

ORIGINAL ARTICLE

Association Between Serum Ferritin, Vitamin D Levels, and Glycemic Control in Patients with Type 2 Diabetes Mellitus

ASIF SAGHEER¹, SADAF SAGHIR², MUHAMMAD BILAL AKBAR³, QAMAR SAJAD⁴, IQRA IQBAL⁵

¹Consultant Physician, District Headquarter Hospital, Mandi Bahauddin

²Women Medical Officer, Allied II Hospital, Faisalabad

³Senior Clinical Fellow, Dr. Greys Hospital, NHS Grampian Scotland.

⁴Assistant Professor Endocrinology, Fatima Memorial Hospital Lahore

⁵Women Medical Officer, District Headquarter Hospital, Mandi Bahauddin

Correspondence to: Asif Sagheer, Email: asifsagheer@gmail.com

ABSTRACT

Background: Diabetes mellitus type 2 is a chronic metabolic disease defined by hyperglycaemia, insulin resistance and decreased insulin production. Changes in iron metabolic and vitamin D status can lead to metabolic dysfunction by oxidative stress, inflammatory mechanisms, and insulin signaling impairment.

Objective: To determine the association between serum ferritin, vitamin D levels, and glycemic control among patients with type 2 diabetes mellitus.

Materials and Methods: This hospital-based analytical cross-sectional study was designed for 140 patients with type 2 diabetes mellitus at DHQ Hospital Mandi Bahauddin, from November 2022 to May 2023. Demographic, clinical history, BMI, ferritin, serum 25-hydroxyvitamin D, fasting blood glucose, and glycated hemoglobin (HbA1c) were evaluated. Patients were classified as having good (HbA1c < 7%) or poor (HbA1c ≥ 7%) glycemic control. Data were to be analyzed statistically using SPSS version 26.0, appropriate group comparisons would be made, spearman correlation and multivariable logistic regression would be done and p-value < 0.05 would be considered as statistically significant.

Results: The analysis included 140 patients with type 2 diabetes mellitus, with a mean age of 52.47 ± 8.77 years. Of these, 77 (55.0%) were male, and 95 (67.9%) had poor glycemic control (HbA1c ≥ 7%). The mean HbA1c was 7.77 ± 1.29%, while the median serum ferritin concentration was 139.00 ng/mL and the mean vitamin D level was 22.76 ± 7.74 ng/mL. Vitamin D deficiency was identified in 47 (33.6%) patients. Serum ferritin showed a significant positive correlation with HbA1c (r=0.450, p<0.001), whereas vitamin D demonstrated a significant negative correlation (r=-0.334, p<0.001). Patients with poor glycemic control had higher ferritin and lower vitamin D concentrations (both p<0.001). Multivariable logistic regression demonstrated significant associations of ferritin (aOR=1.150, 95% CI: 1.062–1.245; p=0.001) and vitamin D (aOR=0.177, 95% CI: 0.082–0.381; p<0.001) with poor glycemic control.

Conclusion: Evaluating serum ferritin and vitamin D alongside conventional glycemic indicators may improve understanding of metabolic abnormalities in type 2 diabetes mellitus. The clinical significance of these biomarkers requires interpretation in conjunction with established indicators of glycemic control and relevant confounding factors.

Keywords: Type 2 diabetes mellitus; serum ferritin; vitamin D; HbA1c; glycemic control; insulin resistance.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is one of the most prevalent public health issues around the world, brought about by chronic hyperglycemia due to decreased insulin secretion, peripheral insulin resistance, and gradual decline of pancreatic beta cell function. It has been associated with a significant morbidity and mortality due to cardiovascular diseases, diabetic nephropathy, neuropathy, retinopathy, and other metabolic complications. The pathogenesis of T2DM is multifactorial and requires interaction of genetic factors, environmental factors, obesity, physical inactivity, and cellular metabolic pathway modifications. Insulin resistance of skeletal muscle, adipose tissue and liver leads to decreased glucose utilization and increased liver glucose production, while pancreatic beta-cell dysfunction gradually decreases the compensatory insulin response. Glycated hemoglobin (HbA1c) is commonly used to assess average blood glucose levels and is a valuable indicator of how well diabetes is being controlled and the probability of developing diabetes-related complications. However, the classical glycemic markers underestimate the underlying inflammatory, oxidative and biochemical abnormalities that contribute to the diabetes progression¹⁻³.

