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Frequency of Raised Serum Ferritin Levels and Its Correlation with HbA1c Among Patients Having Diabetes at a Tertiary Care Hospital

Fizza Fatima[1], Maha Zainab[2], Zaka-ul-Rehman[3], Azka Zainab[4], Muhammad Bin Amjad[5], Muhammad Umair Khalid[6]

[1]Consultant Chemical Pathologist, Bakhtawar Amin Medical and Dental College, Multan
[2]Registrar Microbiology CMH Multan, [3]Registrar Orthopaedic Surgery, RTEH Muzaffargarh
[4]Final Year Resident Radiology, CMH Quetta, [5]Final Year Resident Urology, MIKD Multan
[6]Final Year Resident General Surgery, CMH Quetta

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Address of Correspondent
Dr Fizza Fatima
Pathologist, Bakhtawar Amin Medical and Dental College, Multan
Hellofizzafatima@gmail.com

ABSTRACT

Objective: To determine the frequency of raised serum ferritin levels and its correlation with HbA1c in patients presenting with diabetes.

Methodology: This Descriptive, Cross-sectional study was conducted in the department of Pathology & in collaboration with Department of General Medicine, Nishtar Hospital, Multan from August 24, 2022, to February 24, 2023. All the cases of diabetes (n=151), fulfilling inclusion criteria were recruited in the study. Baseline data such as age, gender, residential status, control of diabetes, duration of diabetes, obesity, family history, hypertension was recorded. Three ml of venous blood was taken for serum ferritin & HbA1c levels.

Results: Mean age of the participants was 48.8 ± 10.8 years. There were 57% females. Median (IQR) HbA1c (%) levels of the participants was 7.7 (3.3). Median (IQR) serum ferritin levels of the participants was 96 (131) ng/ml. Raised serum ferritin was found in 30.5% of the participants. A weak positive correlation (r=0.252) was found between HbA1c levels and serum ferritin levels that was statistically significant (p=0.002).

Conclusion: Serum ferritin levels can be used as a marker for glycemic control in diabetic patients.

Keywords: Ferritin, Diabetes Mellitus, Glycated Hemoglobin

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Introduction

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Annual incidence of diabetes is on the rise and it is expected that every 1 person out of 10 will be diabetic by year 2035.[1,2]

Recent research from various population subsets has shown that serum ferritin levels and fasting blood glucose (FBG) levels in type 2 diabetic patients have a linear relationship. This has led researchers to focus on the relationship between inflammatory markers and type 2 DM patients. [3] Serum ferritin levels in healthy individuals indicate the state of iron reserves under normal circumstances; however, high ferritin levels have been linked by various researchers to diabetic complications, including retinopathy, nephropathy, and vascular dysfunction, in patients with DM and elevated FBG. [4] Serum ferritin levels were shown to be significantly correlated with HbA1c and FBG in a prospective cohort study carried out in China6; epidemiological investigations corroborated this finding.

Increased body iron storage have been linked to the emergence of insulin resistance syndrome, type 2 diabetes, gestational diabetes, and glucose intolerance, according to recent studies.[5]

Higher ferritin levels have also been observed in DM patients with elevated glucose levels, and these levels are linked to comorbidities such as retinopathy, nephropathy, and vascular dysfunction. [6]

Different studies have reported correlation of serum ferritin levels with increasing HbA1c levels, a study conducted by Canturk et al [8] has conducted a study on 329 diabetic patients, reported that 26% patients had raised serum ferritin level and 27.33% patients had raised serum ferritin levels among poorly controlled diabetic patients (P<0.001) while another study conducted by Son et al [3] from Turkey has also reported mean serum ferritin level was 109.37±47.00 ng/ml among poorly controlled versus 69.56±27.68 ng/ml among controlled type 2 diabetic patients, (P<0.001).

This proposed study has been planned to ascertain current magnitude of the problem of raised serum ferritin levels in the patients having diabetes in our local population of Southern Punjab as there is no such study done in our population. The results of this study will highlight early diagnosis followed by timely management of raised serum ferritin levels to protect this population from the complications including retinopathy, nephropathy and vascular dysfunction. The results will help clinicians to create awareness among patients regarding control of diabetes to protect them from future complications and to improve their quality of life.

