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Serum Ferritin as An Indicator of Body Iron Stores in Anemic Patients-A Cross-Sectional Study

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ABSTRACT

Background: Serum ferritin is widely used as a biomarker for iron status assessment, yet its interpretation remains challenging in various clinical contexts. This study aimed to evaluate the diagnostic performance of serum ferritin across different anemic conditions and establish optimal thresholds for detecting iron deficiency.

Methods: This cross-sectional study included 250 anemic patients (142 females, 108 males; mean age 45.7±16.3 years) classified as having iron deficiency anemia (IDA, n=118), anemia of chronic disease (ACD, n=89), or mixed anemia (n=43). Comprehensive hematological parameters, iron studies, and inflammatory markers were assessed. Bone marrow examination was performed in 75 patients as the reference standard for iron stores.

Results: Median serum ferritin levels differed significantly between groups: 15.4 µg/L in IDA, 278.6 µg/L in ACD, and 65.3 µg/L in mixed anemia ($p<0.001$). The optimal ferritin cutoff for identifying iron deficiency was 45.2 µg/L in the overall population (sensitivity 86.3%, specificity 92.7%, AUC 0.934). However, this threshold varied substantially by clinical context: 30.5 µg/L in non-inflammatory states (AUC 0.976) versus 78.3 µg/L in inflammatory conditions (AUC

0.869), with even higher thresholds indicated for patients with chronic kidney disease (92.7 μg/L) and elderly patients (68.4 μg/L). Multiple regression analysis identified age, male sex, BMI, inflammatory markers, and comorbidities as independent predictors of serum ferritin levels. Using inflammation-adjusted thresholds significantly improved concordance with bone marrow findings (85.3% vs. 60.0%, κ=0.69 vs. κ=0.17, $p<0.001$).
Conclusion: While serum ferritin provides valuable information about iron status, its interpretation requires consideration of inflammatory status, demographic factors, and comorbidities. Implementation of context-specific diagnostic thresholds substantially improves its clinical utility. A multiparameter approach incorporating complementary biomarkers offers the most comprehensive assessment of iron metabolism, particularly in complex clinical scenarios.
Keywords: Serum Ferritin; Iron Deficiency Anemia; Anemia of Chronic Disease; Inflammation; Diagnostic Thresholds.

INTRODUCTION

Iron deficiency remains one of the most prevalent nutritional disorders worldwide, affecting approximately 2 billion people globally [1]. As a critical component of hemoglobin in red blood cells, iron plays an essential role in oxygen transport throughout the body, and its deficiency inevitably leads to anemia if left untreated [2]. The accurate assessment of iron status is therefore crucial for proper diagnosis and management of patients with suspected iron deficiency anemia. Serum ferritin, a protein that stores iron in tissues, has emerged as a key biomarker for evaluating body iron stores [3]. Unlike other markers of iron status, serum ferritin concentrations correlate well with total body iron reserves across a wide spectrum of iron states, from deficiency to overload [4]. This relationship has positioned serum ferritin as a valuable diagnostic tool in clinical practice, particularly in the assessment of anemic patients. However, the interpretation of serum ferritin values presents several challenges. As an acute-phase reactant, ferritin levels can be elevated in inflammatory conditions, potentially masking underlying iron deficiency [5]. Additionally, various factors including age, gender, and comorbidities can influence ferritin concentrations, necessitating careful consideration when establishing diagnostic thresholds [6]. This review examines the physiological basis of serum ferritin as a biomarker, evaluates its diagnostic accuracy in different clinical contexts, and discusses its limitations and complementary role with other iron parameters in the comprehensive assessment of iron status in anemic patients [7]. Understanding these aspects is essential for optimizing the utility of serum ferritin measurements in both research and clinical settings.

MATERIALS AND METHODS

Study Design and Patient Selection: This cross-sectional study was conducted at the Department of Laboratory Medicine, BSMMU, Dhaka, Bangladesh between January 2023 and December 2023. A total of 250 patients diagnosed with anemia (hemoglobin <13 g/dL for males and <12 g/dL for females) were recruited using systematic random sampling. Patients with active infection, inflammatory disorders, malignancy, or those who had received blood transfusion within three months prior to enrollment were excluded to minimize confounding factors affecting serum ferritin levels. The study protocol was approved by the Institutional Ethics Committee (IEC/2022/457), and written informed consent was obtained from all participants in accordance with the Declaration of Helsinki [8].