The deranged iron metabolism has been recognized as a possible metabolic imbalance in T2DM patients. Iron is a macro nutrient that is essential for the transport of oxygen, function of mitochondria and plays a role in various enzymatic pathways but excess of biologically available iron may lead to oxidative stress and cell injury. Because of its possible association with insulin resistance, hyperglycemia, and metabolic dysfunction, serum ferritin, an indicator of body iron stores, has been the focus of attention. The greater availability of iron could lead to the

production of more reactive oxygen species, disrupts the insulin-signaling pathways within cells and could add to the insulin-producing pancreatic beta cells being damaged. Also, chronic low-grade inflammation and alterations in hepatic metabolism may contribute to elevation of serum ferritin levels independent of whole body iron stores. Thus, high ferritin levels can be associated with concurrent iron storage, inflammatory and metabolic disorders. The understanding of these mechanisms is especially relevant when examining biochemical factors of poor glycemic control in people with T2DM⁴⁻⁶.

Another important biological factor which may alter glucose homeostasis is vitamin D; apart from its known role in calcium and bone metabolism, vitamin D acts in other ways. Vitamin D receptors are found in a variety of tissues relevant to metabolic regulation such as the pancreatic beta cells, skeletal muscle and adipose tissue. Vitamin D signaling has been associated with calcium-dependent insulin secretion, control of inflammatory cytokines and normal insulin responsiveness. Low vitamin D levels can lead to the development of insulin resistance, oxidative stress and glucose metabolism disturbances. In addition, vitamin D deficiency is often associated with obesity, decreased physical activity, decreased sun exposure, nutritional abnormalities, and all of these factors could affect glycemic control. The biological mechanism by which vitamin D may link to diabetes is reasonable, but the magnitude and consistency of the metabolic effects of vitamin D remain inconsistent. Variability in observed relationships may be due to differences in baseline vitamin D status, diabetes duration, treatment patterns and associated comorbidities^{7,8}.

The combined assessment of serum ferritin and vitamin D may provide a broader understanding of biochemical abnormalities associated with glycemic regulation in patients with T2DM. These biomarkers represent distinct but potentially interrelated pathways involving iron metabolism, oxidative stress, inflammation, and

Received on 15-01-2023

Accepted on 25-06-2023

insulin sensitivity. Despite increasing interest in their metabolic roles, uncertainty remains regarding whether ferritin and vitamin D are independently associated with HbA1c after accounting for conventional clinical factors such as age, body mass index, and duration of diabetes. In addition, evidence regarding the clinical utility of interpreting these markers together remains limited, particularly in routine hospital-based diabetic populations. Further evaluation of their relationships with fasting blood glucose and HbA1c may help clarify their potential relevance to the metabolic assessment of T2DM. Therefore, the present study was designed to determine the association between serum ferritin, vitamin D levels, and glycemic control among patients with type 2 diabetes mellitus at DHQ Hospital, Sargodha, and to evaluate their relationships with selected demographic, clinical, and biochemical characteristics^{9, 10}.

MATERIALS AND METHODS

Study Design, Setting, and Duration: This hospital-based analytical cross-sectional study was conducted at District Headquarters (DHQ) Hospital Mandi Bahauddin, Punjab, Pakistan, over a period of six months, from November 2022 to May 2023. The study was designed to evaluate the association between serum ferritin concentrations, vitamin D levels, and glycemic control among patients diagnosed with type 2 diabetes mellitus (T2DM). The primary objective was to determine the relationship of serum ferritin and vitamin D with glycated hemoglobin (HbA1c), while secondary objectives included evaluating their associations with fasting blood glucose and identifying clinical and biochemical factors associated with inadequate glycemic control.

