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Original article: Level of Serum ferritin and Glycated hemoglobin (HbA1C) in type 2 diabetes mellitus

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Abstract

Background: Serum Ferritin, an acute phase reactant is a marker of iron stores in the body. Ferritin is a protein in the body that binds to iron; most of the iron stored in the body is bound to ferritin. The HbA1c fraction is abnormally elevated in chronic hyperglycemic diabetic patients and it correlates positively with the glycaemic control this study was carried out to examine and establish a relationship between Serum Ferritin with Type 2 diabetes mellitus and metabolic syndrome and to examine whether a correlation between S. ferritin and FBS, HbA1c exists.

Material & Method: 100 type 2 diabetes subjects (M:F - 64:36, mean age 54.5±8.5 years, mean BMI 24.85kg/m^2) which included 24 patients with metabolic syndrome were studied and compared with controls. S. ferritin, Hb, ESR, FBS, PPBS, HbA1c and fasting lipid profile were measured.

Results: Serum ferritin was significantly higher in diabetic patients when compared to controls and serum ferritin had a positive correlation with increasing duration of diabetes.

Conclusions: There was a positive correlation between serum ferritin and FBS, HbA1c. There was no correlation between serum ferritin and age, sex, metabolic syndrome, coexistent hypertension, total cholesterol, LDL and serum triglycerides.

Keywords: Ferritin, Diabetes, FBS

Introduction

The explosive increase of Diabetic population worldwide is a major public health concern both in developing and developed countries. Metabolic syndrome is also on an increasing trend. The metabolic syndrome is closely linked to insulin resistance and numerous studies indicate a link to iron overload. Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance, such as elevated blood glucose and insulin levels [1]. The glycation of proteins is enhanced by elevated glucose concentrations. The major form of protein glycation with a clinical consideration is glycated haemoglobin (HbA1c). HbA1c is majorly affected by the blood glucose levels alone. However, certain studies have proven that the HbA1c levels are altered by various other coexisting factors, along with diabetes, especially that of iron defiiciency anaemia, which is a major public health problem in developing countries like India.

In addition, two prospective studies have identified an independent association between baseline elevations in iron stores and the incidence of diabetes. Low Vitamin D levels are a risk factor for impaired glucose tolerance and T2DM [2, 3]

However, increased glycated haemoglobin levels have been documented in iron deficiency anaemic patients without any history of diabetes. Recent studies indicate that increased body iron stores and subclinical hemochromatosis has been associated with the development of glucose intolerance, type 2 diabetes, metabolic syndrome and possibly the development of diabetic retinopathy, nephropathy and vascular dysfunction. Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver, and interference with insulin's ability to suppress hepatic glucose production [4-6].

Raised Serum Ferritin may possibly be related to the occurrence of long term complications of diabetes, both micro vascular and macro vascular [7, 8].

Hence this study was carried out to examine the relationship between serum ferritin and type 2 diabetes mellitus and metabolic syndrome and to establish a correlation between S. ferritin and FBS, HbA1c.

Material and Method

This retrospective study was done at index medical college hospital and research center, indore, m.p, india from june 2014 to November 2014. 100 type 2 diabetes patients who were treated on an outpatient department of medicine in our hospital were included in the study. Age and sex matched normal healthy controls were selected for the study.

Inclusion criteria

Diagnosed type 2 diabetes mellitus patients on treatment, in the age group-45-65 years.

Control: Healthy controls in the age group 45-65 years

Exclusion criteria

Overt thyroid dysfunction
Chronic kidney disease
Chronic liver disease
On corticosteroid therapy

Data collection

A detailed proforma was filled up for each patient which included age, sex, past history of coronary artery disease, cerebrovascular accident, history of hypertension. The age of onset and duration of diabetes was recorded. As also recorded was whether the patient was treated with oral hypoglycemic

agents or insulin or whether the patient was on diet control alone.

Laboratory parameters including Serum ferritin, Hemoglobin, ESR, fasting and postprandial blood sugar(FBS,PP2BS), glycosylated hemoglobin(HbA1C), renal function tests, liver function tests, serum total cholesterol, serum triglycerides, LDL cholesterol, HDL cholesterol were estimated.

Blood was collected from patients after an overnight (10 hr) fasting and 2 hr postprandial (after a breakfast meal).

Data obtained was analyzed statistically by calculation online student t-test calculator. P-value <0.05 was considered as a significant.