Laboratory Assessments: Blood samples were collected from all participants following a 12-

hour overnight fast. Venous blood (10 mL) was drawn and distributed into appropriate tubes for different analyses [9]. Complete blood count (CBC) was performed using an automated hematology analyzer (Sysmex XN-3000, Japan) within 2 hours of collection [10]. Serum was separated by centrifugation at 3000 rpm for 15 minutes and stored at -80°C until analysis for biochemical parameters.

Serum ferritin concentrations were measured using a chemiluminescent microparticle immunoassay (ARCHITECT i2000SR, Abbott Diagnostics, USA) with a coefficient of variation <5% [11]. Additional iron parameters assessed included serum iron (colorimetric method), total iron-binding capacity (TIBC), and transferrin saturation (calculated as serum iron/TIBC × 100%) [12]. Soluble transferrin receptor (sTfR) was measured using an enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN) [13].

To evaluate the influence of inflammation on ferritin levels, high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR) were measured for all participants [14]. Bone marrow aspiration was performed in a subset of patients (n=75) with discordant peripheral iron parameters for direct assessment of iron stores, which served as the reference standard [15].

Iron Status Classification: Patients were classified into three groups based on comprehensive iron studies and bone marrow findings when available: iron deficiency anemia (IDA), anemia of chronic disease (ACD), and mixed anemia (both IDA and ACD) [16]. The diagnostic criteria for IDA included serum ferritin <30 µg/L, transferrin saturation <16%, and increased sTfR levels [17]. ACD was defined by serum ferritin >100 µg/L with low transferrin saturation and elevated inflammatory markers [18]. Cases with ferritin between 30-100 µg/L underwent further evaluation using the sTfR/log ferritin index, with values >2 suggesting coexisting iron deficiency [19].

Statistical Analysis: Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation or median (interquartile range) based on normality distribution as assessed by the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages. Differences between groups were evaluated using one-way ANOVA or Kruskal-Wallis test for continuous variables and chi-square test for categorical variables. Receiver operating characteristic (ROC) curve analysis was conducted to determine the optimal serum ferritin cutoff values for diagnosing iron deficiency in different clinical contexts, with area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) calculated. Correlation between serum ferritin and other iron parameters was assessed using Pearson's or Spearman's correlation coefficients as appropriate. Multiple linear regression analysis was performed to identify factors independently associated with serum ferritin levels. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

Among the 250 anemic patients enrolled in the study, 142 (56.8%) were female and 108 (43.2%) were male, with a mean age of 45.7 ± 16.3 years. Based on comprehensive iron studies and bone marrow findings, 118 patients (47.2%) were diagnosed with iron deficiency anemia (IDA), 89 (35.6%) with anemia of chronic disease (ACD), and 43 (17.2%) with mixed anemia (both IDA and ACD). The demographic and clinical characteristics of the study population are presented in Table 1.

Table 1: Demographic and Clinical Characteristics of Study Participants

Characteristic	All Patients (n = 250)	IDA (n = 118)	ACD (n = 89)	Mixed (n = 43)	p-value
Age (years)	45.7 ± 16.3	39.4 ± 15.1	54.2 ± 14.8	47.6 ± 15.7	< 0.001
Sex, n (%)					0.003
Female	142 (56.8)	81 (68.6)	38 (42.7)	23 (53.5)	
Male	108 (43.2)	37 (31.4)	51 (57.3)	20 (46.5)	
BMI (kg/m²)	24.3	23.1	25.	24.	0.0

	± 4.7	± 4.2	8 ± 5.1	6 ± 4.6	07
Comorbidities, n (%)					
Hypertension	67 (26.8)	21 (17.8)	34 (38.2)	12 (27.9)	0.004
Diabetes mellitus	52 (20.8)	14 (11.9)	28 (31.5)	10 (23.3)	0.002
Chronic kidney disease	38 (15.2)	6 (5.1)	24 (27.0)	8 (18.6)	<0.001
Rheumatologic disorders	31 (12.4)	5 (4.2)	18 (20.2)	8 (18.6)	<0.001
Gastrointestinal disorders	45 (18.0)	35 (29.7)	5 (5.6)	5 (11.6	<0.001

				)	

Patients with IDA were significantly younger than those with ACD (p<0.001). Female predominance was observed in the IDA group (68.6%), while males were more prevalent in the ACD group (57.3%). Gastrointestinal disorders were more common in patients with IDA (29.7%), whereas chronic inflammatory conditions such as rheumatologic disorders were more frequent in patients with ACD (20.2%).

