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Original Research Article

Association of Serum Ferritin in Type 2 Diabetes Mellitus Patients- An Observational Study

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Abstract

Introduction: Serum ferritin and iron load are proposed to be having significant role in etiopathogenesis of type 2 diabetes mellitus. Our study intends to determine the association of serum ferritin levels in type 2 diabetics of South Indian origin.

Methodology: Consecutive type 2 diabetic patients attending medicine op department of a tertiary care centre between the age group of 40 to 70 years are included in the study. The data regarding clinical history, physical investigation and relevant biochemical investigations including HbA1c, Serum Ferritin, Fasting blood sugars were collected of the study population using pre validated questionnaire.

Results: 150 patients were studied with mean duration of diabetes of 6.69 ± 3.63 years were included in the study. Mean HbA1c and serum ferritin levels of study population were 8.84 ± 1.68 and 159.40 ± 84.72 respectively. HbA1c, fasting blood sugar and serum triglyceride values had statistically significant correction with serum ferritin levels whereas there was no significant correlation noted with duration of diabetes. A simple linear regression showed that patients' average HbA1c level increased 0.01 % for every 1ng/ml rise in serum ferritin value.

Conclusion: Study shows that serum ferritin is having strong correlation with HbA1c levels and is a good marker of overall diabetic control.

Keywords: Type 2 Diabetes Mellitus, Ferritin, Hba1c, Iron.

Introduction

Type 2 diabetes mellitus is one of the most common non communicable diseases which causes significant morbidity and mortality worldwide. The pathogenesis of Type 2 diabetes mellitus is complex and multifactorial, and many theories have been proposed to explain its etiopathogenesis. Recent evidence suggests that iron and serum ferritin may have a role in the pathogenesis of type 2 diabetes mellitus.

Iron is a strong pro-oxidant and high body iron levels are associated with increased levels of oxidative stress that may elevate the risk of developing type 2 diabetes. Many epidemiological studies have reported a positive association between high body iron stores, as measured by circulating ferritin level, and the risk of type 2 diabetes and insulin resistant state such as metabolic syndrome[1,2,3,4]. Serum

ferritin is routinely measured to assess the status of iron storage but it is not a specific marker of iron storage and many additional factors including inflammation, infection and malignancies can elevate serum ferritin levels. Whether elevated serum ferritin levels have potential to precipitate type 2 diabetes in itself or whether high serum ferritin levels indicate underlying chronic inflammation associated with Type 2 diabetes mellitus is highly debated.

The relationship of serum ferritin levels with various clinical and biochemical parameters of type 2 Diabetes mellitus including glycemic control and diabetic complications are still not clear. Studies in this regard are limited in our population. This study was conducted to determine the association of serum ferritin levels with clinical and biochemical parameters of type 2 diabetics in South Indian population.

Methodology:

This was a cross sectional observational study conducted in a tertiary care academic institution in North Kerala for a period of one year. All consecutive patients with type 2 diabetes mellitus of age group between 40-70 years attending medicine outpatient department during the one-year study period were included in the study. Patients with anemia of any cause, chronic infections, pregnancy, chronic kidney disease, chronic liver disease and those on long term corticosteroids were excluded from the study. Ethical clearance was obtained from the institutional ethical committee and informed written consent was taken from all the study subjects before data collection. Data was collected using a pre-validated proforma containing detailed clinical history, physical examination and relevant blood investigations. Body mass index was calculated from height (in meters) and weight (in Kg) measurements using standard weighing machine and measuring tape. Blood investigations done included Serum Ferritin, HbA1c, fasting blood sugar and fasting lipid profile. Blood samples for biochemical investigations were done during the initial OP visit. Measurement principle of HBA1c was turbidimetric immunoinhibition using the Beckman Coulter–AU5800 machine. Measurement principle of Ferritin was chemiluminescence immunoassay using Cobas e411 machine.

Statistical analysis:

Data entry and coding was done using Microsoft Excel 2007 and analyzed by PSPP open-source statistical software. Descriptive data was represented using frequency, percentages, mean and standard deviation. For data analysis Pearson correlation coefficient, ANOVA and linear regression methods were used appropriately. P value <0.05 was considered as cut off for statistical significance for all analytical tests. Scatter plots were drawn using R programming software.

Results:

The study was conducted in a tertiary care academic institution in North Kerala. 150 consecutive patients attending medicine OP department during the study period satisfying the inclusion and exclusion criteria were included in the study. Mean age of the study population was 54.74 ± 8.59 years. 63.33% (95) of the study population were males and rest 36.67% (55) were females. Mean duration of diabetes among them was 6.69 ± 3.63 years. 31.33 % (47) of them were hypertensive and 24% (36) were overweight **(Table 1)**.

