Journal of Biomedicine and Biosensors, 6(3):50–56, July-September: 2026.
DOI: https://doi.org/10.58613/jbb636

Journal of Biomedicine and Biosensors
ISSN (Online): 2583-3170

Journal homepage: https://gpub.org/journal-details.php?journal-id=45

Research Article

Assessment of Serum Ferritin Levels in Patients with Type 1 and Type 2 Diabetes Mellitus

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Article Info

Keywords: *Diabetes Mellitus, Type 1 Diabetes, Type 2 Diabetes, Serum Ferritin, HbA1c, Iron Metabolism, Oxidative Stress, Insulin Resistance, C-Peptide, Transferrin Saturation, Hyperferritinemia, Acute-Phase Reactant.*

Received: *04.08.2026;*
Accepted: *10.09.2026;*
Published: *16.09.2026*

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Abstract

Background: Diabetes Mellitus (DM) is a metabolic disease of chronic hyperglycemia. New evidence suggests that iron metabolism, specifically serum ferritin, is involved in its pathogenesis. **Objectives:** To evaluate and compare serum ferritin levels in patients with Type 1 DM (T1DM), Type 2 DM (T2DM) and healthy controls and to determine independent predictors of raised ferritin by multivariable analysis. **Methods:** 75 patients (29 T1DM, 21 T2DM and 25 age and sex matched healthy controls) were recruited in a cross-sectional study. Serum ferritin, HbA1c, C-peptide, transferrin saturation (TSAT) and fasting blood sugar were determined. One-way ANOVA test with Bonferroni post hoc test, Pearson's correlation and multiple linear regression (MLR) were used for data analysis. Normality was confirmed using the Shapiro-Wilk test and effect sizes are expressed as Cohen's d. **Results:** Ferritin was significantly elevated in T2DM (193.3 $\pm$ 65.4 ng/mL) compared to both T1DM (55.4 $\pm$ 32.1 ng/mL) and controls (62.1 $\pm$ 28.7 ng/mL), both P $<$0.001. There is no significant difference between the ferritin levels of T1DM and control (P = 0.84). MLR identified diabetes type (β = 0.61, P $<$0.001) and BMI (β = 0.22, P = 0.014) as the strongest independent predictors of ferritin (R^2 = 0.71). When confounders were taken into account, HbA1c was not an independent predictor (P = 0.152). **Conclusion:** Hyperferritinemia in T2DM is mainly due to insulin resistance and adiposity, not glycemic dyscontrol. Ferritin testing in T2DM may be useful to identify patients with greater inflammatory and oxidative risk, who should be studied over the long term. What is known: There is a link between iron metabolism and oxidative stress in diabetes mellitus. What is new: Factors influencing diabetes mellitus and iron metabolism include HbA1C, total iron binding protein, and serum ferritin.

1. Introduction

Diabetes Mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia due to defective insulin production, action or both. It can be diagnosed as Type 1 (T1DM) related to autoimmune damage to the beta cells or Type 2 (T2DM) associated with insulin resistance and relative insulin deficiency [1]. DM is a significant epidemic worldwide with increasing morbidity associated with vascular, renal and neurological complications [2]. Now, iron metabolism has come into light as a modulator of DM pathogenesis. Ferritin is the main intracellular iron-storage protein, and is a positive acute-phase reactant, which increases when inflammation occurs in a wider systemic

context [3]. Too much iron can create reactive oxygen species (ROS) through the Fenton reaction, leading to peripheral insulin resistance and beta-cell apoptosis [4]. High levels of ferritin have been associated with an increased risk of developing T2DM, even when metabolic risk factors are taken into account, in large prospective cohorts [5, 6].

Although these connections have been made, it has not been fully explored in comparative work whether the mechanism for ferritin upregulation in inflammatory diseases is the same or different from that induced by iron deposition. Furthermore, few previous studies included healthy control groups and/or failed to employ multivariable analyses to determine the independent effect of diabetes type, BMI, age, and glycemic control on ferritin levels.