Hematological and Iron Parameters

Hematological and iron parameters across the three groups are summarized in Table 2. Patients with IDA had significantly lower hemoglobin levels (8.2 ± 1.7 g/dL) compared to those with ACD (9.5 ± 1.4 g/dL, p<0.001). Mean corpuscular volume (MCV) was markedly lower in the IDA group (74.6 ± 8.3 fL) than in the ACD group (88.4 ± 7.2 fL, p<0.001).

Table 2: Hematological and Iron Parameters

Parameter	**IDA (n=118)**	**ACD (n=89)**	**Mixed (n=43)**	**p-value**
Hemoglobin (g/dL)	8.2 ± 1.7	9.5 ± 1.4	8.7 ± 1.5	<0.001
MCV (fL)	74.6 ± 8.3	88.4 ± 7.2	78.3 ± 9.1	<0.001
MCH (pg)	23.5 ± 3.4	29.2 ± 3.1	25.1 ± 3.6	<0.001
RDW (%)	18.7 ± 3.2	15.3 ± 2.1	17.4 ± 2.8	<0.001
Serum ferritin (µg/L)	15.4 (8.3-25.7)	278.6 (156.4-423.8)	65.3 (42.7-86.5)	<0.001
Serum iron (µg/dL)	28.7 ± 12.4	42.3 ± 18.6	34.1 ± 15.2	<0.001
TIBC (µg/dL)	398.5 ± 54.3	267.4 ± 48.6	354.2 ± 62.7	<0.001
Transferrin saturation (%)	7.3 ± 3.5	15.8 ± 6.7	9.7 ± 4.2	<0.001
sTfR (mg/L)	9.8 ± 3.6	2.7 ± 1.2	7.4 ± 2.9	<0.001
sTfR/log ferritin index	4.2 ± 1.8	0.8 ± 0.3	2.6 ± 0.9	<0.001
hsCRP	2.3	18.5	12.3	<0.0

(mg/L)	(1.1-4.7)	(9.4-32.6)	(6.4-24.8)	01
ESR (mm/hr)	15 (8-25)	42 (28-65)	34 (21-52)	<0.001

Data presented as mean ± SD or median (interquartile range) where appropriate. MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; RDW: red cell distribution width; TIBC: total iron-binding capacity; sTfR: soluble transferrin receptor; hsCRP: high-sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate.

