

Association of Serum Ferritin Levels with Glycemic Control in type-2 Diabetes Mellitus

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ABSTRACT

Submitted: 18-03-2014

Accepted: 29-03-2014

Several recent studies concluded that, serum ferritin was found to be high in uncontrolled type 2 diabetic patients. There is paucity of information regarding association of serum ferritin levels with glycemic control in type 2 diabetic patients in India. This study was undertaken to identify the serum ferritin levels in poorly controlled type 2 diabetic patients and in well controlled type 2 diabetic patients taken as controls. The case control study was conducted and compared serum ferritin levels in 50 poorly controlled type 2 diabetics with 50 well controlled type 2 diabetics as controls. Chi square, Student t-test, Pearson correlation and Fisher exact test were used for statistical analysis. There was statistically significant ($p < 0.001$) elevation of serum ferritin levels (of about 66%) in poorly controlled type 2 diabetics compared to control group (4%). The elevation of serum ferritin levels in poorly controlled diabetics compared to control group and it was statistically significant ($p < 0.001$). Additional observations showed the positive correlation of serum ferritin levels with fasting blood sugar, post prandial blood sugar, and glycosylated hemoglobin and body mass index. The study shows positive association of serum ferritin levels with glycemic control in Type 2 Diabetic patients.

Keywords: Diabetes mellitus, Glycemic control, Glycosylated haemoglobin, Fasting blood sugar, Post prandial blood sugar, Serum ferritin, Type 2 DM

INTRODUCTION

Diabetes Mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of Diabetes Mellitus, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization and increased glucose production.¹ It is a disease of epidemic proportions. Although increase in both the prevalence and incidence of type 2 diabetes have occurred globally, they have been especially dramatic in societies in economic transition, in newly industrialized countries and in developing countries.²

Excessive iron accumulation can induce organic damage that leads to diabetes. 50% of transfusion treated thalassemia patients have an abnormal glucose tolerance³ and up to 65% of hereditary hemochromatosis patients develop diabetes mellitus.⁴ Several recent studies found that, high serum ferritin levels in uncontrolled Type 2 Diabetic patients and it has been shown that lowering elevated serum ferritin levels correlated well with diabetic control and improved fasting plasma glucose and glycosylated hemoglobin.⁵ It has been suggested that serum ferritin could be a marker of Insulin resistance syndrome.⁶

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There is paucity of information regarding association of serum ferritin levels with glycemic control in type 2 diabetic patients in India. Hence the present study was undertaken to study the serum ferritin levels in poorly controlled type 2 diabetic patients and in well controlled type 2 diabetic patients taken as controls.

METHODOLOGY

MATERIALS AND METHODS

The study was conducted at a tertiary care teaching Hospital, Bangalore, for a period of two years. The 50 patients who have fulfilled study criteria and diagnosed to have poorly controlled type 2 diabetes mellitus with glycosylated haemoglobin more than 8% were included in the study. 50 patients who were well controlled type 2 diabetics with glycosylated haemoglobin less than 6.5% were taken as controls. Sample size estimation was done and all the patients were evaluated by following parameters like detailed clinical history, general physical and systemic examination, evaluation of diabetic control by fasting blood glucose, post prandial blood glucose and glycosylated haemoglobin and detailed case report form was completed in each case documenting the information regarding all parameters from the cases and controls.

Diagnosis of Type 2 Diabetes Mellitus was made by taking detailed history, thorough general physical, systemic examination and blood glucose levels according to American Diabetic Association guidelines (ADA).⁷

After the fasting and post prandial sugars were done, patients were deemed to have diabetes as per the American Diabetic Association criteria. Further, the diabetes was said to be uncontrolled if glycosylated haemoglobin was more than 8% as per the Diabetes Control and Complications Trial (DCCT) recommendations.

In the control group, the diabetes status was said to be well controlled if Glycosylated Haemoglobin was less than 6.5%.

Serum ferritin was estimated in all cases and controls by Radioimmunoassay method. Mouse monoclonal antibodies directed against two different epitopes of ferritin molecule. The samples of calibrators are incubated in tubes coated with the first monoclonal antibody in the presence of the second monoclonal antibody labeled with iodine 125. After incubation, the content of tubes is aspirated and the tubes are rinsed so as to remove unbound ¹²⁵I-labeled antibody. The bound radioactivity is then determined in a gamma counter. The ferritin concentrations in the samples are obtained by interpolation from the standard curve. The concentration of ferritin in the samples is directly proportional to the radioactivity.

10 ml of venous blood sample collected from both the cases and controls and centrifuged to separate the serum and stored at 2-8 degree centigrade.

The Statistical software's SPSS 11.0 and Systat 8.0 were used for the analysis of the data.

RESULTS

50 patients diagnosed to have poorly controlled type 2 diabetes mellitus were studied along with 50 age matched well controlled type 2 diabetics as controls.