Sample Size and Sampling Technique: The proposed sample size was 140 patients with type 2 diabetes mellitus. Sample size estimation was based on Fisher's z-transformation for correlation analysis, considering an anticipated correlation coefficient of 0.25 [11], a 95% confidence level, 80% statistical power, and a 5% level of significance. The minimum estimated sample size was approximately 124 participants, which was increased to 140 to accommodate potentially incomplete observations. The sample size calculation followed the approach described by Hulley et al. [12]. A non-probability consecutive sampling technique was specified for recruiting eligible patients presenting to the medical outpatient department or diabetes clinic during the study period.

Eligibility Criteria: Patients were eligible for inclusion if they were older than 18 years, diagnosed with type 2 diabetes mellitus and of either gender. Documented clinical history, medical records, antidiabetic treatment and accepted diagnostic criteria, such as HbA1c $\geq 6.5\%$, fasting plasma glucose ≥ 126 mg/dL, or documented previous diagnosis of T2DM were used for diagnosis. The eligible patients were those receiving oral antidiabetic meds, insulin, or both. Patients with known iron-storage disorders, chronic liver disease, advanced chronic kidney disease, malignancy, gestational diabetes, acute infections, and type 1 diabetes mellitus were excluded as these conditions may affect ferritin levels or vitamin D metabolism or glycemic indices on their own. Patients who consumed iron supplements, a recent blood transfusion, or high doses of vitamin D were also excluded to avoid any potential biochemical interference. Other exclusion criteria included pregnancy as well as hematological disorders that might influence the accuracy of HbA1c levels.

Data Collection and Clinical Assessment: Data collection proforma was used to gather demographic and clinical data. The following variables were recorded: age, sex, family history of diabetes, history of hypertension, and antidiabetic treatment. Anthropometric measurements were body weight and height, and the body mass index (BMI) was calculated as body weight in kg/m². BMI was classified based on the different BMI classifications used as follows: normal weight, overweight, and obesity. Clinical records and patient interviews were used to obtain information about diabetes duration and treatment.

Laboratory Investigations: Blood samples were drawn from the veins, under aseptic conditions, for the measurement of serum

ferritin, 25-hydroxyvitamin D [25(OH)D], fasting blood glucose and HbA1c. Blood glucose levels were measured following an 8–12 hour overnight fast. Laboratory immunoassay was used to measure serum ferritin, which was expressed in ng/mL, and serum 25(OH)D was expressed in ng/mL. Standardized laboratory methodology was used to determine HbA1c as a percentage; this was regarded as the primary measure of long-term glycemic control. Hematological and renal status was also evaluated by hemoglobin and serum creatinine. Laboratory results were reported in standardized units and standard internal quality-assurance protocols were deemed to be essential to provide analytical reliability.

Classification of Vitamin D Status and Glycemic Control: The vitamin D status was classified according to the commonly used clinical cut-off as vitamin D deficiency (serum 25(OH)D < 20 ng/mL), vitamin D insufficiency (serum 25(OH)D $20 - < 30$ ng/mL), and vitamin D sufficiency (serum 25(OH)D ≥ 30 ng/mL). HbA1c levels were used as a measure of glycemic control. HbA1c $< 7\%$ was considered to represent good glycemic control, while those with $\geq 7\%$ were considered to represent poor glycemic control. Group comparisons were conducted to explore differences in serum ferritin, vitamin D and other clinical characteristics, by these categories. In addition, serum ferritin and vitamin D were also analyzed as continuous variables, to maintain its quantitative information.