Aims of the Study

Primary objective: To compare serum ferritin levels between three groups of subjects (T1DM, T2DM and healthy controls) using appropriate statistical methods such as one-way ANOVA, Bonferroni correction and effect size estimation.

Secondary aim: Using multiple linear regression model to identify independent predictors of ferritin elevation after adjusting for age, BMI, sex, disease duration and HbA1c.

Tertiary aim: To assess transferrin saturation index with ferritin to differentiate between actual iron overload and inflammatory hyperferritinemia in T2DM.

2. Methods

Study Design and Setting

The research was an Iraqi cross-sectional comparative study done at diabetes clinic in Najaf Governorate. The study was done in compliance with the Declaration of Helsinki.

Participants

They recruited participant to 3 groups:

Group 1 — T1DM (n=29): Confirmed Type 1 Diabetes.

Group 2 — T2DM (n=21): Type 2 Diabetes mellitus patients were those patients with confirmed Type 2 Diabetes.

Group 3 — Healthy Controls (n=25): Age and sex matched participants who had no history of diabetes, chronic disease or iron supplementation. Outpatients from a hospital with their accompanying family members were chosen for the controls. The addition of this group was to serve as a normative reference baseline for ferritin and to allow for comparisons between diabetic and non-diabetic iron status after the study was completed.

Inclusion Criteria

Diabetic groups: Age 15-70 years; confirmed diabetes medical records; diabetes duration >1 year; stable therapy > 6 months; complete lab data; no acute illness at sampling; BMI 18-35 kg/m^2; HbA1c 7-12%.

Control group: Age 18-70 years; fasting glucose <100 mg/dL; HbA1c < 5.7%; No chronic inflammatory, hepatic, renal or hematologic disease; No iron supplements or blood transfusion in past 6 months; non-pregnant.

Exclusion Criteria

The three groups differed in the exclusion of participants with: active infection or malignancy; chronic liver disease (ALT/AST > 3 × upper normal); chronic kidney disease (eGFR < 60); hemoglobinopathies (thalassemia, sickle cell); known hemochromatosis or iron overload; pregnancy; HbA1c > 20% or ferritin > 1000 ng/mL (suspected data error); medications significantly altering iron metabolism other than recorded supplements.

Questionnaire and Data Collection Sheet

The demographic characteristics and glycemic and iron profile parameters of the diabetic patients are presented in Table 1.

Laboratory Measurements

Serum Ferritin, C Peptide

500 μL of serum was transferred into a Hitachi cup and introduced into the Zybio fully-automated analyzer.

Result of ferritin: Press [FERRITIN] then press [START] and the result will be displayed in 28 minutes.

To check C-Peptide, press [C-P] to display, press [START] and display the result in 32 minutes.

Transferrin Saturation Calculated as:

$$\text{TSAT}(\%) = \frac{\text{Serum Iron}(\mu g/dL)}{\text{TIBC}(\mu g/dL)} \times 100.$$

Serum iron and TIBC colorimetrically measured on the same analyzer.

HbA1c

Measured by high-performance liquid chromatography (HPLC) or by laboratory standard operating procedure (immunoturbidimetry).

Table 1: Questionnaire and data collection sheet for demographic, glycemic and iron profile parameters among diabetic patients

Participant ID	_____
Sex (M/F)	Male / Female
Age (years)	_____
Height (cm)	_____
Weight (kg)	_____
Type (Diabetic / Control)	☐ T1DM ☐ T2DM ☐ Healthy Control
Duration of Diabetes (years)	_____ (N/A for Control)
Age at Diagnosis (years)	_____
Fasting Blood Glucose (mg/dL)	_____
HbA1c (%)	_____
C-peptide (ng/mL)	_____
Serum Ferritin (ng/mL)	_____
Serum Iron (µg/dL)	_____
Transferrin Saturation (%)	_____
TIBC (µg/dL)	_____
Blood Pressure (mmHg)	_____
Liver Function Status	☐ Normal ☐ Mild Elevation ☐ Abnormal
Anti-Diabetic Therapy	☐ Insulin ☐ Metformin ☐ Other
Iron/Vitamin Supplements	☐ Yes (specify): _____ ☐ No
CRP (mg/L) [Optional]	_____
Comorbidities / Notes	_____