Age in years	TEST (Poorly controlled)		CONTROL (well controlled)	
	No	%	No	%
	≤40	5	10.0	5
41-50	20	40.0	21	42.0
51-60	23	46.0	22	44.0
>60	2	4.0	2	4.0
Total	50	100.0	50	100.0

Majority of patients were in the age group of 41-60 years in both test as well as control group

Sex	TEST		CONTROL	
	No	%	No	%
Male	31	62.0	30	60.0
Female	19	38.0	20	40.0
Total	50	100.0	50	100.0

S. Ferritin	TEST		CONTROL	
	No	%	No	%
Normal	17	34.0	48	96.0
Elevated	33	66.0	24.0	
Total	50	50.0	50	50.0

Inference: Of 50 patients of poorly controlled Type 2 Diabetes Mellitus, 33 (66%) patients had elevated Serum ferritin which was statically significant (p <0.001) and in 17 (34%) patient's serum ferritin levels were within normal range.

Of 50 patients in control group, only 2 (4%) patients had elevated serum Ferritin and in 48 (96%) patient's serum ferritin levels were within normal range.

Parameters	Type 2 DM (Mean±SD)				
	TEST		CONTROL		P value
	Range	Mean±SD	Range	Mean±SD	
S.FERRITIN	26-720	392.80±175.57	14-398	91.26±11.69	<0.001**
Log S.FERRITIN	1.41-2.86	2.52±0.30	1.15-2.60	1.81±0.05	<0.001**

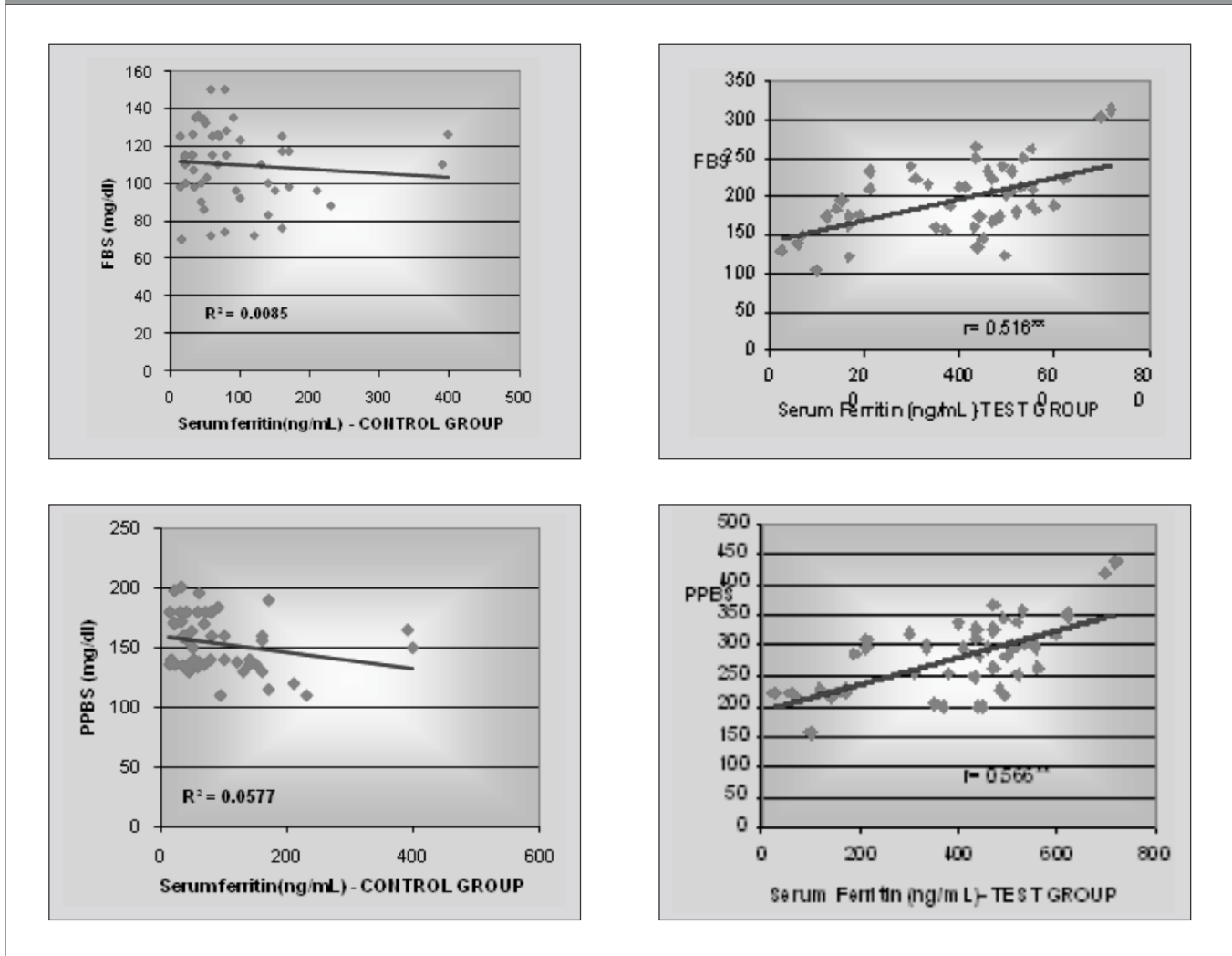
There was statically significant association (p <0.001) between elevated serum Ferritin levels and poorly controlled type 2 Diabetics.

