONCLUSION

To conclude, the major issue arises whether to estimate Serum ferritin levels routinely in all type 2 diabetes patients and whether to set a cutoff value of serum ferritin for good glycemic control.

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