Statistical Analysis

Data were analyzed statistically in SPSS v26. A significance level of $P < 0.05$ was used.
In order to perform parametric testing,
Step 1 — Normality testing: Shapiro-Wilk test [7] was performed for all continuous variables. Variables that had a $P > 0.05$ were assumed to be normally distributed. Homogeneity of variances was examined using the Levene test.
Step 2 — Group comparisons: One-way ANOVA was conducted to compare the levels of ferritin, HbA1c, BMI, and transferrin saturation among the three groups. A familywise error rate was controlled using Bonferroni post-hoc correction.
Step 3 — Effect size: Cohen's d [8] calculated for each significant pairwise comparison, d = 0.2 (small), 0.5 (medium) and ≥ 0.8 (large effect).
Step 4 — Correlation analysis: Pearson's r was calculated for normally distributed continuous variables. As there was a small sample (N=50 diabetic patients), only the correlations which showed $|r| \geq 0.30$ and $P < 0.05$ were practically meaningful. The T1DM and T2DM subgroups were analyzed separately in order to avoid Simpson's paradox obscuring differences between the subgroups.
Step 5 – Multiple linear regression (MLR): The serum ferritin was used as a dependent variable and a hierarchical MLR model [9] was developed. Demographic data (age, sex, BMI) were entered into Block 1. Clinical variables (diabetes type, duration of diabetes, HbA1c) were entered in Block 2. The Variance Inflation Factor (VIF < 5 = acceptable) was used to evaluate multicollinearity. The Shapiro-Wilk test was used for normality of residuals on standardized residuals and was found to be satisfactory. Incremental contribution of each block was assessed by the F-change test.
Step 6 — Point-biserial correction: The correlation between ferritin (continuous) and diabetes type (binary) was computed as a point-biserial rpb, rpb = 0.78 = Cohen's d = 2.5 (very large effect) indicating that the difference was substantially clinically significant, not just statistically.

3. Results

3.1. Demographic and Clinical Characteristics

All of these subjects were enrolled (25 healthy controls, 21 T2DM and 29 T1DM). Details of demographic and baseline clinical data are presented in Table 2. The T2DM group was significantly older (mean 48.3 $\pm$ 9.1 years) than T1DM (22.4 $\pm$ 5.8 years) and controls (38.6 $\pm$ 10.2 years; $P < 0.001$). The groups were balanced in terms of sex (P = 0.98). The BMI of the patients with T2DM was significantly higher than of T1DM patients and controls (P = 0.003). There was a significant increase in both diabetic groups when compared to controls, with regards to fasting blood sugar ($P < 0.001$).

Table 2: Demographic and Clinical Characteristics of All Groups

Parameter	T1DM (n=29)	T2DM (n=21)	Control (n=25)	P-value
Age (years)	22.4 ± 5.8	48.3 ± 9.1	38.6 ± 10.2	<0.001*
Sex (M/F)	15/14	11/10	13/12	0.98 (NS)
BMI (kg/m²)	24.1 ± 4.8	28.4 ± 5.2	24.8 ± 4.1	0.003*
Disease Duration (years)	6.2 ± 3.9	9.1 ± 5.4	N/A	0.04*
FBS (mg/dL)	178.3 ± 42.1	194.6 ± 55.3	88.4 ± 10.5	<0.001*

Data presented as Mean $\pm$ SD unless stated. NS = Not Significant. * $P < 0.05$.
ANOVA with Bonferroni post-hoc correction.

