Section: Miscellaneous

Original Research Article

ASSOCIATION OF SERUM FERRITIN WITH GLYCEMIC CONTROL AND LIPID PROFILE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Alterations in iron metabolism and oxidative stress have been involved in the pathogenesis of insulin resistance and Type 2 Diabetes Mellitus (T2DM). The aim of this study was to evaluate serum ferritin (SF) levels in patients with T2DM and to assess their association with HbA1c and lipid parameters. **Materials and Methods:** A cross-sectional study was conducted at the Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, Manipur, among 300 participants aged 30–60 years. The study included 270 patients with T2DM and 30 apparently healthy controls. Fasting venous blood samples were analyzed for serum ferritin using a chemiluminescence immunoassay, HbA1c using an ion-exchange resin method, and fasting lipid profile parameters using enzymatic methods. **Results:** Mean serum ferritin levels were significantly higher in patients with T2DM than in healthy controls (172.7 ± 117.9 ng/mL vs. 102.5 ± 75.4 ng/mL; $p = 0.013$). Mean HbA1c was significantly higher in patients with T2DM than in controls (9.33 ± 1.34% vs. 5.52 ± 0.7%; $p < 0.001$). Among patients with T2DM, serum ferritin showed a positive correlation with HbA1c ($r = 0.145$, $p = 0.017$). Serum ferritin was not significantly correlated with total cholesterol, triglycerides, or LDL-C, whereas a weak negative correlation was observed with HDL-C ($r = -0.135$, $p = 0.027$). **Conclusion:** Serum ferritin levels were significantly higher in patients with T2DM than in healthy controls. Among patients with T2DM, serum ferritin showed an association with HbA1c and HDL-C, while no significant correlations were observed with total cholesterol, triglycerides, or LDL-C. Further prospective studies are required to determine the clinical significance of serum ferritin in T2DM.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder with multiple genetic and environmental factors and a major global public health challenge.[1] India is facing a growing burden of T2DM, due to urbanization, sedentary lifestyle, and dietary changes.[2] T2DM is linked with significant morbidity and mortality because of microvascular complications such as retinopathy, nephropathy and neuropathy and macrovascular complications such as cardiovascular and cerebrovascular disease.[3] Chronic hyperglycemia in T2DM promotes the formation of advanced glycation end products (AGEs) and is often associated with atherogenic dyslipidemia characterized by hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C) and increased low-density lipoprotein cholesterol (LDL-C).[4] HbA1c is a well established biomarker of long term glycemic control and reflects the glycemic exposure over an average of 2–3 months.[5]

Changes in iron homeostasis have also been involved in the pathophysiology of T2DM.[6] Serum ferritin, an acute phase reactant and a measure of body iron stores, has been associated with glucose intolerance and insulin resistance.[7] Excess free iron may generate reactive oxygen species (ROS) and induce oxidative stress and cell injury.[8] These mechanisms have been involved in pancreatic beta-cell dysfunction and impaired insulin action. Several potential confounding factors complicate the

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interpretation of the association between serum ferritin and T2DM. Increased ferritin concentrations can be seen in the setting of systemic inflammation, obesity, metabolic syndrome, liver disease and other conditions.[9] Further studies are required to delineate the relationship of serum ferritin with glycemic control and lipid abnormalities.

Hence, the aim of this study was to evaluate serum ferritin levels in patients with T2DM and to assess its association with HbA1c and lipid profile parameters.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Departments of Biochemistry and Endocrinology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, Manipur from September 2017 to August 2019. The Institutional Ethics Committee of JNIMS approved the study and 300 participants were enrolled. The study population consisted of 270 patients with T2DM and 30 apparently healthy non-diabetic controls.

Inclusion criteria: Patients aged 30–60 years with T2DM diagnosed according to the American Diabetes Association criteria, who provided informed consent were included. Eligible participants included inpatients and outpatients. The exclusion criteria were patients with type 1 diabetes mellitus, hemoglobinopathies such as thalassemia, disorders of iron metabolism such as hemochromatosis, chronic organ disease, malignancy, acute infection or pregnancy. Patients on iron supplements, corticosteroids, antioxidants or thiazide diuretics were also excluded.