Statistical Analysis: IBM SPSS Statistics 26.0 was used to analyze data. Normality of continuous variables was tested by the Shapiro–Wilk test and the visual inspection of the data distribution. Quantitative variables were expressed as mean with standard deviation (SD), and median with interquartile range (IQR) for variables that were not normally distributed. Categorical variables were expressed in terms of frequencies and percentages. Independent-samples t-tests were used for normally distributed continuous variables, and Mann–Whitney U tests were used for variables that did not have a normal distribution, when a comparison was made between patients with good glycemic control and those with poor glycemic control. The chi-square test or Fisher's exact test was used to assess associations between categorical variables. The relationships between serum ferritin, vitamin D, BMI and duration of diabetes with HbA1c level and fasting blood glucose level were determined using spearman's rank correlation coefficient. Multivariable binary logistic regression was used to assess each factor independently of the other factors (age, gender, BMI, duration of diabetes, serum ferritin, serum vitamin D and hypertension) associated with poor glycemic control (HbA1c $\geq 7\%$). Reported adjusted odds ratios (aORs) with 95% confidence intervals (CIs). A p value of < 0.05 was deemed to be statistically significant.

RESULTS

A total of 140 patients with Type 2 Diabetes Mellitus (T2DM) were included in the cohort with a mean age at 52.47 ± 8.77 years. Most patients were between 41 and 60 years of age (72.1%), and 77 (55.0%) were male. The mean BMI was 27.50 ± 3.76 kg/m², with 64 (45.7%) participants classified as overweight and 38 (27.1%) as obese. The average duration of diabetes was 8.03 ± 4.11 years. A family history of diabetes was noted in 89 (63.6%) patients and hypertension in 52 (37.1%). The number of patients treated with insulin was documented in 45 (32.1%).

The median concentration of serum ferritin was 139.00 ng/mL (IQR: 102.59–183.24) and the mean concentration of serum vitamin D was 22.76 ± 7.74 ng/mL. Forty-seven (33.6%) patients were found to be vitamin D deficient, 69 (49.3%) vitamin D insufficient and 24 (17.1%) vitamin D sufficient. The mean fasting blood glucose level was 174.47 ± 39.86 mg/dL, and the mean HbA1c was $7.77 \pm 1.29\%$. Ninety-five (67.9%) patients had poor glycemic control (HbA1c $\geq 7\%$).

Patients having poor glycemic control had significantly higher levels of serum ferritin than did patients with good glycemic control (157.8 versus 109.8 ng/mL; $p < 0.001$). In contrast, patients

with poor glycemic control had significantly low levels of vitamin D (20.83 ± 7.34 ng/mL) compared to those with good glycemic control (26.84 ± 7.00 ng/mL; $p < 0.001$). The poor-control group also had a significantly greater length of diabetes ($p = 0.035$). Deficiency in vitamin D was significantly more common in those with poor-control glucose (44.2% vs 11.1%, $p < 0.001$). There were no significant differences in age, BMI or hypertension.

Table 1: Demographic and clinical characteristics of patients with type 2 diabetes mellitus (n=140)

Variables	Frequency (%) / Mean $\pm$ SD
Age (years)	52.47 $\pm$ 8.77
≤ 40 years	13 (9.3%)
41–50 years	49 (35.0%)
51–60 years	52 (37.1%)
>60 years	26 (18.6%)
Male	77 (55.0%)
Female	63 (45.0%)
BMI (kg/m ²)	27.50 $\pm$ 3.76
Normal BMI	38 (27.1%)
Overweight	64 (45.7%)
Obese	38 (27.1%)
Duration of diabetes (years)	8.03 $\pm$ 4.11
≤ 5 years	31 (22.1%)
6–10 years	70 (50.0%)
>10 years	39 (27.9%)
Family history of diabetes	89 (63.6%)
Hypertension	52 (37.1%)
Insulin-based treatment	45 (32.1%)
Other antidiabetic treatment	95 (67.9%)

Table 2: Biochemical parameters and glycemic control among study participants (n=140)

Variables	Mean $\pm$ SD / Median (IQR) / n (%)
Serum ferritin (ng/mL)	139.00 (102.59–183.24)
Serum vitamin D (ng/mL)	22.76 $\pm$ 7.74
Vitamin D deficiency (<20 ng/mL)	47 (33.6%)
Vitamin D insufficiency (20–<30 ng/mL)	69 (49.3%)
Vitamin D sufficiency (≥ 30 ng/mL)	24 (17.1%)
Fasting blood glucose (mg/dL)	174.47 $\pm$ 39.86
HbA1c (%)	7.77 $\pm$ 1.29
Good glycemic control (HbA1c <7%)	45 (32.1%)
Poor glycemic control (HbA1c $\geq 7\%$)	95 (67.9%)
Hemoglobin (g/dL)	13.01 $\pm$ 1.25
Serum creatinine (mg/dL)	0.98 $\pm$ 0.19