3.2. Comparison of Biochemical Parameters Across Three Groups

The main biochemical results are given in Table 3. One-way ANOVA revealed significant group differences in ferritin ($F(2,72) = 48.3$, $P < 0.001$), HbA1c ($F(2,72) = 112.4$, $P < 0.001$), C-peptide ($F(2,72) = 87.1$, $P < 0.001$), and transferrin saturation ($F(2,72) = 9.7$, $P < 0.001$). The HbA1c and C-peptide were normally distributed as determined by Shapiro-Wilk testing ($P > 0.05$). Ferritin in the T2DM group was slightly right skewed ($W = 0.94$, $P = 0.24$), but this was within acceptable value for parametric analysis ($N > 20$).

Table 3: Biochemical Parameters by Group (with Control Comparison)

Parameter	T1DM (n=29)	T2DM (n=21)	Control (n=25)	P-value
Serum Ferritin (ng/mL)	55.4 ± 32.1	193.3 ± 65.4	62.1 ± 28.7	<0.001*
HbA1c (%)	8.01 ± 0.9	8.15 ± 1.1	5.2 ± 0.4	<0.001*
C-Peptide (ng/mL)	0.45 ± 0.2	2.18 ± 0.8	1.85 ± 0.6	<0.001*
Transferrin Sat. (%)	26.1 ± 8.4	34.8 ± 9.1	25.3 ± 7.2	0.001*

Data as Mean ± SD. TSAT = Transferrin Saturation. One-way ANOVA; * $P < 0.05$ after Bonferroni correction. NS = Not Significant.

3.3. Post-Hoc Pairwise Comparisons for Serum Ferritin

According to the Bonferroni-corrected post hoc analysis Table 4, the T2DM group had a higher concentration than T1DM and control groups ($P < 0.001$, mean difference +137.9 and +131.2 ng/mL, respectively) but no difference between T1DM and control groups ($P = 0.84$, mean difference -6.7 ng/mL). This is a very important discovery because it shows that there is no difference between the ferritin levels of patients with T1DM and healthy controls, but T2DM ferritin is pathologically elevated in both. Note that Cohen's d for T2DM vs T1DM = 2.7 (very large effect).

Table 4: Post-Hoc Pairwise Comparisons for Serum Ferritin (Bonferroni Correction)

Comparison	Mean Diff.	P (Bonferroni)	Interpretation
T2DM vs. T1DM	+137.9	<0.001*	Highly Significant
T2DM vs. Control	+131.2	<0.001*	Highly Significant
T1DM vs. Control	-6.7	0.84 (NS)	Not Significant (T1DM ≈ Control)

Post-hoc analysis following significant one-way ANOVA ($F(2,72) = 48.3$, $P < 0.001$).

3.4. Gender-Stratified Ferritin Analysis

The results presented by sex Table 5 reveal that males tended to have a higher ferritin than females in each group as per the lower and upper limits of physiological reference range, but both males and females of the T2DM group had higher ferritin than upper limits of their sex-specific ranges. The blood glucose levels of males with T1DM (61.2 ng/mL) and females with T1DM (49.8 ng/mL) were normal. Measures were concordant with T1DM and thus yielded convergent validity of the reference values.

Table 5: Gender-Stratified Serum Ferritin with Sex-Specific Reference Ranges

Group	Gender	Mean Ferritin (ng/mL)	Reference Range
T1DM	Male	61.2 ± 28.5	12-300 ng/mL (Normal)
	Female	49.8 ± 34.1	12-150 ng/mL (Normal)
T2DM	Male	210.5 ± 55.2	12-300 ng/mL (Elevated)
	Female	179.8 ± 71.3	12-150 ng/mL (Above Normal)
Control	Male	65.3 ± 24.1	12-300 ng/mL (Normal)
	Female	51.8 ± 22.9	12-150 ng/mL (Normal)

Reference ranges applied per IFCC guidelines: Males 12–300 ng/mL; Females 12–150 ng/mL. T2DM females (179.8 ng/mL) exceed the female upper limit; T2DM males are within range but close to upper normal, contextually elevated given disease burden.

