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Original Research Article

Association of glycated haemoglobin and serum ferritin levels in type 2 diabetics of rural population

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ABSTRACT

Background: Serum ferritin, an acute phase reactant, is an indicator of the body's iron reserves. Increased body iron reserves and subclinical hemochromatosis have been linked to the development of hyperglycaemia, type 2 diabetes, metabolic syndrome, and potentially diabetic retinopathy, nephropathy, and vascular dysfunction, according to recent research. The objective of this study was to see if there was a link between Serum Ferritin and Type 2 diabetes and metabolic syndrome, as well as to see if there was a link between S. ferritin and HbA1c.

Materials and Methods: The present study included 50 diagnosed cases of type 2 diabetes mellitus (males: 32, females: 18) and 50 healthy controls of same age (males: 28, females: 22). Serum ferritin levels, glycated hemoglobin were measured and compared.

Results: When diabetic patients were compared to controls, serum ferritin was considerably greater, and serum ferritin had a positive correlation with the duration of diabetes and glycated hemoglobin.

Conclusions: Positive correlation was found between serum ferritin levels and glycated hemoglobin and duration of disease.

1. Introduction

Diabetes mellitus, a chronic metabolic and endocrine condition that affects people all over the world, is a major public health concern in both developing and developed countries. Diabetes mellitus (DM), one of the most common endocrine disorders in the world, has now reached pandemic proportions worldwide. In this regard, India, a forerunner, has a very large number of diabetics and has won the dubious distinction of being the world's diabetes hub. 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.

However, with the discovery of new iron metabolism disorders, it is clear that iron overload, regardless of the aetiology, contributes to an increased occurrence of type 2 diabetes. a) An increased occurrence of type 2 diabetes due to various sources of iron overload, and b) a reversal or improvement of diabetes (glycemic control) with a decrease in iron load accomplished by phlebotomy or iron chelation therapy, suggest that iron plays a role in diabetes aetiology. The increased insulin sensitivity and secretion associated with regular blood donation, as well as lower iron levels, suggest that iron excess is a causal factor. [1,2]

Recent research has linked the onset of glucose intolerance, gestational diabetes, type 2 diabetes, and insulin resistance syndrome to increased body iron storage. [3–7]

Insulin resistance is the predominant symptom of type 2 diabetes, followed by a growing degree of -cell dysfunction. [8] Many people die as a result of DM

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complications.[9] The HbA1c percentage represents the average glucose levels during the previous 6 to 8 weeks.

In chronic diabetes patients, the HbA1c fraction is higher, and it correlates with glycemic control.[10] Insulin resistance, metabolic syndrome, and type 2 diabetes have all been linked to chronic systemic subclinical inflammation. Inflammation causes the creation of several acute phase proteins in the liver, including serum ferritin, which has a role in insulin resistance and atherosclerosis. High blood ferritin levels have been linked to an increased risk of type 2 diabetes. Insulin resistance is defined by elevated blood glucose and insulin levels, which are frequently caused by bodily iron excess, resulting in a rise in serum ferritin.[11,12] Elevated iron reserves can cause diabetes by a variety of processes, including oxidative damage to pancreatic beta cells, disruption of hepatic insulin extraction by the liver, and insulin suppression of hepatic glucose synthesis. Hepcidin affects iron metabolism; hepcidin induces excessive production of cytokines IL-6 in chronic inflammatory diseases, including type 2 diabetes mellitus, by directly activating hepatocytes.[13] Glycation of proteins, including haemoglobin, is enhanced in chronic hyperglycemia, culminating in the production of Advanced Glycated End Products (AGE).[14] It has been claimed that there is a link between elevated serum ferritin and poor glycemic control, as measured by greater HbA1c, in diabetes individuals.[15]

Raised serum ferritin may cause long-term microvascular and macrovascular problems in diabetics.[16] Iron is a transitional metal with high pro-oxidant activity, which results in the generation of reactive oxygen species, which raises oxidative stress levels.[17] It's uncertain what role ferritin plays as an iron overload marker in hyperglycemia caused by pancreatic injury or peripheral insulin resistance.[18] There are few research that indicate the optimal serum ferritin cut-off value in type 2 diabetes mellitus.

The aim of the current study was to assess long-term glycemic control (HbA1c) among subjects with type 2 diabetes mellitus and the correlation among HbA1c as well as serum ferritin levels which are responsible for diabetes mellitus complications.

2. Aim

To correlate Glycated Haemoglobin and serum Ferritin levels in Type 2 Diabetes Mellitus

3. Material and Methods

The present study was carried out at clinical biochemistry laboratory, Dept. of Biochemistry of a tertiary teaching hospital of Vidarbha region, India.

3.1. Study group

50 diagnosed patients of type 2 diabetes mellitus of duration more than 1 year, aged 30 years and above from Medicine indoor and outdoor will be recruited in the study.

Cut off values for Fasting Blood Sugar Level >126 mg/dl and Post Meal Blood Sugar > 200 mg/dl will be considered as diagnostic criteria.

Patients with history of Hypertension (HT), Obesity, Renal diseases, Liver disease, Valvular heart diseases, smoking, Family history of Diabetes will be excluded.

50 Healthy controls of same age will be included for comparison.

3.2. Study period

Study period will be for the duration of 6 months.

3.3. Study type

Case-control study.