Diagnosis of T2DM was made based on the American Diabetes Association criteria.[10]

All participants underwent venous blood collection (5 mL) following fasting under aseptic conditions. Serum ferritin: Serum ferritin was measured by sandwich chemiluminescence immunoassay on the LIAISON® analyzer. HbA1c: HbA1c was measured in EDTA-anticoagulated whole blood by the ion-exchange resin method. Lipid profile: Total cholesterol, triglyceride and HDL-C were measured by enzymatic colorimetric methods. LDL-C was calculated by the Friedewald formula.[11]

Statistical analyses were conducted using IBM SPSS Statistics version 16. Categorical variables were expressed as frequency and percent. Continuous variables are reported as mean ± standard deviation. Differences in continuous variables between groups were tested using independent- samples Student's t-test and categorical variables were compared using chi-square test. The Pearson's correlation coefficient was used to determine the correlation between serum ferritin and the glycemic and lipid parameters. Statistical significance was set at $p<0.05$.

RESULTS

Three hundred subjects were enrolled, including 270 patients with T2DM and 30 healthy controls. Mean age was 46.40 ± 9.8 years in T2DM patients and 47.27 ± 11.89 years in controls, with no significant difference between the two groups ($p = 0.657$). In the T2DM group, there were 135 males (50.0%) and 135 females (50.0%) and in the control group, there were 9 males (30.0%) and 21 females (70.0%). There was no statistically significant difference in sex distribution ($p=0.053$).

The mean serum ferritin level was significantly elevated in T2DM patients as compared to healthy controls (172.7 ± 117.9 vs. 102.5 ± 75.4 ng/mL; $p = 0.013$). The mean HbA1c was significantly higher in T2DM patients than controls (9.33 ± 1.34% vs. 5.52 ± 0.7%; $p < 0.001$). Serum ferritin was positively correlated with HbA1c in T2DM patients ($r = 0.145$, $p = 0.017$). [Table 1 and Figure 1]

The mean total cholesterol (221.79 ± 30.2 vs. 135.17 ± 24.0 mg/dL), triglycerides (181.38 ± 30.2 vs. 113.0 ± 24.88 mg/dL) and LDL-C (140.89 ± 37.2 vs. 68.83 ± 22.2 mg/dL) were significantly higher in T2DM patients than in controls ($p < 0.001$ for all). Mean HDL-C was comparable in patients with T2DM and control subjects (43.50 ± 14.6 vs. 44.13 ± 7.0 mg/dL; $p = 0.686$). In T2DM patients, serum ferritin was not significantly correlated with total cholesterol ($r = 0.012$, $p = 0.837$) (Figure 2), triglycerides ($r = 0.056$, $p = 0.333$) or LDL-C ($r = 0.006$, $p = 0.916$). Serum ferritin was weakly negatively correlated with HDL-C ($r = -0.135$, $p = 0.027$). [Table 2]

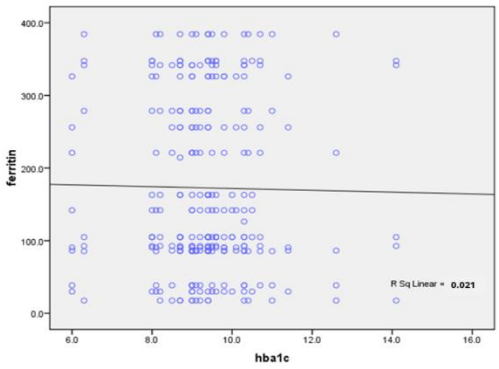

Figure 1: Scatter plot showing the correlation between serum ferritin and HbA1c among patients with type 2 diabetes mellitus

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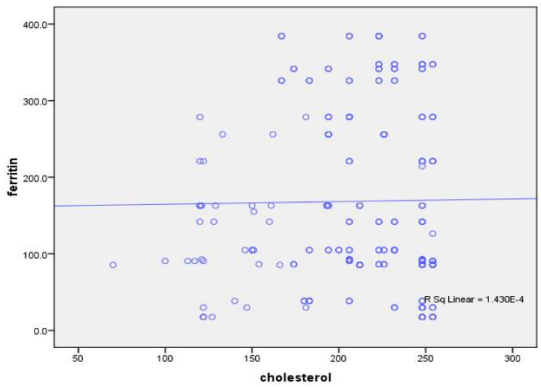