Methodology

After receiving institutional ethical committee approval, the study was carried out. This descriptive, cross-sectional study was carried out at Nishtar Medical University/Hospital in Multan in cooperation with the Department of General Medicine at the Department of Pathology from August 24, 2022, to February 24, 2023. A total of 151 diabetic patients meeting the inclusion criteria were recruited. The sample size of 151 was calculated using the formula $n = z^2pq/d^2$, where *z* = 1.96 at a 95% confidence level, *p* = 26% (frequency of raised serum ferritin in diabetes), *q* = 100 – *p*, and *d* = 7% (margin of error). Non-probability consecutive sampling was used for patient selection. Written informed consent was obtained from all participants, who were briefed about the study objectives, assured of confidentiality, and informed that their participation carried no risks.

Patients aged 30–70 years of both genders with type 2 diabetes (diagnosed for over two years) were included, while those on iron therapy, with anemia (Hb <11.5 mg/dL for females, <13 mg/dL for males), recent infections, blood donations within three months, comorbidities such as coronary artery disease, acute infections, stroke, thyrotoxicosis, hemochromatosis, chronic renal or liver disease, pregnant women, and those declining consent were excluded. Baseline demographic and clinical data, including age, gender, residential status, diabetes control, duration, obesity, family history, and hypertension, were recorded. A 3 mL venous blood sample was collected from each participant for serum ferritin and HbA1c analysis, with results documented in a structured proforma.

Type 2 diabetes was defined as a self-reported history of anti-diabetic medication use for more than two years following diagnosis by a physician. Controlled diabetes was classified as HbA1c <7%, while uncontrolled diabetes was HbA1c ≥7%. A positive family history of diabetes was recorded if first-degree relatives had the condition. Serum ferritin levels were considered elevated if they exceeded 250 ng/mL in males or 120 ng/mL in females. The BMI, which is derived by dividing weight in kilogrammes by height in meters squared, was used to identify obesity (>27.5 kg/m²). A history of antihypertensive medication for longer than two years was considered hypertension.

Statistical Package for Social Sciences (SPSS v. 25) was employed for data analysis. For continuous variables, descriptive statistics such as mean ± standard deviation were employed, whereas frequencies and percentages were utilised to represent categorical variables. The association between serum ferritin and HbA1c levels was evaluated using Pearson's correlation coefficient; a *p*-value ≤0.05 was deemed statistically significant.

Potential confounding variables such as age, gender, hypertension, diabetes control, family history, residential status, and obesity were controlled through stratification, and post-stratification chi-square tests were performed to evaluate their influence on serum ferritin levels. A *p*-value ≤0.05 was deemed significant for all statistical analyses.

Results

Mean age of the participants was 48.8 ± 10.8 years. There were 57% (n=86) females and 43% (n=65) male participants. Mean body mass index of the study participants was 26.9 ± 1.9 kg/m2 and 36.4% (n=55) were obese. From rural area, 52.3% (n=79) and from urban area, 47.7% (n=72) patients belonged. Of all the participants, 39.7% (n=600 was hypertensive and 69.5% (n=105) had positive family history of hypertension. Median (IQR) HbA1c (%) levels of the participants was 7.7 (3.3) and only 41.1% (n=62) were having controlled

diabetes. Median (IQR) serum ferritin levels of the participants was 96 (131) ng/ml. Table I. Raised serum ferritin was found in 30.5% (n=46) of the participants [Figure-1].

Table I: Demographic characteristics of diabetic patients. (N=151)

Age (years), mean ±SD	48.8 ± 10.8
Gender	N(%)
Male	65 (43)
Female	86 (57)
Body Mass Index (kg/m^2) mean ±SD	26.9 ± 1.9
Obesity – Yes	55 (36.4)
Area of residence	N(%)
Rural	79 (52.3)
Urban	72 (47.7)
Hypertension - Yes	60 (39.7)
Family history of diabetes – Yes	105 (69.5)
HbA1c (%) median (IQR)	7.7 (3.3)
Controlled diabetes – Yes	62 (41.1)
Serum Ferritin (ng/ml) median (IQR)	96 (131)