Table 1: Baseline characteristics of the study population

Variable	Frequency (N=150)	Percentage
Gender		
Male	95	63.33
Female	55	36.67
Duration of diabetes		
< 5 years	61	40.67
6-10 years	66	44.00
> 10 years	23	15.33
BMI category		
Under weight	7	4.67
Normal weight	107	71.33
Overweight	31	20.67
Obese	5	3.33
BP category		
Normotensive	49	32.67
Pre hypertensive	54	36.00
Hypertensive	47	31.33

Table 2: Mean values of biochemical parameters of the study population

Variable	Mean	Std Deviation	Minimum	Maximum
Ferritin	159.40	84.72	10.07	693.40
FBS	161.83	52.07	73.00	359.00
HbA1C	8.84	1.68	6.50	13.30
S Cholesterol	194.04	45.89	110.00	391.00
Triglyceride	147.95	84.10	49.00	524.00
LDL	114.39	31.42	52.00	273.00

A one-way ANOVA was performed to compare the effect of BMI category on serum ferritin levels. It revealed that there was a statistically significant difference in mean serum ferritin level between at least two BMI categories ($F(3,146) = 3.06$, $p = 0.03$). Tukey's HSD Test for multiple comparisons found that the mean value of serum ferritin was significantly different between overweight and obese category ($p = 0.024$, 95% CI [11.0, 218.94]). There was no statistically significant difference between ferritin values of other BMI categories.

A Pearson correlation coefficient was computed to assess the linear relationship between duration of diabetes and serum ferritin level. There was no statistically significant correlation between these two variables [$r(148) = 0.13$, $p = 0.108$] (Figure 1). Pearson correlation coefficients were computed to assess the linear relationship between various biochemical parameters namely FBS, HbA1C, Serum cholesterol, triglyceride, serum LDL and serum ferritin level. FBS [$r(148) = 0.43$, $p < 0.001$], HbA1C [$r(148) = 0.60$, $p < 0.001$] and triglyceride levels [$r(148) = 0.19$, $p = 0.018$] had statistically significant positive correlation with ferritin values (Figure 2). Whereas others like serum cholesterol and serum LDL did not show any significant correlation with serum ferritin levels.

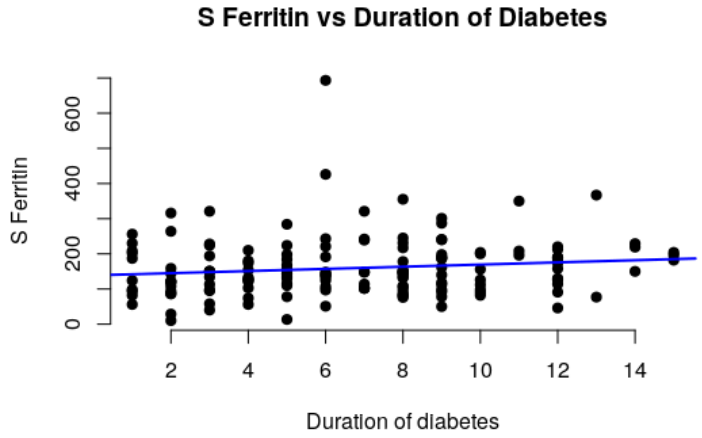

Figure 1: Scatter plot - Serum ferritin level vs Duration of diabetes

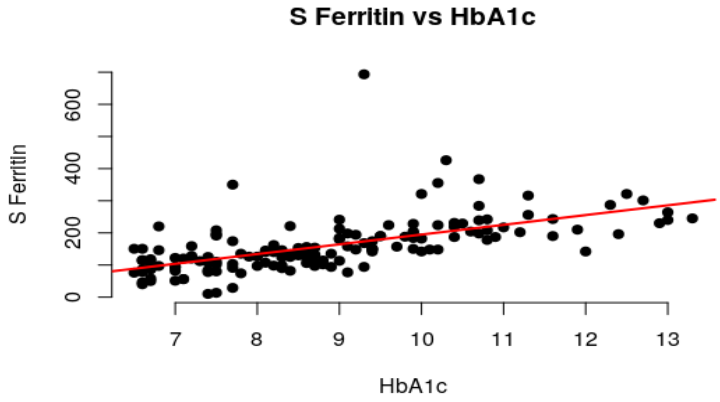

Figure 2: Scatter plot - Serum ferritin vs HbA1c levels

A simple linear regression was calculated to predict the patients HbA1c level based on their serum ferritin level. A significant regression equation was found (F (1,148) =83.85, p<0.001), with an R^2 of 0.36. Patient's predicted HbA1c is equal to 6.94+ 0.01(Ferritin) % when ferritin is measured in ng/ml. Patients' average HbA1c level increased 0.01 % for every 1ng/ml rise in serum Ferritin value.