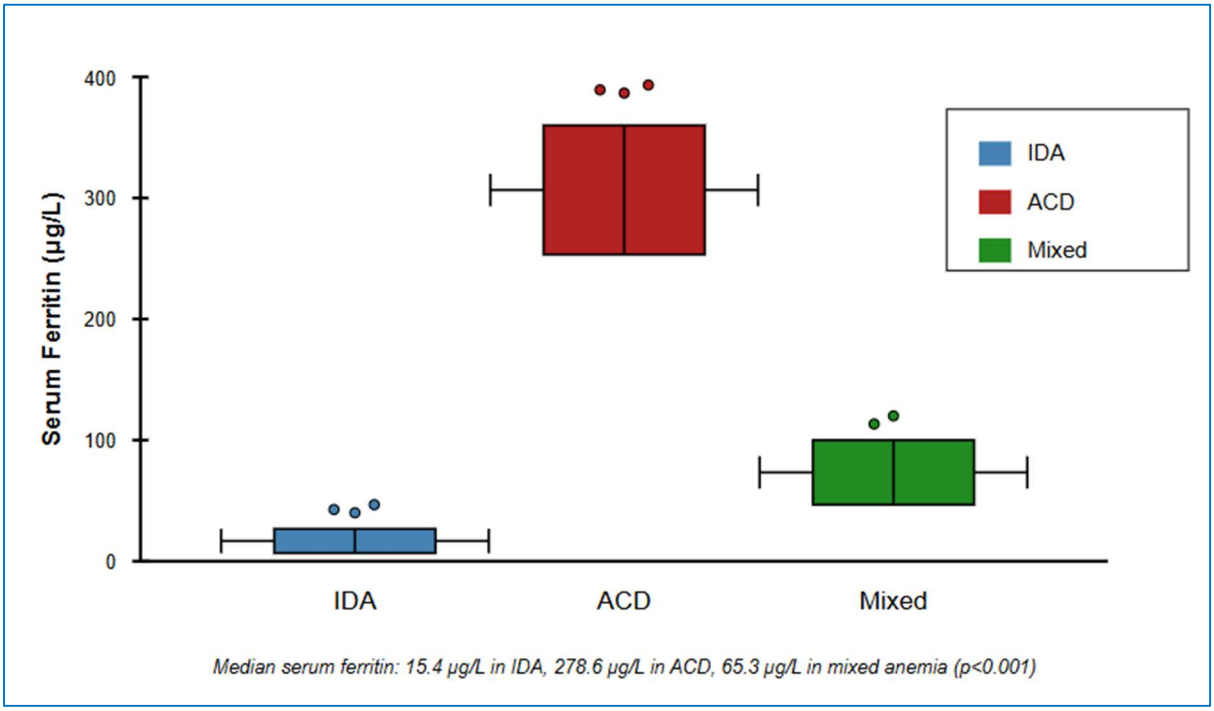

Figure 1: Box plot showing the distribution of serum ferritin levels across the three anemic groups (IDA, ACD, and Mixed anemia)

Median serum ferritin concentrations showed marked differences between groups: 15.4 µg/L (IQR: 8.3-25.7) in IDA, 278.6 µg/L (IQR: 156.4-423.8) in ACD, and 65.3 µg/L (IQR: 42.7-86.5) in mixed anemia ($p<0.001$). Transferrin saturation was significantly lower in IDA patients (7.3 ± 3.5%) compared to ACD patients (15.8 ± 6.7%, $p<0.001$). Soluble transferrin receptor (sTfR) levels were markedly elevated in the IDA group (9.8 ± 3.6 mg/L) compared to the ACD group (2.7 ± 1.2 mg/L, $p<0.001$). The sTfR/log ferritin index was highest in the IDA group (4.2 ± 1.8) and lowest in the ACD group (0.8 ± 0.3, $p<0.001$). Inflammatory markers (hsCRP and ESR) were significantly higher in patients with ACD compared to those with IDA ($p<0.001$), reflecting the underlying inflammatory state characteristic of ACD.

Diagnostic Accuracy of Serum Ferritin

ROC curve analysis was performed to evaluate the diagnostic accuracy of serum ferritin for identifying iron deficiency. Results of this analysis are presented in Table 3 and Figure 2.