3.5. Correlation Analysis

The Pearson's correlation coefficients are shown in Table 6. The overall correlation between ferritin and HbA1c ($r = 0.32$, $P = 0.04$) was significant, but not for T1DM alone ($r = 0.09$, $P = 0.64$) which was largely attributed to the T2DM group ($r = 0.47$, $P = 0.03$). This subgroup-stratified analysis is important because it will not lead to the ecological fallacy of assuming a pooled correlation is representative of both subtypes. There was a moderate correlation between ferritin and BMI ($r = 0.52$, $P = 0.001$) and transferrin saturation ($r = 0.63$, $P < 0.001$) with the latter indicating that part of the ferritin rise in T2DM is driven by true elevation in iron stores rather than inflammation.

Table 6: Pearson's Correlation Coefficients between Serum Ferritin and Key Variables

Variables	R	P-value	Interpretation
Ferritin vs. Diabetes Type	0.78	<0.001	Strong Positive Correlation
Ferritin vs. HbA1c (Overall)	0.32	0.04*	Weak Positive Correlation (interpret with caution, N=50)
Ferritin vs. HbA1c (T2DM only)	0.47	0.03*	Moderate Positive Correlation
Ferritin vs. HbA1c (T1DM only)	0.09	0.64 (NS)	No Significant Correlation
Ferritin vs. Age	0.41	0.02*	Moderate Correlation
Ferritin vs. BMI	0.52	0.001*	Moderate-Strong Correlation
Ferritin vs. Disease Duration	0.15	0.22 (NS)	No Significant Correlation
Ferritin vs. Transferrin Saturation	0.63	<0.001	Strong Correlation

$P < 0.05$. NS = Not Significant. r-values for "Diabetes Type" computed as point-biserial r, appropriate for binary grouping variables. Subgroup r-values computed independently within each diabetes type.

3.6. Multiple Linear Regression Analysis — Independent Predictors of Ferritin

A hierarchical MLR was conducted to identify variables that were predictive of serum ferritin independent of other variables Table 7. The full model explained 71% of ferritin variance ($R^2 = 0.71$, Adjusted $R^2 = 0.67$, F(6,43) = 17.6, P <0.001).

The three independent predictors that were significant were:

- The strongest predictor was diabetes type (T2DM vs. T1DM) with a standardized β of 0.61 ($P < 0.001$) which indicated that the diagnosis of T2DM is an independent factor for increasing the concentration of ferritin by about 118 ng/mL after adjusting for all other variables.
- BMI was an independent contributor to the levels of ferritin ($\beta = 0.22$, P = 0.014), contributing about 4.8 ng/mL per unit increment of BMI, which is indicative of the relationship between adiposity and inflammation.
- Age was an independent modest contributor ($\beta = 0.18$, P = 0.038).
- After adjusting for diabetes type and BMI, HbA1c was NOT found to be an independent predictor ($\beta = 0.11$, P = 0.152). This is an important finding, indicating that there is likely an interaction between disease type and adiposity that biases the apparent ferritin–HbA1c correlation observed in univariate analyses.

Table 7: Multiple Linear Regression — Independent Predictors of Serum Ferritin

Predictor Variable	β (Unstd.)	Std. Error	β (Std.)	P-value	95% CI
Diabetes Type (T2DM vs T1DM)	118.4	18.2	0.61	<0.001*	[82.1 - 154.7]
BMI (kg/m²)	4.8	1.9	0.22	0.014*	[1.0 - 8.6]
Age (years)	1.3	0.6	0.18	0.038*	[0.1 - 2.5]
HbA1c (%)	6.1	4.2	0.11	0.152 (NS)	[-2.3 - 14.5]
Disease Duration (years)	0.9	1.1	0.06	0.411 (NS)	[-1.3 - 3.1]
Sex (Male=1)	21.3	14.6	0.12	0.151 (NS)	[-7.8 - 50.4]

Model fit: $R^2 = 0.71$, Adjusted $R^2 = 0.67$, F(6,43) = 17.6, $P < 0.001$. Dependent variable: Serum Ferritin (ng/mL).
Variance Inflation Factor (VIF) < 3.0 for all predictors, confirming absence of multicollinearity.
Normality of residuals confirmed by Shapiro-Wilk test (P = 0.24).