Table 3: Comparison of biochemical and clinical parameters according to glycemic control

Variables	Good control (n=45)	Poor control (n=95)	p-value
Age (years)	51.38 $\pm$ 8.49	52.99 $\pm$ 8.90	0.305
BMI (kg/m ²)	27.23 $\pm$ 4.14	27.63 $\pm$ 3.58	0.582
Duration of diabetes (years)	7.3 (4.3–9.5)	8.4 (6.0–11.0)	0.035
Serum ferritin (ng/mL)	109.8 (82.5–140.2)	157.8 (124.3–203.2)	<0.001
Serum vitamin D (ng/mL)	26.84 $\pm$ 7.00	20.83 $\pm$ 7.34	<0.001
Fasting blood glucose (mg/dL)	140.64 $\pm$ 22.45	190.49 $\pm$ 36.13	<0.001
Vitamin D deficiency	5 (11.1%)	42 (44.2%)	<0.001
Hypertension	21 (46.7%)	31 (32.6%)	0.135

Values are presented as mean $\pm$ SD, median (IQR), or frequency (%). Bold p-values indicate statistical significance.

Table 4: Correlation of serum ferritin and vitamin D with glycemic parameters

Variables	HbA1c (r)	p-value	Fasting glucose (r)	p-value
Serum ferritin	0.450	<0.001	0.354	<0.001
Serum vitamin D	-0.334	<0.001	-0.155	0.068
BMI	0.063	0.460	0.081	0.342
Duration of diabetes	0.261	0.002	0.279	<0.001

Spearman's rank correlation coefficient was used.

Table 5: Multivariable logistic regression analysis of factors associated with poor glycemic control

Independent variables	Adjusted OR	95% CI	p-value
Age (years)	1.036	0.974–1.102	0.264
Male sex	0.897	0.360–2.231	0.814
BMI (kg/m ²)	1.074	0.952–1.212	0.248
Duration of diabetes (years)	1.121	0.985–1.275	0.082
Serum ferritin (per 10 ng/mL)	1.150	1.062–1.245	0.001
Vitamin D (per 10 ng/mL)	0.177	0.082–0.381	<0.001
Hypertension	0.346	0.131–0.915	0.032

Dependent variable: Poor glycemic control (HbA1c $\geq 7\%$). OR: odds ratio; CI: confidence interval.

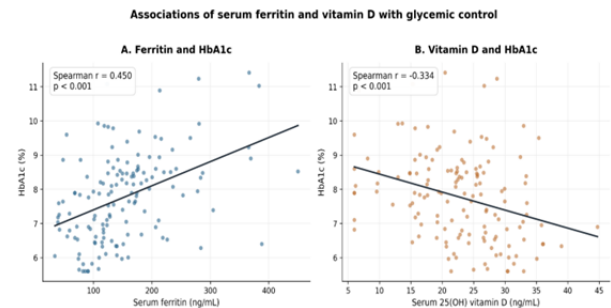


Fig. 1: Scatter plots demonstrating a positive correlation between serum ferritin and HbA1c ($r = 0.450$, $p < 0.001$) and a negative correlation between serum vitamin D and HbA1c ($r = -0.334$, $p < 0.001$).

The moderate positive correlation between the serum ferritin and HbA1c ($r = 0.450$, $p < 0.001$) was observed on Spearman's correlation analysis, suggesting that higher levels of ferritin were associated with poorer glycemic control. The HbA1c level was significantly negatively associated with serum vitamin D ($r = -0.334$, $p < 0.001$). Fasting blood glucose also was positively correlated with ferritin ($r = 0.354$, $p < 0.001$). Vitamin D wasn't associated with fasting glucose ($p = 0.068$). There were positive correlations between duration of diabetes and HbA1c and fasting glucose.