Figure 2: Scatter plot showing the correlation between serum ferritin and total cholesterol among patients with type 2 diabetes mellitus

Table 1: Clinical and biochemical characteristics of the study participants

Parameter	T2DM (n=270)	Controls (n=30)	p-value
Age (years), mean ± SD	46.40 ± 9.8	47.27 ± 11.89	0.657
Male, n (%)	135 (50.0)	9 (30.0)	0.053
Female, n (%)	135 (50.0)	21 (70.0)	0.053
HbA1c (%), mean ± SD	9.33 ± 1.34	5.52 ± 0.7	<0.001
Serum ferritin (ng/mL), mean ± SD	172.7 ± 117.9	102.5 ± 75.4	0.013
Total cholesterol (mg/dL), mean ± SD	221.79 ± 30.2	135.17 ± 24.0	<0.001
Triglycerides (mg/dL), mean ± SD	181.38 ± 30.2	113.0 ± 24.88	<0.001
LDL-C (mg/dL), mean ± SD	140.89 ± 37.2	68.83 ± 22.2	<0.001
HDL-C (mg/dL), mean ± SD	43.50 ± 14.6	44.13 ± 7.0	0.686

Table 2: Correlation of serum ferritin with glycemic and lipid parameters among patients with type 2 diabetes mellitus

Parameter	Correlation coefficient (r)	p-value
HbA1c (%)	0.145	0.017*
Total cholesterol (mg/dL)	0.012	0.837
Triglycerides (mg/dL)	0.056	0.333
LDL-C (mg/dL)	0.006	0.916
HDL-C (mg/dL)	-0.135	0.027*

**Indicates statistical significance ($p < 0.05$)*

DISCUSSION

Serum ferritin levels were significantly higher in patients with T2DM than in healthy controls in the present study. This is consistent with previous studies which reported an association between high serum ferritin and T2DM.[12,13] Several mechanisms have been proposed to explain this association, such as oxidative stress, inflammation and changes in iron metabolism. However, high ferritin may be a marker of inflammatory and metabolic processes rather than of iron overload alone. Therefore, the increase in serum ferritin observed should be interpreted with caution.[14]

Our study, in line with the studies of Prashant et al. and Raj et al., showed a statistically significant positive correlation of serum ferritin with HbA1c levels in diabetics.[15,16] This means that high body iron stores are intrinsically linked with poor long-term glycemic control. These findings are further supported by other researchers who have similarly demonstrated that elevated serum ferritin is closely associated with increased HbA1c levels in diabetic populations.[17] In addition, although we hypothesized a relationship between serum ferritin and a broader atherogenic lipid profile, our analysis showed no significant relationship between serum ferritin and total cholesterol, triglycerides, or low-density lipoprotein (LDL-C) in patients with T2DM. However, a significant weak negative correlation was found between serum ferritin and high-density lipoprotein (HDL-C). This specific finding of HDL-C is consistent with some aspects of studies by Sheth et al,[18] and Salonen et al,[19] who characterized low HDL together with high ferritin as elements of insulin resistance syndrome. In our cohort, there were no significant correlations with other lipid parameters, indicating that the relationship between iron stores and dyslipidemia may not be a simple one. Although hyperferritinemia may serve as a clinical marker of glucotoxicity, its role as a direct marker of broader lipotoxicity needs to be explored further.[20] This study has some limitations. The cross-sectional design prevents causal inferences, and the heavily imbalanced sample size (270 T2DM vs. 30 controls) limits statistical power. Additionally, other iron metabolism markers were not assessed. Future longitudinal studies with matched cohorts are needed.

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CONCLUSION

Serum ferritin levels were significantly increased in patients of Type 2 Diabetes Mellitus as compared to healthy controls. Serum ferritin showed a positive association with HbA1c in patients with T2DM and a weak negative correlation with HDL-C. Serum ferritin was not significantly associated with total cholesterol, triglycerides or LDL-C. The results of the present study indicate that serum ferritin may be associated with some metabolic parameters in T2DM. However, because the study is cross-sectional, causal inference is not possible. Larger prospective studies with detailed assessment of iron status and confounding factors are required to determine the clinical significance of serum ferritin in T2DM.

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Conflicts of Interest Statement

The authors declare no conflicts of interest. The authors received no specific funding for this study.

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