4. Discussion

The Central Finding: T2DM-Specific Hyperferritinemia vs. Normal Ferritin in T1DM: The most striking finding of this study is that the ferritin levels in T2DM patients are pathologically elevated relative to both T1DM patients and healthy controls, and that ferritin levels in both T1DM patients and healthy controls are not statistically different (P = 0.84). This finding offers two important messages: first, hyperferritinemia did not occur in all patients with diabetes, but only in patients with T2DM, even when both sets of patients have had poor glycemic control (HbA1c > 8%); second, the ferritin levels in T1DM are not different from healthy controls, indicating that the autoimmune disease process (in the absence of metabolic syndrome) does not have a chronic effect on iron homeostasis. It is consistent with Jiang et al. [5] and Bonfils et al. [10] and is in contrast to the simplistic notion that all types of diabetes increase ferritin.

Mechanistic Interpretation: Inflammation-Adiposity Rather Than Glycemia is responsible for the increase in Ferritin in T2DM: The MLR analysis clearly shows that type of diabetes and BMI, and not HbA1c, are factors independently associated with increased ferritin levels. This is a significant improvement compared to the univariate correlation analysis (r = 0.32) between ferritin and HbA1c where all the correlation was observed in the T2DM group, as revealed in the subgroup analysis. The following is concluded hereafter, after controlling for disease type and BMI: HbA1c does not have predictive power (P = 0.152) meaning that the increase in HbA1c in T2DM is not a phenomenon of glucose-toxicity, but rather a phenomenon of adiposity and inflammation. Ferritin in T2DM should be regarded as the indicator of the metabolic syndrome milieu, rather than as a marker of glycemic control, as this milieu is produced by visceral fat by producing IL-6 [11] and TNF-α which promotes the synthesis of hepatic ferritin [3].

This section covers the iron overload-inflammatory hyperferritinemia relationship: The moderate correlation between ferritin and TSAT (r = 0.63, $P < 0.001$) in T2DM patients, in addition to the mean TSAT (34.8%) that is elevated but not high enough to be a diagnostic criterion for iron overload, suggest an intermediate picture: some part of the elevation of ferritin in T2DM reflects actual increased amounts of iron stores, consistent with DIOS [12], and the rest reflects inflammatory process. This difference has clinical implications as patients with

T2DM and a TSAT $>$ 45% might be candidates for stool testing for secondary hemochromatosis or DIOS and might benefit from therapeutic phlebotomy [4]. Conversely, individuals with high ferritin levels and normal levels of TSAT should not be treated with iron reduction, but instead with anti-inflammatory metabolic management, such as weight reduction, exercise and anti-inflammatory medications.

Reinterpreting the Ferritin–HbA1c Relationship

The modest overall r = 0.32 between ferritin and HbA1c hides, however, important heterogeneity: moderate (and clinically relevant) association in T2DM (r = 0.47, P = 0.03); no association in T1DM (r = 0.09, P = 0.64). This difference is in line with the biological model, where the inflammatory and metabolic processes that affect the regulation of glycemia overlap and underlie the difference in ferritin levels between T1DM and T2DM, but do not directly cause the elevation of ferritin. It is still possible that glycated ferritin, free iron, oxidative stress and then, worsened HbA1c [13] are amplifying mechanisms in T2DM and should not be applied to T1DM without independent evidence.

Gender analysis and contextualization of reference ranges

Gender-specific analysis revealed that females with T2DM (179.8 ng/mL) exceed the upper reference limit of 150 ng/mL for females and males with T2DM (210.5 ng/mL) are approaching, but not exceeding, the male upper reference limit (300 ng/mL). This apparent sex dimorphism in "clinical significance" highlights the need for sex-specific interpretation, which is not consistently adopted in previous literature [14]. Of note, T1DM males and females were not significantly elevated either and again demonstrate the T2DM specificity of ferritin elevation in this study.

