Research Article

Correlation between serum ferritin and glycaemic control in patients of type 2 diabetes mellitus: a case control study

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ABSTRACT

Background: Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Ferritin is a ubiquitous intracellular protein complex that reflectes the iron stores of the body. Many cross-sectional studies indicate that increased body iron stores have been associated with the development of glucose intolerance, type 2 diabetes, metabolic syndrome. This study was carried out to find out the relationship between serum ferritin and type 2 diabetes and to see the influence of body iron stores on HbA1c and blood glucose.
Methods: This study includes 50 patients suffering from type 2 diabetes and compared with controls at Sir T hospital, Bhavnagar. S. ferritin, Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS) and HbA1c were measured.
Results: Serum ferritin was significantly higher ($p<0.0001$) in the patients suffering from type 2 diabetes and the correlation between serum ferritin and HbA1c was positive. Patients with type 2 diabetes with increased level of serum ferritin had poor glycemic control reflected by increased levels of HBA1c ($r=0.701$, $p<0.0001$)
Conclusions: There is a positive association between elevated iron stores measured by serum ferritin levels and type 2 diabetes mellitus. Ferritin levels also correlated FBS, PP2BS and HbA1c.

Keywords: Type 2 diabetes mellitus, Ferritin, HbA1c

INTRODUCTION

Diabetes Mellitus (DM) is a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of diabetes mellitus, factors contributing hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.[1]

Measurement of glycated proteins primarily HbA1c (glycated hemoglobin) is effective in monitoring long-term glucose control in people with diabetes mellitus.[2]

Chronic hyperglycemia causes increased glycation of protein including hemoglobin resulting in the formation of Advanced Glycated End products (AGE).[3]

It has been suggested that in the diabetic patients a positive correlation between increased serum ferritin and poor glycaemic control reflected by higher HbA1c.[4]

Increased ferritin 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.[5]

It's also observed that ferritin levels correlated with individual components of the metabolic syndrome particularly serum triglycerides and plasma glucose as well as markers of insulin resistance.[6]

Thus present study is designed to evaluate the correlation between serum ferritin and glycaemic control in patients of type 2 diabetes mellitus which will help to understand the significance of ferritin for the better management of type 2 diabetes mellitus.

METHODS

The study was designed as a case control study. The study was conducted over a period of one year from July 2012 to June 2013. In the present study 50 cases of known type 2 diabetes mellitus and 50 apparently healthy subjects as a control group were studied. They were primarily diagnosed by clinical examination and further evaluated by biochemical investigations.

All cases were selected from the patients attending diabetic clinic at Sir T. General Hospital, Bhavnagar and the control subjects were selected randomly. Informed consent was taken from all the participants. The study was reviewed and approved by the human ethics committee of Govt. Medical College, Bhavnagar.

To find out the influence of body iron stores on various biochemical parameters diabetics underwent the following investigations: Serum Ferritin (SF) levels, fasting, postprandal blood glucose, glycosylated Hb levels using standard methods at NABL accredited clinical biochemistry section, Sir T Hospital, Bhavnagar

In data analysis, comparison of all parameters between control and study group was carried out by applying unpaired t-test and correlation of ferritin with other parameters were also studied by applying Pearson correlation test.

RESULTS

In the present study the Mean ± SD of age in study group was 49.58 ± 8.82 years as compared to 46.98 ± 8.977 in control group. The male:female ratio in study group patient was 1.08:1.

Table 1 shows the comparison of FBS, PP2BS, HbA1c and ferritin in study and control group. As per Table 1 values of FBS, PP2BS, HbA1c and Ferritin are significantly higher ($p<0.0001$) in the cases compared to the controls.

Table 2 shows that levels of serum ferritin were positively correlated with values of FBS (r=0.600, $p<0.0001$), PP2BS (r=0.526, $p<0.0001$), HbA1c (r=0.701, $p<0.0001$).

Table 1: Comparison of biochemical parameters between study & control group.

Parameter	Biological reference interval	Study			Control			Significance
		Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD	
FBS	70-100 mg/dl	109.0	554.0	218.5 ± 96.15	76.0	99.0	87.88 ± 5.989	t=9.585 **$p<0.0001$
PP2BS	80-140 mg/dl	136	570.0	260.0 ± 95.37	88.0	125.0	105.5 ± 9.83	t=11.40 **$p<0.0001$
HbA1c	<7.0 %	5.0	13.0	8.308 ± 1.971	3.80	5.40	4.272 ± 0.3839	t=14.21 **$p<0.0001$
Ferritin	M - 30-220 ng/ml F - 20-110 ng/ml	20.0	716.0	319.7 ± 133.6	23.0	134.0	67.40 ± 30.53	t=13.02 **$p<0.0001$

Note: *$p<0.05$ – significant; **$p<0.001$ - highly significant; #$p\geq0.05$ - not significant

Table 2: Correlation of serum ferritin with other biochemical parameters in study group.