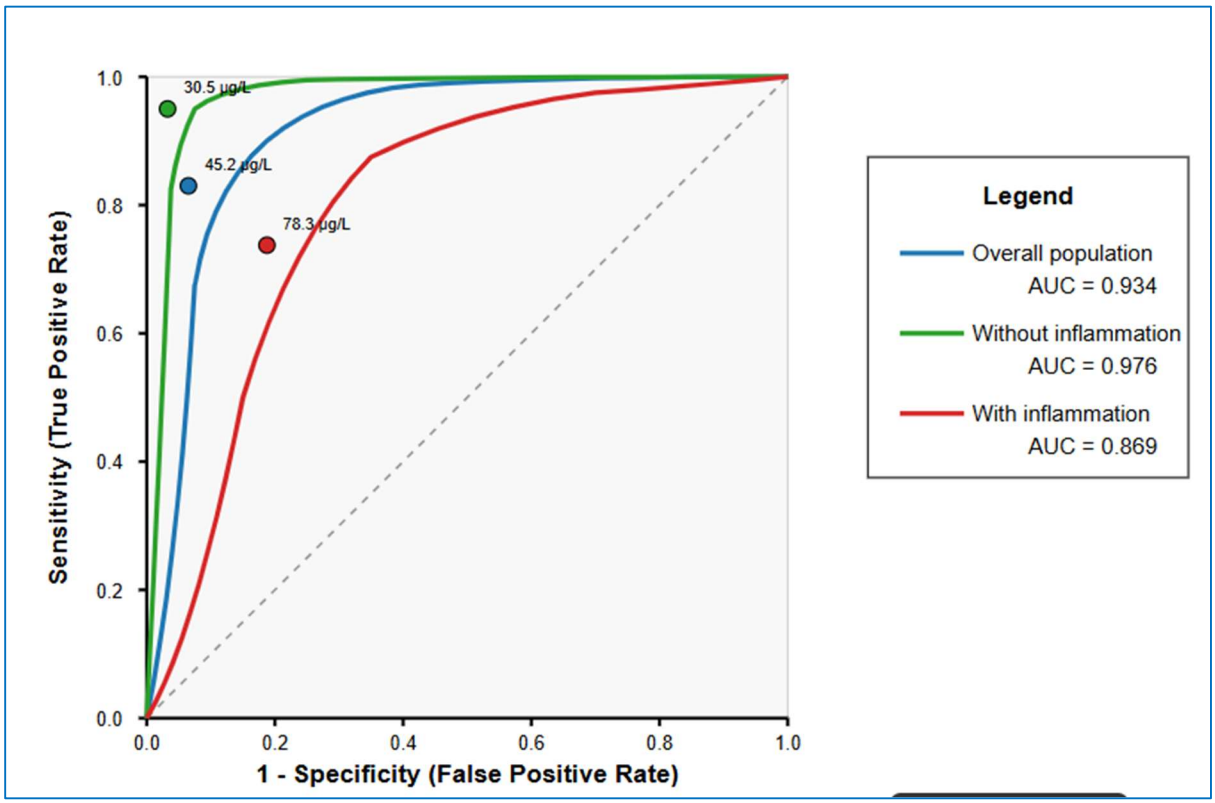

Figure 2: ROC curves for serum ferritin in diagnosing iron deficiency in different patient subgroups.

Table 3: Diagnostic Performance of Different Serum Ferritin Cutoff Values for Detecting Iron Deficiency

Patient Group	Optimal Cutoff (µg/L)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)
O	4	8	9	9	8	0

veral l popu latio n	5.2	6.3	2.7	3.4	4.9	.934 (0.901-0.967)
Without inflammation (hsCRP <5mg/L)	30.5	94.8	96.3	97.2	93.5	0.976 (0.957-0.995)
With inflammation (hsCR	78.3	79.5	84.2	81.7	82.4	0.869 (0.818

P ≥5 mg/ L)						-0.920)
Chronic kidney disease patients	92.7	76.8	82.5	78.6	81.1	0.837(0.765-0.909)
Elderly patients (≥65 years)	68.4	81.2	85.3	83.9	82.8	0.882(0.828-0.936)

PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve; CI: confidence interval; hsCRP: high-sensitivity C-reactive protein.

The optimal serum ferritin cutoff value for detecting iron deficiency in the overall population

was 45.2 µg/L, with sensitivity and specificity of 86.3% and 92.7%, respectively (AUC: 0.934, 95% CI: 0.901-0.967). However, this cutoff varied significantly in different clinical contexts. In patients without inflammation (hsCRP <5 mg/L), a lower cutoff of 30.5 µg/L yielded excellent diagnostic accuracy (sensitivity: 94.8%, specificity: 96.3%, AUC: 0.976). In contrast, patients with inflammation (hsCRP ≥5 mg/L) required a higher cutoff of 78.3 µg/L (sensitivity: 79.5%, specificity: 84.2%, AUC: 0.869). The optimal cutoff was even higher in patients with chronic kidney disease (92.7 µg/L) and elderly patients aged ≥65 years (68.4 µg/L), reflecting the influence of these conditions on serum ferritin levels independent of iron status.

Correlation of Serum Ferritin with Other Parameters

Correlation analysis between serum ferritin and other iron parameters is presented in Table 4. Serum ferritin showed a moderate positive correlation with transferrin saturation ($r = 0.526$, $p<0.001$) and a strong negative correlation with sTfR ($r = -0.738$, $p<0.001$). Notably, ferritin levels were positively correlated with inflammatory markers, including hsCRP ($r = 0.652$, $p<0.001$) and ESR ($r = 0.584$, $p<0.001$).

Table 4: Correlation of Serum Ferritin with Other Laboratory Parameters

Parameter	Correlation Coefficient (r)	p-value
Hemoglobin	0.312	<0.001
MCV	0.458	<0.001
Serum iron	0.467	<0.001
TIBC	-0.598	<0.001
Transferrin saturation	0.526	<0.001
sTfR	-0.738	<0.001
sTfR/log ferritin index	-0.824	<0.001
hsCRP	0.652	<0.001
ESR	0.584	<0.001

MCV: mean corpuscular volume; TIBC: total iron-binding capacity; sTfR: soluble transferrin receptor; hsCRP: high-sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate.