Higher serum Ferritin levels and lower vitamin D levels were found as independent significant correlates of poor glycemic control in multivariable logistic regression analysis. Each 10 ng/mL increase in ferritin was associated with 15.0% higher adjusted odds of poor glycemic control (aOR=1.150; 95% CI: 1.062–1.245; $p = 0.001$). On the other hand, the odds of having poor glycemic control decreased as vitamin D levels increased (aOR=0.177; 95% CI: 0.082–0.381; $P < 0.001$). Age, sex, BMI and diabetes duration were not statistically significant in the adjusted model, but hypertension showed an inverse adjusted association (aOR=0.346; $p = 0.032$). These associations do not imply causation.

DISCUSSION

Type 2 diabetes mellitus is a complex metabolic disorder characterized by persistent hyperglycemia, insulin resistance, progressive pancreatic beta-cell dysfunction, and disturbances in several biochemical pathways. In addition to conventional glycemic indicators, increasing attention has been directed toward the possible contributions of iron metabolism and vitamin D status to metabolic regulation. Serum ferritin is an important indicator of body iron stores but also reflects inflammatory activity, whereas vitamin D participates in several physiological processes involving glucose homeostasis, immune regulation, and cellular metabolism. Disturbances in these biomarkers may coexist with inadequate glycemic control and contribute to the metabolic abnormalities associated with diabetes. HbA1c remains an essential indicator of long-term glycemic status because it reflects average blood glucose concentrations over approximately three months. However, the interpretation of glycemic control should also consider disease duration, treatment adherence, obesity, associated comorbidities, and individual patient characteristics^{13–15}.

Serum ferritin has been the focus of much interest as a biochemical marker with association to abnormalities of glucose metabolism. An excess of iron could facilitate the production of ROS and cause cell damage, lipid peroxidation and impair insulin signaling by iron-dependent oxidative reactions. In the case of the pancreatic beta cell, the relatively weak antioxidant protection is especially susceptible to oxidative stress. An increase in oxidative activity may affect insulin secretion and lead to progressive beta-cell dysfunction. Moreover, changes in iron metabolism could affect hepatic glucose output, insulin sensitivity in skeletal muscle and inflammatory pathways that contribute to the pathogenesis of insulin resistance. However, the level of serum ferritin should not be used as sole evidence of iron overload as it can also rise with chronic inflammatory conditions, liver dysfunction and metabolic disturbances. Therefore, there is a need to assess the role of ferritin in relation to diabetes and its control in conjunction with other relevant clinical and biochemical parameters^{16,17}.

Another biological relevant factor, which could also be involved in metabolic regulation in patients with type 2 diabetes mellitus, is vitamin D. In addition to its known actions in calcium and bone metabolism, vitamin D can affect activity of the pancreatic beta cells, insulin secretion, inflammatory signaling and peripheral insulin sensitivity. Vitamin D receptors are found in many metabolically active tissues indicating vitamin D signaling may be involved in glucose regulation in many ways. Low vitamin D levels may be linked with impaired calcium-insulated insulin secretion, enhanced inflammatory activity and decreased insulin sensitivity. The relationship between vitamin D and glycemic control is complex, however, and could be influenced by other factors such as obesity, nutritional status, sunlight exposure, age, physical activity, and length of diabetes. While vitamin D has shown a positive effect on some metabolic markers, results on HbA1c have not been consistent in clinical studies. Thus, vitamin D status needs to be viewed as an additional possibly relevant metabolic factor, rather than a known independent risk factor for glycemic control^{18,19}.