Discussion:

There are only limited studies looking into the association of serum ferritin in diabetic population from Indian population. This study was conducted in one hundred and fifty South Indian Type 2 diabetic patients. The study population had an average serum ferritin level of 159.40 ± 84.72 ng/ml with a range from 10.07 to 693.40 ng/ml. In a study conducted by Pankaj Bansal et al in 200 North Indian male diabetic patients aged 35-65 years and age & sex matched healthy controls; serum ferritin values were significantly increased in type 2 diabetic patients compared to the control group 185 ± 3.5 ng/ml & 113 ± 4.6 ng/ml, respectively[5]. In a study conducted by Borah M et al in 92 Type 2 diabetic patients of a North eastern state of India, the mean level of serum ferritin in diabetic cases were found to be 150.35±74.43 ng/mL and in age and gender matched healthy group it was found to be 47.42±21.71 ng/ml[6].

Studies from other populations also revealed that serum ferritin levels were elevated in patients with Type 2 diabetes mellitus[7]. In our study population also serum ferritin levels were comparable to previous studies and ferritin levels were higher in our diabetic patients.

In this study a statistically significant correlation exists between fasting plasma glucose and HbA1c with serum ferritin levels. Poor glycemic control was strongly associated with higher ferritin values. A linear regression analysis for prediction of HbA1c value from serum ferritin level showed a significant regression equation predicting 0.01 % rise in HbA1c for every 1 ng/ml rise in serum ferritin value. These finding were also evident in previous studies; Ali Momeni et al conducted a quasi-experimental study in 67 patients with type 2 diabetes serum ferritin, Fasting Blood Sugar (FBS), post prandial sugar and glycosylated Hemoglobin level (HbA1c) were checked before and 3 months after the control of hyperglycemia and hyperlipidemia. Mean serum ferritin, before and after the control of hyperglycemia were 115 ± 109.4 ng/mL and 91.4 ± 61.9 ng/mL. Serum ferritin significantly decreased after 3 months follow-up, indicating that serum ferritin decreased with reducing serum FBS and post-prandial sugar levels[8].

These findings suggest that better glycemic control may reduce serum ferritin levels in diabetic patients. Apart from diabetic control we also analyzed the correlation between duration of diabetes and serum ferritin level. It was observed that duration of diabetes had no significant correlation with serum ferritin values and longer disease duration did not result in higher ferritin levels. Serum ferritin has more correlation with existing diabetic control and not to the duration of illness in this study. We also observed a significant difference between serum ferritin levels and different BMI categories. The ferritin level was having significant difference especially between overweight and obese individuals showing the importance of ferritin as an indicator of underlying insulin resistance syndrome. This was in accordance with previous studies which also showed significant rise in serum ferritin levels in patients with signs of insulin resistance[9].

The specific mechanisms that led to elevated ferritin levels in type 2 diabetic patients is still not well established. It is well accepted that chronic inflammatory conditions were associated with an increase in ferritin levels[10]. Inflammatory cytokines such as tumor necrosis factor-α and interleukin-6 have been detected in significant amounts in patients with either insulin resistance syndrome or diabetes[11-12]. So high ferritin levels observed in diabetic patients could reflect an inflammatory phenomenon as a part of chronic inflammation. Also the role of iron load in the development of type 2 diabetes also is postulated. Our study being a cross sectional design limited its ability to answer such an enquiry. But it clearly shows that higher serum ferritin is an indicator of poor glycaemic control and does not directly correlate with duration of disease. Rather high ferritin can be considered as an acute phase reactant in a patient with uncontrolled type 2 diabetes. This also means that such patients having higher ferritin levels may have higher probability of developing microvascular complication owing to the chronic inflammation and high oxidative stress. Further detailed prospective study may be required to ascertain the correlation of serum ferritin with diabetes and its complication.

Conclusion:

This study showed a strong positive correlation between serum ferritin and HbA1c levels. It points to the fact that serum ferritin level may be representative of overall diabetic control. There was also significant difference between serum

ferritin values of overweight and obese individuals. This shows that serum ferritin can be considered as an indicator of insulin resistance in patients with diabetes.

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