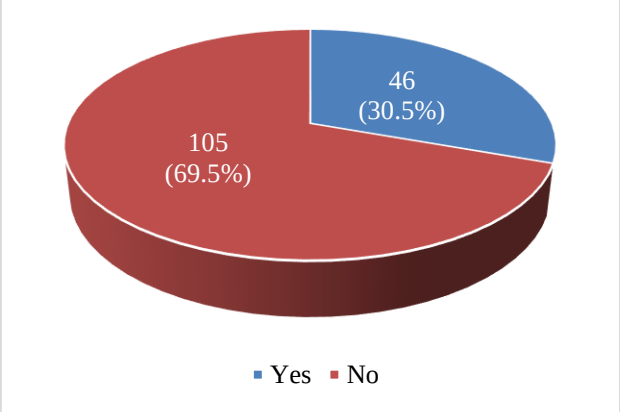

Figure 1. Frequency of raised serum ferritin levels in diabetic patients.

A weak positive correlation (rs=0.252) was found between HbA1c levels and serum ferritin levels that was statistically significant (p-value=0.002). [Figure 2].

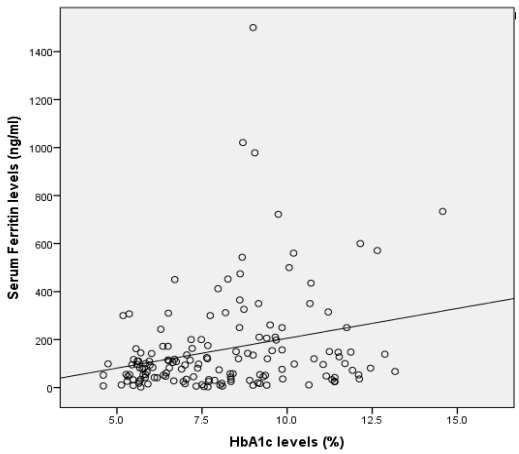

Figure 2. Correlation of HbA1c (%) and Serum ferritin levels (ng/ml) in diabetic patients.

Frequency of raised serum ferritin levels was high in patients with family history of diabetes compared to no family history (37.1% vs. 15.2%). Frequency of raised serum ferritin levels was high in patients with uncontrolled diabetes compared to controlled (44.9% vs. 9.7%). Table II

Table II: Comparison of serum ferritin levels on the basis of demographic characteristics in diabetic patients.(N=151)

Demographic characteristics		Serum Ferritin levels		p-value*
		Raised	Normal	
Age	Up to 50-years	21 (26.2)	59 (738)	0.232
	> 50-years	25 (35.2)	46 (64.8)	
Gender	Male	17 (26.2)	48 (73.8)	0.317
	Female	29 (33.7)	57 (66.3)	
Obesity	Yes	22 (40)	33 (60)	0.054
	No	24 (25)	72 (75)	
Area of residence	Rural	21 (26.6)	58 (73.4)	0.278
	0Urban	25 (34.7)	47 (65.3)	
Hypertension	Yes	20 (33.3)	40 (66.7)	0.534
	No	26 (28.6)	65 (71.4)	
Family history of hypertension	Yes	39 (37.1)	66 (62.9)	0.007
	No	7 (15.2)	39 (84.8)	
Control of Diabetes	Controlled	6 (9.7)	56 (90.3)	< 0.001
	Un-controlled	40 (44.9)	49 (55.1)	

Correlation between HbA1c and serum ferritin levels remained positive after stratification on demographic characteristics. However, statistically significant correlation was observed with respect to age, female gender, presence of obesity, in patients coming from rural areas, in patients without hypertension and no family history of hypertension. Table III

Discussion

The participants in our study had an average age of 48.8 ± 10.8 years. Females made up 57% (n=86). Thirty-five percent of subjects had elevated serum ferritin. In a parallel investigation, Momeni A et al. found that 45 patients (67.2%) were female and that their mean age was 56.5 ± 9.7 years. 8. According to the current study, there is a weak positive connection (p=0.002) between serum ferritin and glycated haemoglobin, suggesting that ferritin

Table III: Correlation between serum ferritin levels and HbA1c levels with respect to demographic characteristics in diabetic patients. (N=151)