3.4. Sample size

Cases: 50 newly diagnosed patients of type 2 diabetes mellitus

Control: 50 healthy controls of same age

3.5. Blood sample collection

5 ml (2.5 + 2.5 ml) random blood sample will be collected in dry plain and EDTA tubes for the estimation of Serum ferritin and Glycated haemoglobin levels simultaneously.

1. **Estimation of Serum Ferritin Levels:** It was done by roche cobas e411 analyzer with Electrochemiluminescence immunoassay (ECLIA).
2. **Estimation of Glycated Haemoglobin levels**: It was done by Vitros 5600 dry chemistry analyzer with Turbidimetric Inhibition Immuno Assay method.

3.6. Statistical analysis

Statistical analysis was done by using descriptive and inferential statistics using Student's unpaired t test and Pearson's correlation coefficient and software used in the analysis were SPSS 27.0 version and Graph Pad Prism 7.0 version and $p<0.05$ is considered as level of significance.

4. Results

Table 1 shows gender wise distribution of patients with 62% of the cases and 56% of the control were males and 36% of the cases & 44% of the controls were females.

As shown in Table 2 mean serum ferritin levels in cases was 535.28 ± 146.40 and in controls it was 182±99.94 by using students unpaired t test. Statistically significant difference was found. ($t=14.22$, $p=0.00015$).

Table 1: Gender wise distribution of patients

Gender	Cases	Controls
Male	32(64%)	28(56%)
Female	18(36%)	22(44%)
Total	50(100%)	50(100%)

Table 2: Comparison of serum ferritin level(μg/L) in two groups student's unpaired t test

Group	N	Mean	Std. Deviation	Std. Error Mean	t-value
Cases	50	535.28	146.40	20.70	14.22
Controls	50	182.00	96.94	13.71	P=0.0001,S

N= No of subjects, S= significant

As given in Table 3, it was found that serum Ferritin Levels (μg/L) were positively correlated with HbA1c Levels (%) (r=0280, p=0.049)

Table 3: Correlation between serum ferritin levels (μg/L) with HbA1c levels (%) Pearson's correlation coefficient

	Mean	Std. Deviation	N	Correlation 'r'	p-value
Sr. Ferritin Level	535.28	146.40	50	0.634	0.0001,S
HbA1c Level	6.59	0.44	50		

N= No of subjects, S= significant

As shown in Table 1, significant positive correlation was found between duration of type 2 diabetes mellitus and serum ferritin levels. (r = 0.280, p= 0.049)

Table 4: Correlation between serum ferritin levels (μg/L) with duration of diabetes in cases Pearson's correlation coefficient

	Mean	Std. Deviation	N	Correlation 'r'	p-value
Duration of diabetes	7.70	3.18	50	-	-
Sr. Ferritin Level	535.28	146.40	50	0.280	0.049,S

N= No of subjects, S= significant

5. Discussion

The majority of the diabetics in the study were men, with an average age of 49.3 years. The majority of the patients were on oral hypoglycemics. Only roughly 12% of the patients were left untreated.

When compared to controls, serum ferritin, a reflector of bodily iron reserves, was significantly higher in diabetic patients, and this increased dramatically as the duration of diabetes increased which is in consistence with our study. This could be due to the development of subclinical hemochromatosis in a diabetic patient with a prolonged history of diabetes.[19] Increased body iron reserves are likely connected with the incidence of glucose intolerance, type-2 diabetes, and gestational diabetes, according to Fernandez et al.[20]

HbA1c had a positive correlation with serum ferritin. This represented the short- and long-term relationship between serum ferritin and glycemic control. In their studies, Cantur KZ et al. confirmed that patients with poorly controlled diabetes exhibited hyperferritinemia.[21] This indicated that in diabetes, serum ferritin levels rose as long as glycemic control was not established. In addition, they discovered a link between ferritin levels and diabetic retinopathy. Eschwege et al. found a link between elevated serum ferritin and poor glycemic control, as measured by greater HbAIc, in diabetics.[22]

In diabetic patients, there was no link between serum ferritin and BMI or metabolic syndrome, according to our findings. S. ferritin had no relationship with age, sex, coexisting hypertension, total cholesterol, LDL, or serum triglycerides. Insulin resistance, hypertension, dyslipidemia with low HDL and elevated triglycerides, obesity, type 2 diabetes mellitus, and accelerated cardiovascular disease are all terms used to describe a cluster 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 reserves, as measured by serum ferritin levels, have been suggested as a determinant in insulin resistance. Serum ferritin levels are considerably higher in men and women with a high BMI (>25 kg/m2), high cholesterol (>200 mg/dl), and high systolic (>160 mmHg) blood pressure, in women with diabetes, and in men with high diastolic (>95 mmHg) blood pressure, according to Wrede et al.[23] This assertion is contradicted by our study.

6. Conclusion

Based on our results, it can be observed that serum ferritin levels were positively correlated with glycemic control of the patient. Serum ferritin levels can be used as one the control indices for patients of diabetes.

6.1. Need of the research in this field

Unfortunately, Serum ferritin levels are not done routinely in rural population of India. Anaemia is prevalent and recognized, and often there is dispensing of Iron and Folic Acid capsules openly and arbitrarily, irregardless of the hemoglobin status even by grass root level workers in persons with Type 2 DM pre-existing, which could hamper an already existing version of a critical situation if it leads to iron overload.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

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