The serum Ferritin and Vitamin D levels could be helpful in gaining insight into the metabolic and inflammatory mechanism of type 2 diabetes mellitus when used together. There is limited direct evidence of a direct interaction, but there is the possibility of interaction between oxidative stress caused by iron and vitamin D-dependent immunomodulatory pathways with insulin resistance and chronic low-grade inflammation. Elevated ferritin levels can be due to either increased iron stores, liver metabolic dysfunction, or inflammatory processes, and decreased vitamin D levels can be associated with obesity and other metabolic risk factors. Both of these mechanisms can be used to investigate these two biomarkers together with HbA1c and fasting blood glucose. However, alteration in biochemical parameters does not necessarily mean that changing ferritin or vitamin D levels will enhance glycemic control. The interpretation should take into consideration the potential for confounding factors such as dietary patterns, medication use, body composition, renal function and lifestyle factors. A thorough evaluation of these factors could help to better understand the diversity in metabolic patterns seen in type 2 diabetes mellitus patients^{20,21}.

Evaluating ferritin and vitamin D has clinical relevance because of their possible role in understanding the metabolic heterogeneity, but not as a substitute for the existing methods of diabetes assessment. HbA1C, fasting glucose, clinical assessment and customised therapy continue to be key elements in diabetes care. Iron disorders, inflammatory diseases, or liver disorders may warrant ferritin measurements; in patients with known clinical risk for vitamin D deficiency, vitamin D testing may be warranted. These biochemical markers will need further investigation to determine if these markers provide better prediction of glycemic outcomes than traditional clinical parameters. The drawbacks of a hospital-based cross-sectional study are the lack of temporal or causal inferences, the potential for selection bias, and the residual confounding due to unmeasured inflammatory, dietetic and lifestyle

factors. Elevated or low levels of a single biochemical marker can also be due to changes in iron status or vitamin D levels over time. Additional prospective multicenter studies with inflammatory markers, comprehensive iron parameters, dietary assessment and repeated glycemic monitoring are suggested to further elucidate these relationships and to assess their clinical relevance.

CONCLUSION

Serum ferritin and vitamin D are biologically relevant markers for investigating metabolic disturbances associated with type 2 diabetes mellitus. Altered iron metabolism, oxidative stress, inflammation, and vitamin D-related mechanisms may contribute to variations in glycemic regulation. However, associations between these biomarkers and HbA1c should not be interpreted as evidence of causation. Further prospective investigations are required to establish their independent clinical value and determine whether targeted management of iron abnormalities or vitamin D deficiency can improve glycemic outcomes.

REFERENCES

1. Himanshu, D., W. Ali, and M. Wamique, Type 2 diabetes mellitus: pathogenesis and genetic diagnosis. *J Diabetes Metab Disord*, 2020. 19(2): p. 1959-1966 DOI: 10.1007/s40200-020-00641-x.
2. James, D.E., J. Stöckli, and M.J. Birnbaum, The aetiology and molecular landscape of insulin resistance. *Nature Reviews Molecular Cell Biology*, 2021. 22(11): p. 751-771 DOI: 10.1038/s41580-021-00390-6.
3. American Diabetes, A., 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. *Diabetes Care*, 2020. 44(Supplement_1): p. S15-S33 DOI: 10.2337/dc21-S002.
4. Eizirik, D.L., L. Pasquali, and M. Cnop, Pancreatic β -cells in type 1 and type 2 diabetes mellitus: different pathways to failure. *Nature Reviews Endocrinology*, 2020. 16(7): p. 349-362 DOI: 10.1038/s41574-020-0355-7.
5. Yong, J., et al., Therapeutic opportunities for pancreatic β -cell ER stress in diabetes mellitus. *Nature Reviews Endocrinology*, 2021. 17(8): p. 455-467 DOI: 10.1038/s41574-021-00510-4.
6. Ali, K., Q. Raza, and T.A. Maka, MEAN SERUM FERRITIN LEVELS IN TYPE-2 DIABETES MELLITUS IN PAKISTANI POPULATION. *Pakistan Armed Forces Medical Journal*, 2021. 71(Suppl-1): p. S15-18 DOI: 10.51253/pafmj.v71iSuppl-1.6194.
7. Szymczak-Pajor, I., J. Drzewoski, and A. Śliwińska, The Molecular Mechanisms by Which Vitamin D Prevents Insulin Resistance and Associated Disorders. *Int J Mol Sci*, 2020. 21(18) DOI: 10.3390/ijms21186644.
8. Yarıbeygi, H., et al., The molecular mechanisms by which vitamin D improve glucose homeostasis: A mechanistic review. *Life Sci*, 2020. 244: p. 117305 DOI: 10.1016/j.lfs.2020.117305.
9. Cojic, M., et al., The Effects of Vitamin D Supplementation on Metabolic and Oxidative Stress Markers in Patients With Type 2 Diabetes: A 6-Month Follow Up Randomized Controlled Study. 2021. Volume 12 - 2021 DOI: 10.3389/fendo.2021.610893.
10. Venkatesan, P., et al., Evidence of dysregulated iron homeostasis in newly diagnosed diabetics, but not in pre-diabetics. *Journal of Diabetes and its Complications*, 2021. 35(9): p. 107977 DOI: https://doi.org/10.1016/j.jdiacomp.2021.107977.
11. Son, N.E., Influence of ferritin levels and inflammatory markers on HbA1c in the Type 2 Diabetes mellitus patients: Inflammatory markers on HbA1c in the Type 2 Diabetics. *Pakistan Journal of Medical Sciences*, 2019. 35(4) DOI: 10.12669/pjms.35.4.1003.