Results

Majority of the patients with diabetes were male (64% vs. 36%). The mean age group of patients with diabetes was 54.5±8.5 years and that of the controls is 52.5±9.1 years. 28 % of the patients in the cases group had a past history of coronary artery disease or cerebrovascular accident compared to 7 % of the controls. Systemic hypertension was seen to be significantly higher in the cases (33% of the cases and 12% of the controls were hypertensive,). The age of onset of diabetes in 80% of patients was between 45 and 50 years. The duration of diabetes was between 5-10 years in 68% and more than 10 years in 32%. 72% of the patients were on oral hypoglycemic agents and 28% were on insulin. The lipid profiles showed significantly higher levels of total cholesterol (p<0.05) and serum triglyceride (p<0.01) in the cases compared to the controls. The HDL, LDL cholesterol levels were not significantly different in the two groups. [Table 1, 2]

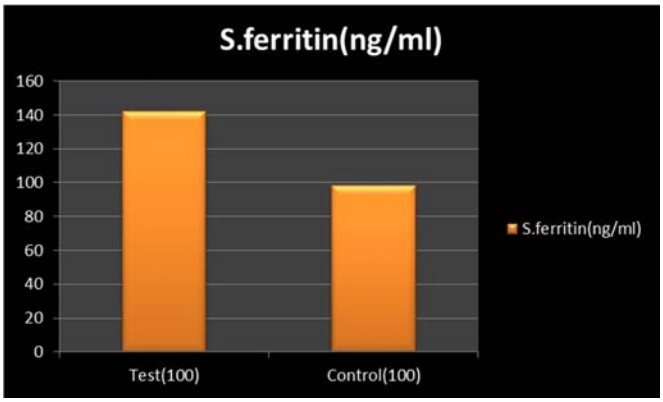
Serum ferritin was significantly higher in the cases (p<0.01) when compared to controls. Serum ferritin was significantly related to the duration of diabetes (p<0.05). As the duration of diabetes increased, serum ferritin also increased. There was a positive correlation between serum ferritin and FBS, HbA1c. Serum ferritin is significantly related to FBS (p<0.01) in cases. Serum ferritin is also significantly related to HbA1c (p<0.05). [Table 2].

Table 1: Age wise comparisons of participant

Group	Age Group(yr)	Number of participant(n)	Mean Age(yr)
Test (Diabetic)	45-65	100	54.5±8.5
Control	45-65	100	52.5±9.1

Table 2: Comparision of various biochemical parameter between diabetic and control group

Parameter	Number of participant(n)	Test Group(Mean SD)	Control(Mean SD)	P-value
Fasting Blood sugar(mg/dl)	100	156±8.3	102±9.5	<0.01(S)
T.cholesterol(mg/dl)	100	240±13.5	170.9±8.3	<0.01(S)
S.HDL(mg/dl)	100	45±6.2	47±11.2	>0.01(NS)
S.Triglyceride(mg/dl)	100	170±11.9	94±6.9	<0.01(S)
S.LDL(mg/dl)	100	141±14.9	139±16.2	>0.01(NS)
S.Ferritin(ng/ml)	100	142±16.2	98.3±10.5	<0.01(S)
HbA1c(%)	100	8.4±1.2	5.3±0.9	<0.01(S)



Graph 1: Graphical presentation of S. ferritin (ng/ml) concentration between test and control group

Discussion

The study population consisted of predominant male diabetics with mean age of 54.3 years. Most of the patients were on oral hypoglycemic agents. Only about 10 % of patients were untreated.

Serum ferritin, a reflector of body iron stores was significantly higher in diabetic patients when compared to controls and this significantly increased as duration of diabetes increased. This possibly reflects the subclinical hemochromatosis developing in a long standing diabetic patient [9]. Fernandez *et al* [10]. In their studies concluded that increased body iron stores are possibly associated with occurrence of glucose intolerance, type-2 diabetes and gestational diabetes.

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* [11] 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* [12].

Our study showed no correlation between serum ferritin and BMI and with metabolic syndrome in diabetic patients. There was also no correlation between S. ferritin and age, sex, coexistent hypertension, total cholesterol, LDL and serum triglycerides. Metabolic syndrome or syndrome X are terms used to describe constellation of metabolic derangements that include insulin resistance, hypertension, dyslipidemia with low HDL and elevated triglycerides, obesity, type 2 diabetes mellitus and accelerated cardiovascular disease. Iron stores expressed as serum ferritin concentration, have been proposed as component of insulin resistance syndrome.

Conclusion

There was a positive correlation between serum ferritin and FBS, HbA1c. There was no correlation between serum ferritin

and age, sex, metabolic syndrome, coexistent hypertension, total cholesterol, LDL and serum triglycerides.

To conclude, the major issue arises whether to estimate S. ferritin routinely in all type 2 diabetes patients and whether to set a cutoff value of serum ferritin for good glycaemic control. Though our study is a pointer in this direction, we would recommend further studies in this path for setting up specific guidelines.

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