Ferritin (319.7 ± 133.6) compared to other parameter		Two tailed p value	Pearson coefficient (r)	Significance
Name of parameter	Mean value			
FBS	218.5 ± 96.15	$p<0.00001$	0.600	Yes
PP2BS	260.0 ± 95.37	$p<0.0001$	0.526	Yes
HbA1c	8.154 ± 2.00	$p<0.0001$	0.701	Yes

Figure 1, 2 and 3 shows the positive correlation between Ferritin and FBS, PP2BS and HbA1c respectively.
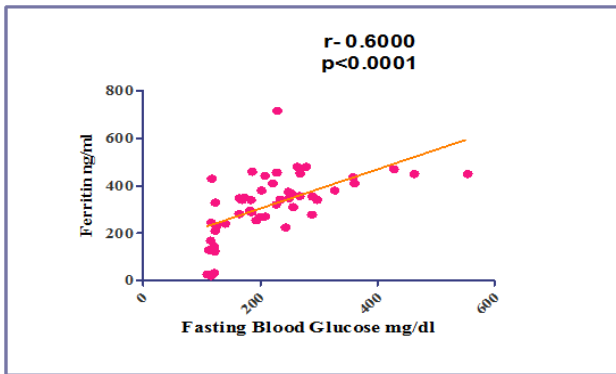

Figure 1: Relationship between ferritin and fasting blood glucose in study group.
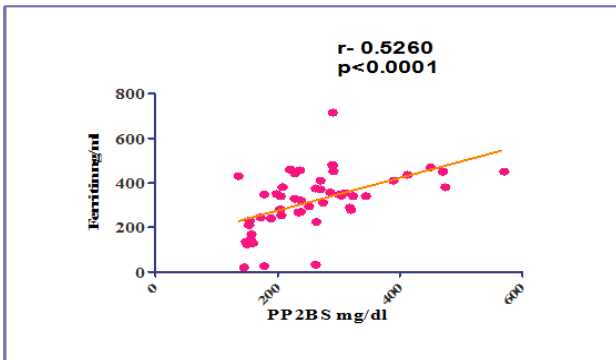

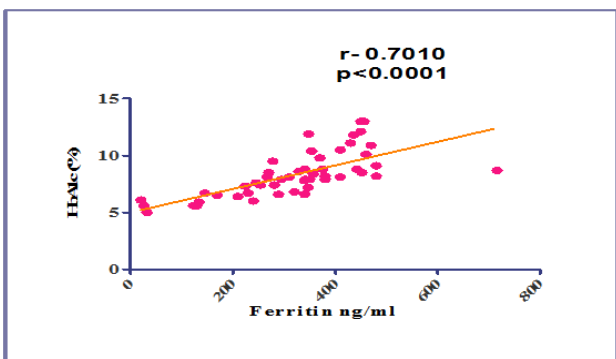**Figure 2: Relationship between ferritin and PP2BS in study group.**

Figure 3: Relationship between ferritin and HbA1c in study group.

DISCUSSION

It's obvious evident from the study that increased body iron stores reflected by SF levels had a statistically significant directly proportional correlation with FBS, PP2BS and HbA1c.

There is an increasing concern about the relationship between iron stores and type 2 diabetes with evidence that moderately elevated body iron stores below levels commonly found in genetic hemochromatosis may be associated with adverse health outcomes. Elevated serum ferritin levels were independently predicted incident of type 2 diabetes in prospective studies among apparently healthy men and women.[6]

Ferritin is an iron-phosphorus-protein complex that is a biomarker for evaluating body iron contents. Tissue and organ damage occurs when iron concentrations are elevated.[7] Increased accumulation of iron affects insulin synthesis and its secretion from the pancreas and interferes with the insulin-extracting capacity of the liver. Iron deposition in muscle decreases glucose uptake because of muscle damage.

Conversely, insulin stimulates cellular iron uptake through increased transferring receptor externalization. Thus, insulin and iron can mutually potentiate their effects leading after a vicious cycle to insulin resistance and diabetes.[8]

In the present study, ferritin levels were significantly higher in patients of type 2 DM (319.7 ± 133.6 vs. 67.40 ± 30.53 ng/ml, p<0.0001) as compared to controls (Table 1) which were consistent with the reports published by F. Sharifi and colleagues. They concluded that the ferritin (101 ± 73 mg/ml vs. 43.5 ± 42 mg/ml, p<0.001) were significantly higher in patients of type 2 diabetes as compared to control subjects.[9]

Our findings are in agreement to by Rui Jiang among type 2 DM cases who reported the mean concentration of Ferritin were significantly higher in study group as compared to control subjects.[10]

It's evident from the study that ferritin levels were positively correlated with FBS, PP2BS and HbA1c. Similar study conducted by Sumeet Smotra et al.[11] and Jeevan K. Shetty et al.[12] found increased levels of Serum Ferritin and also reported that diabetics with increased level of Serum Ferritin had significantly poor glycaemic control reflected by higher levels of HbA1c as compared to diabetes cases under good glycaemic control and healthy controls.

Positive correlation between FBS and HbA1c as well as ferritin and HBA1c indicates hyperglycemia causing increased glycation of hemoglobin and increased release of free iron from glycated proteins like hemoglobin. This makes a vicious cycle of hyperglycemia, glycation of hemoglobin and increase in levels of free iron and ferritin. This increased presence of iron pool will enhance oxidant generation leading damage to biomolecules.[12]

CONCLUSION

Our findings suggest that iron overload reflected by increased SF levels has the potential role in the development of type 2 diabetes. Therefore, in agreement

with previous studies we suggest that serum ferritin should be included in standard screening protocol to identify patients who are at risk of developing type 2 DM and also to assess the glyacemic control in patients who have already developed the disease.

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