12. Browner, W.S., et al., Designing clinical research. 2022: Lippincott Williams & Wilkins.
13. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2021. *Diabetes Care*, 2021. 44(Suppl 1): p. S73-s84 DOI: 10.2337/dc21-S006.
14. Liu, J., et al., Iron metabolism and type 2 diabetes mellitus: A meta-analysis and systematic review. *J Diabetes Investig*, 2020. 11(4): p. 946-955 DOI: 10.1111/jdi.13216.
15. Pitchika, A., et al., Associations of iron markers with type 2 diabetes mellitus and metabolic syndrome: Results from the prospective SHIP study. *Diabetes Res Clin Pract*, 2020. 163: p. 108149 DOI: 10.1016/j.diabres.2020.108149.
16. Zhang, R., et al., Serum ferritin as a risk factor for type 2 diabetes mellitus, regulated by liver transferrin receptor 2. *Endocr Connect*, 2021. 10(12): p. 1513-1521 DOI: 10.1530/ec-21-0316.
17. Pitchika, A., et al., Hepatic steatosis and hepatic iron overload modify the association of iron markers with glucose metabolism disorders and metabolic syndrome. *Liver Int*, 2021. 41(8): p. 1841-1852 DOI: 10.1111/liv.14868.
18. Restrepo-Gallego, M., L.E. Díaz, and P.H.C. Rondó, Classic and emergent indicators for the assessment of human iron status. *Crit Rev Food Sci Nutr*, 2021. 61(17): p. 2827-2840 DOI: 10.1080/10408398.2020.1787326.
19. Emadzadeh, M., et al., A systematic review and meta-analysis of the effect of Vitamin D-fortified food on glycemic indices. *Biofactors*, 2020. 46(4): p. 502-513 DOI: 10.1002/biof.1632.
20. Gharekhani, A., et al., The Effect of Treating Vitamin D Deficiency or Insufficiency on Serum Adiponectin, Leptin and Insulin Resistance of Type 2 Diabetes Mellitus Patients: A Pilot Study. *Iran J Pharm Res*, 2020. 19(3): p. 86-94 DOI: 10.22037/ijpr.2020.112067.13512.
21. Kwak, J.H., Y.H. Choi, and J.K. Paik, Vitamin D Status, Fiber Intake, and Type 2 Diabetes in U.S. Adults. *J Med Food*, 2020. 23(7): p. 711-718 DOI: 10.1089/jmf.2019.4528.

This article may be cited as: Sagheer A., Saghir S., Akbar M.B., Sajad Q., Iqbal I., Association Between Serum Ferritin, Vitamin D Levels, and Glycemic Control in Patients with Type 2 Diabetes Mellitus. *Pak J Med Health Sci*, 2023; 17(7): 228-232.