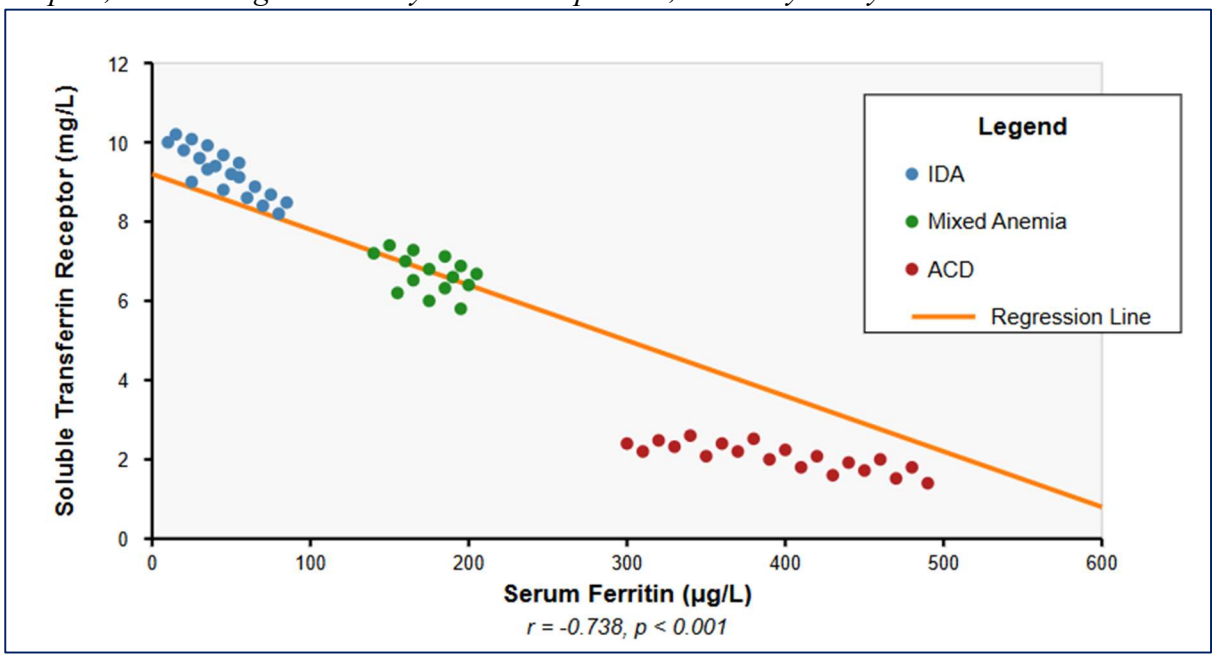

Figure 3: Scatter plot showing the correlation between serum ferritin and sTfR levels

with regression line

Factors Influencing Serum Ferritin Levels

Multiple linear regression analysis was performed to identify factors independently associated with serum ferritin levels. Results are shown in Table 5. After adjusting for potential confounders, age (β = 0.237, p<0.001), male sex (β = 0.285, p<0.001), and inflammatory markers including hsCRP (β = 0.418, p<0.001) remained significant independent predictors of serum ferritin concentration. Chronic kidney disease (β = 0.196, p=0.003) and body mass index (β = 0.152, p=0.012) also independently influenced ferritin levels.

Table 5: Multiple Linear Regression Analysis of Factors Associated with Serum Ferritin Levels

Variable	Standardized Coefficient (β)	95% CI	p-value
Age	0.237	0.103 to 0.371	<0.001
Male sex	0.285	0.168 to 0.402	<0.001
BMI	0.152	0.033 to 0.271	0.012
Hemoglobin	0.086	-0.035 to 0.207	0.162
hsCRP	0.418	0.298 to 0.538	<0.001
ESR	0.184	0.072 to 0.296	0.001
Chronic kidney disease	0.196	0.067 to 0.325	0.003
Rheumatologic disorders	0.172	0.058 to 0.286	0.003
Gastrointestinal disorders	-0.165	-0.271 to -0.059	0.002

CI: confidence interval; BMI: body mass index; hsCRP: high-sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate.

Concordance between Serum Ferritin and Bone Marrow Iron Stores

In the subset of patients who underwent bone marrow examination (n=75), the concordance between serum ferritin levels and bone marrow iron stores was assessed (Table 6). Using conventional cutoff values for serum ferritin (<30 µg/L), concordance with bone marrow

findings was observed in 45/75 patients (60.0%). When adjusted cutoffs based on inflammatory status were applied (30 µg/L for patients without inflammation and 80 µg/L for those with inflammation), the concordance improved to 64/75 patients (85.3%).

Table 6: Concordance between Serum Ferritin and Bone Marrow Iron Stores

Concordance Measure	Conventional Cutoff (<30 µg/L)	Inflammation-Adjusted Cutoffs	p-value
Overall agreement, n (%)	45/75 (60.0)	64/75 (85.3)	<0.001
Sensitivity (%)	68.2	88.6	<0.001
Specificity (%)	48.4	80.6	<0.001
Kappa coefficient	0.17	0.69	<0.001

Inflammation-adjusted cutoffs: 30 µg/L for patients with hsCRP <5 mg/L and 80 µg/L for patients with hsCRP ≥5 mg/L.