The results are compared to published literature in Section.

The mean for our T2DM (193.3 ng/mL) is comparable to Canturk et al. [15] (poorly controlled T2DM: $\sim$ 185 ng/mL) and Padwal et al. [16] ($\sim$ 198 ng/mL). In the EPIC-Norfolk study [6] level of ferritin in the highest quartile ($>$170 ng/mL in women and $>$ 285 ng/mL in men) was associated with a 2.4 fold greater risk of T2DM over 10 years. Our T2DM females (179.8 ng/mL) are also in this high risk quartile, indicating that the current cohort has a similar risk profile. The values for T1DM (55.4 ng/mL) are consistent with those of the controls from the same study population (62.1 ng/mL).

Weaknesses and Limitations

Weaknesses: (1) Inclusion of a healthy control group in which the results can be compared to a normative sample that is not available in most local studies; (2) Multiple linear regression with six potential confounders controlled simultaneously; (3) Transferrin saturation measured along with ferritin to distinguish iron overload from inflammatory hyperferritinemia; (4) Diabetes was biochemically confirmed using C-peptide; (5) Effect sizes (Cohen's d) reported for all major comparisons; (6) Subgroup-stratified correlations, thus avoiding the ecological fallacy.

Limitations: (1) Cross-sectional design precludes causal inference; (2) small sample (N=75) limits statistical power for sub-group analyses and may give unstable regression coefficients; (3) CRP and IL-6 were not measured thus iron sequestration due to inflammation was not directly quantified; (4) Dietary iron intake was not assessed; (5) convenienced sampling at one centre limits generalizability.

5. Conclusions

T2DM-specific hyperferritinemia: The hyperferritinemia is statistically significantly higher in T2DM than in T1DM and healthy controls (P $<$ 0.001, Cohen's d = 2.7). There is no statistical difference between T1DM and healthy controls (P = 0.84), confirming that hyperferritinemia is not a typical part of chronic hyperglycemia but is a part of the metabolic milieu seen in T2DM. There is a high correlation between adiposity and disease type (type 1 diabetes vs type 2 diabetes), rather than glycemia, and ferritin (Conclusion 2). These confounders do not explain the relationship between HbA1c and ferritin independently (P = 0.152). This clearly indicates that high ferritin in T2DM is linked to insulin resistance and inflammation from the fat and not simply due to glucose toxicity.
Mixed iron overload and inflammation in T2DM: The moderate ferro-TSAT correlation (r = 0.63) and the mean ferro-TSAT level of 34.8% in T2DM indicate a mixed mechanism: some iron accumulation is true, which is characteristic of DIOS, and another is inflammatory upregulation. Ferritin and TSAT should be measured together to inform clinical management decisions.
Subgroup-specific ferritin–HbA1c correlation: The ferritin–HbA1c correlation was only present in the T2DM subgroup (r = 0.47, P = 0.03) but not for the T1DM group (r = 0.09, P = 0.64). The overall correlation should not be averaged over the different diabetes types because this will not reveal this biological difference.

Article Information

Funding: This research received no external funding.

Author Contributions: Z.A.A.N. - Writing – review & editing, Supervision; A.N.A. - Conceptualization, Writing – original draft; B.A.A. - Methodology, Formal analysis; M.A.A. - Data curation.

Ethical Approval: The study was approved by the Ethical Committee of the University of Kufa, Iraq. All procedures involving human participants were performed in accordance with the ethical standards of the institutional research committee and the Helsinki Declaration.

Informed Consent: Informed consent was obtained from all participants involved in the study.

Conflict of Interest: The authors declare no competing interests.

Data Availability Statement: The data used in this study are available from the corresponding author upon reasonable request, subject to the preservation of participant confidentiality and privacy.

Clinical Trial Registration: Not applicable.

Reporting Guidelines Statement: Not applicable.

Acknowledgments: The authors wish to express their sincere thanks and gratitude to the staff of the Diabetes Clinic in Najaf Governorate and to all the participants who contributed to this study.

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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