Parameters	Type 2 DM				
	TEST		CONTROL		P value
	Range	Mean±SD	Range	Mean±SD	
BMI	20.55-38.58	28.96±4.39	15.97-44.85	27.05±5.43	0.052+
FBS	105-314	196.18±44.49	70-150	109.88±20.22	<0.001**
PPBS	156-439	273.76±58.95	110-201	153.92±23.52	<0.001**
HBA1C	8.10-13.80	9.60±1.44	5.10-6.40	6.00±0.35	<0.001**

Parameters	Type II DM	
	TEST GROUP	CONTROL GROUP
Age vs S.FERRITIN	-0.023(0.872)	-0.027(0.856)
BMI vs S.FERRITIN	0.133(0.352)	0.082(0.572)
FBS vs S.FERRITIN	0.516**(0.001)	-0.093(0.522)
PPBS vs S.FERRITIN	0.566**(0.001)	-0.296(0.037)

There was no statistical association between serum ferritin levels and age, however there was statistically significant association between serum ferritin levels and fasting blood sugar (FBS), post prandial blood sugar (PPBS) as well as Body mass index (BMI).

Fig. 1: Pearson correlation of serum Ferritin with age, BMI, FBS and PPBS parameters



DISCUSSION

The elevation of serum ferritin levels in poorly controlled type 2 diabetics (study group or test group) is statistically significant ($P < 0.001$) compared to well controlled type 2 diabetics as controls. In poorly controlled type 2 diabetics 66% of patients had elevated serum ferritin level compared to only 4% in control group.

Our finding was consistent with the study done by Canturk Z, Cetinarslan B, Tarkun et al.⁶ They evaluated the association between serum ferritin concentration and nature of type 2 diabetes mellitus and examined association of serum ferritin concentration, fasting and post prandial blood glucose levels and glycosylated hemoglobin in 329 patients with type 2 diabetes mellitus and 269 healthy controls, confirmed that serum ferritin was increased in type 2 diabetic patients as long as glycemic control was not achieved and concluded that there was independent positive association between serum ferritin concentration and markers of glucose homeostasis.

Similar findings were also observed by Paul Cutler³ about 50% of patients with poorly controlled type 2 diabetes mellitus had elevated serum ferritin levels, further went on to investigate if decreasing the high ferritin levels with Desferoxamine given as 10 mg/kg I/V for 5-13 weeks would control diabetes and found that decreasing ferritin correlated well with diabetes control and improved FBS and HbA1c in 8 of 9 patients with high ferritin levels.

However, Cutler's observations were refuted by JB REDMON, Kathryn L, Pyzdrowski et al⁵ studied 9 individuals with type 2 Diabetes Mellitus and elevated serum ferritin levels. Patients were given twice weekly Desferoxamine (DFO) infusion. Although 8 out of 9 subjects achieved normal or near normal serum ferritin levels after Desferoxamine and found little evidence that it produced beneficial effects on glycemic control. FBS levels pre and post Desferoxamine therapy were unchanged, HbA1c levels declined slightly after Desferoxamine therapy; however, this effect was small

and was not associated with elimination or even substantial reduction in insulin or Oral hypoglycemic therapy.

In this study, we found that serum ferritin had a positive statistically significant correlation with FBS, PPBS, HBA1C and also positively correlated with BMI. These findings were consistent with study done by Nan Hee Kim, Jung Heon Oh et al.⁸ They found that the value of log Ferritin was higher in type 2 diabetes mellitus patients than the control subjects. Log ferritin correlated with FBS level and Body mass index (BMI).

Similarly, other studies done by Yan Ren, HaomingTian et al⁹ and TomiPekkaTuomainen et al¹⁰ showed an independent positive association exists between S.Ferritin concentration and FBS, PPBS, HBA1C and BMI.

The effect of lowering S.Ferritin levels on metabolic control of type 2 diabetes mellitus was studied by Cutler by giving Desferoxamine who reported that it resulted in decrease in HBA1C in patients with poorly controlled type 2 Diabetes Mellitus. But, this was contradicted by J.B.Redmon, Pyzdrowski et al,found no such benefit by decreasing S.Ferritin levels. However, our study did not attempt to look into this particular aspect.

According to the observations made in this study, it is evident that positive correlation exists between serum ferritin levels and glycemic control. This highlights the need for strict glycemic control in these subjects. It would be interesting to assess if decreasing serum ferritin levels would help in glycemic control in such subjects, which provides scope for future research.

CONCLUSION

To conclude, in this case control study involving 50 poorly controlled type 2 diabetic patients with equal number of controls

- Serum Ferritin was found to be significantly elevated ($p < 0.001$) in 66% of the patients with poor glycemic control.
- Serum Ferritin also positively correlated with fasting blood sugar, post prandial blood sugar, glycosylated hemoglobin and Body mass index.
- This study shows positive association of Serum Ferritin levels with glycemic control.

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