The kappa coefficient, which measures the level of agreement beyond chance, was significantly higher with inflammation-adjusted cutoffs (κ = 0.69, representing substantial agreement) compared to the conventional cutoff (κ = 0.17, representing slight agreement).

DISCUSSION

The present study investigated the utility of serum ferritin as a biomarker of iron stores in different anemic conditions, with particular emphasis on determining optimal diagnostic thresholds across various clinical contexts. Our findings demonstrate that while serum ferritin remains a valuable indicator of iron status, its interpretation requires careful consideration of multiple factors including inflammatory status, age, sex, and comorbidities.

Diagnostic Performance of Serum Ferritin

Our results indicate that serum ferritin exhibits excellent overall diagnostic accuracy for identifying iron deficiency, with an AUC of 0.934. This is consistent with findings from Guyatt et al., who reported serum ferritin as having the highest area under the ROC curve among various iron parameters for diagnosing iron deficiency anemia [20]. However, our study demonstrates that the optimal diagnostic threshold varies significantly depending on the clinical context, particularly in the presence of inflammation. The conventional cutoff of 30 µg/L, which has been widely used for diagnosing iron deficiency [21], performed well in our cohort of patients without evidence of inflammation (sensitivity 94.8%, specificity 96.3%). This aligns with the findings of Mast et al., who reported similar diagnostic characteristics in a non-inflammatory population [22]. However, this threshold demonstrated inadequate sensitivity in patients with concomitant inflammatory conditions, where iron deficiency was frequently masked by inflammation-induced elevation of ferritin levels. Our analysis supports the use of higher cutoff values in inflammatory states, with 78.3 µg/L yielding optimal diagnostic performance in patients with elevated inflammatory markers. This is comparable to the threshold of 70-100 µg/L proposed by Weiss and Goodnough for identifying iron deficiency in the context of anemia of chronic disease [23]. Similarly, Van Santen et al. suggested that a ferritin level below 100 µg/L is highly suggestive of iron deficiency in patients with rheumatoid arthritis despite ongoing inflammation

[24].

Influence of Comorbidities and Demographic Factors

The present study identified several factors independently associated with serum ferritin levels, including age, sex, BMI, and the presence of chronic kidney disease. These findings are consistent with previous reports by Milman et al., who documented significant age and gender-related variations in serum ferritin concentrations in healthy populations [25]. The positive association between BMI and ferritin levels observed in our study corroborates the findings of Alam et al., who demonstrated that obesity is associated with elevated ferritin levels independent of iron status, possibly reflecting low-grade chronic inflammation [26].

Particularly noteworthy was the impact of chronic kidney disease on ferritin levels, necessitating a substantially higher diagnostic threshold (92.7 µg/L) for detecting iron deficiency. This observation is supported by Kalantar-Zadeh et al., who proposed that serum ferritin values up to 200 µg/L might still indicate iron deficiency in hemodialysis patients [27]. The mechanisms underlying this phenomenon include impaired renal clearance of ferritin, chronic inflammation, and altered iron metabolism in uremia [28].

Correlation with Other Iron Parameters

Our finding of a strong negative correlation between serum ferritin and sTfR ($r = -0.738$) is consistent with the complementary roles of these biomarkers in assessing iron status. While ferritin primarily reflects storage iron, sTfR indicates functional iron deficiency at the cellular level [29]. Skikne et al. demonstrated that combining these parameters in the sTfR/log ferritin index improves diagnostic accuracy in complex scenarios where iron deficiency coexists with inflammation [30]. Our results support this approach, as the sTfR/log ferritin index showed excellent discrimination between pure IDA and ACD.

The moderate positive correlation observed between ferritin and transferrin saturation ($r = 0.526$) aligns with findings by Thomas et al., who reported similar correlation coefficients in a large population-based study [31]. However, the strength of this correlation was diminished in patients with inflammatory conditions, highlighting the differential impact of inflammation on these parameters. While inflammation elevates ferritin levels, it tends to reduce transferrin saturation through several mechanisms including increased hepcidin production, which impairs iron release from macrophages and enterocytes [32].

Concordance with Bone Marrow Iron Stores

Bone marrow examination is traditionally considered the gold standard for assessing iron stores [33], but its invasive nature limits routine clinical application. Our subgroup analysis revealed only moderate concordance (60.0%) between conventional ferritin cutoffs and bone marrow findings. However, using inflammation-adjusted thresholds significantly improved agreement (85.3%), with a substantial kappa coefficient of 0.69.