Demographic characteristics		Pearson Correlation	p-value
Age	Up to 50-years	0.318	0.004
	> 50-years	0.232	0.051
Gender	Male	0.232	0.062
	Female	0.291	0.006
Obesity	Yes	0.332	0.013
	No	0.197	0.054
Area of residence	Rural	0.337	0.002
	Urban	0.212	0.074
Hypertension	Yes	0.081	0.541
	No	0.429	< 0.001
Family history of hypertension	Yes	0.127	0.197
	No	0.636	< 0.001
Control of Diabetes	Controlled	0.196	0.126
	Un-controlled	0.105	0.329

may be used as a marker of diabetes complications and glycemia control. Thus, serum ferritin can be utilized as a marker to screen for type 2 diabetes and insulin resistance.

Elevated serum ferritin levels have been linked to gestational diabetes, metabolic syndrome, insulin resistance, and metabolic syndrome.[11] In patients with iron deficiency anaemia who also have diabetes, the HbA1c value is correlated with both the patient's iron status and blood sugar level. [12] Serum ferritin levels were correlated with hyperglycemia and fell as serum blood glucose levels rose.[8]

A chronic metabolic illness called type 2 diabetes mellitus is brought on by inadequate or inefficient insulin levels that do not adequately control blood glucose levels. All around the world, the prevalence of DM-type 2 has been progressively rising. People with type 2 diabetes mellitus are more susceptible to both short-term and long-term problems, which frequently cause them to die soon.[13] The main causes of T2DM include unhealthy lifestyles and excessive body weight. Unfortunately, encouraging good habits and weight control hasn't been able to stop the rising public health burden of T2D. The pathophysiology of T2DM problems is heavily influenced by oxidative stress.[14] The main components that appear to be formed are superoxide and hydrogen peroxide. These reactive oxygen species contribute to the production of other, more reactive oxidants, such as the extremely reactive hydroxyl radicals, which are catalyzed reactions involving iron salts. The metal catalyzed Haber-Weiss reaction is the name given to this process.[15] The reversal or improvement of diabetes (glycaemic control) with a reduction in iron load achieved by either phlebotomy or iron chelation treatment, as well as the higher prevalence of type 2 diabetes in several causes of iron overload, demonstrate that iron plays a role in the pathogenesis of diabetes. [16]

Hydrogen peroxide and superoxide seem to be the main species produced. These reactive oxygen species contribute to the production of more and more reactive oxidants, such as the extremely reactive hydroxyl radicals, which are produced when iron salts catalyse a process. This reaction is known as the Haber-Weiss reaction that is catalysed by metal. [15] A higher incidence of type 2 diabetes in a variety of iron overload causes and the reversal or improvement of diabetes (glycaemic control) with a reduction in iron load accomplished by either phlebotomy or iron chelation therapy suggest the role of iron in the pathophysiology of diabetes. [16] Ferritin has been identified as an indicator of insulin resistance because of iron buildup in the liver, which results in hepatic insulin resistance and elevated hepatic glucose synthesis. [17]

In some cases of diabetes, pancreatic damage brought on by some degree of subclinical hemochromatosis has been taken into consideration.[18] Studies by Garcia-Casol MN, et al[19] and Aregbesola A, et al [20] found a significant correlation between an elevated serum ferritin level and a higher risk of developing diabetes.

The findings of our study are consistent with those of Thanna RC et al., [21] Momeni A et al., [8] and Rawat N et al., [22] who observed hyperferritinemia in individuals with poorly managed diabetes. Serum ferritin levels in diabetes individuals were significantly greater than those in the control group ($p<0.001$)., according to a study by Al-Miraj AK et al. HbA1c and serum ferritin showed a favorable correlation.[23] This demonstrated that, as long as glycemic control was not established, serum ferritin was elevated in diabetes.

Conclusion

According to our evaluation, patients with type 2 diabetes mellitus had a weakly positive but statistically significant relationship among serum ferritin and glycated haemoglobin, and elevated serum ferritin was noticed in 30.5% of cases. It demonstrates that in diabetic patients, serum ferritin may be used as a measure for glycaemic management.

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