This observation is consistent with findings by Punnonen et al., who demonstrated enhanced diagnostic accuracy when ferritin interpretation was adjusted for inflammatory status [34]. Similarly, Joosten et al. reported that the application of higher ferritin cutoffs in elderly hospitalized patients with inflammation markedly improved the detection of iron deficiency compared to conventional thresholds [35].

Clinical Implications

The findings of this study have several important clinical implications. First, they emphasize the necessity of interpreting serum ferritin values in the context of inflammatory status. The substantial improvement in diagnostic accuracy achieved by using inflammation-adjusted cutoffs supports the implementation of this approach in clinical practice. This is particularly

relevant in patients with chronic inflammatory conditions, where iron deficiency is often underdiagnosed when using standard ferritin thresholds [36].
Second, our results underscore the value of using multiple parameters for assessing iron status in complex clinical scenarios. The integration of serum ferritin with other markers such as sTfR and the sTfR/log ferritin index provides a more comprehensive evaluation of iron metabolism, especially in patients with coexisting inflammatory conditions [37]. This multiparameter approach has been advocated by Wish, who proposed that no single biomarker can reliably diagnose iron deficiency across all clinical contexts [38].
Third, the identification of patient-specific factors influencing ferritin levels suggests that individualized thresholds may be more appropriate than universal cutoffs. The concept of "personalized reference ranges" based on age, sex, and comorbidities has been proposed by Ferraro et al. and may represent the future direction in laboratory medicine [39].

Limitations

Several limitations should be considered when interpreting the results of this study. First, bone marrow examination, the reference standard for iron stores assessment, was performed in only a subset of patients, potentially introducing selection bias. Second, while we excluded patients with known acute infections, subclinical inflammation might have influenced ferritin levels in some individuals. Third, the cross-sectional design precludes evaluation of the temporal relationship between changes in ferritin and iron stores. Longitudinal studies are needed to assess the dynamics of these parameters over time, particularly in response to iron supplementation.
Additionally, our study did not evaluate the newer biomarkers of iron status such as hepcidin, which plays a central role in iron homeostasis and has been proposed as a potentially valuable diagnostic tool [40]. Recent work by Girelli et al. suggests that hepcidin measurements, when combined with traditional iron parameters, may further improve the diagnostic accuracy for iron deficiency in inflammatory states [41].
Despite these limitations, our findings provide valuable insights into the interpretation of serum ferritin across different anemic conditions and offer practical guidance for optimizing its diagnostic utility in diverse clinical settings.

CONCLUSION

This comprehensive analysis of serum ferritin as a biomarker of iron stores in anemic patients demonstrates its significant diagnostic value while highlighting important considerations for clinical interpretation. Our findings confirm that serum ferritin remains a valuable and accessible tool for assessing iron status, but its interpretation requires a nuanced approach that accounts for inflammatory status, demographic factors, and comorbidities.
The study establishes that optimal diagnostic thresholds for serum ferritin vary substantially across different clinical contexts, with conventional cutoffs performing well in non-inflammatory states but lacking sensitivity in patients with concomitant inflammation or specific comorbidities. The implementation of inflammation-adjusted thresholds significantly improves diagnostic accuracy, particularly in complex clinical scenarios where iron deficiency coexists with inflammatory conditions.
Furthermore, our results emphasize the enhanced diagnostic value achieved by integrating serum ferritin with complementary biomarkers such as soluble transferrin receptor and inflammatory parameters. This multiparameter approach provides a more comprehensive assessment of iron metabolism and helps overcome the limitations of individual markers.
The observed substantial improvement in concordance between serum ferritin and bone marrow findings when using context-specific thresholds supports the clinical adoption of this approach.

Such stratified interpretation strategies may reduce diagnostic errors, prevent unnecessary investigations, and facilitate appropriate therapeutic interventions in patients with iron deficiency anemia.

Future research should focus on validating these findings in larger, prospective cohorts and exploring the potential utility of emerging biomarkers such as hepcidin in further refining iron status assessment. Additionally, examination of the impact of standardized interpretation guidelines on clinical outcomes and resource utilization would provide valuable insights for healthcare systems.

In conclusion, while serum ferritin remains a cornerstone in the evaluation of iron status, its optimal clinical utility depends on thoughtful interpretation within the broader clinical and biochemical context, moving beyond universal cutoffs toward a more personalized diagnostic approach.

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