

Serum Ferritin an Indicator of Iron Deficiency Anemia in Children with Normal Hemoglobin

Serum Ferritin
an Indicator of
Iron Deficiency
Anemia in
Children

Hafsa Hashmi¹, Sughra Wahid² and Maliha Akhtar Qureshi³

ABSTRACT

Objective: To determine the diagnostic accuracy of serum ferritin in diagnosis of iron deficiency in children with normal haemoglobin taking composite non-invasive laboratory reference as gold standard.

Study Design: A cross-sectional validation study

Place and Duration of Study: This study was conducted at the Department of Paediatrics KRL Hospital Islamabad Pakistan, from 15th January to 15th July 2026.

Methods: A total of 165 children aged 6 months to 5 years with normal haemoglobin and clinical suspicion of iron deficiency were included. Serum ferritin was compared with a composite non-invasive laboratory reference comprising adjusted serum ferritin, soluble transferrin receptor, transferrin saturation and reticulocyte haemoglobin content. Data were analysed using Statistical Package for the Social Sciences version 26. Diagnostic performance was assessed by calculating sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy and receiver operating characteristic curve.

Results: The mean age was 2.86 ± 1.29 years, mean weight was 16.52 ± 3.93 kilograms and mean serum ferritin level was 35.03 ± 22.99 micrograms per litre. There were 91 (55.2%) males and 74 (44.8%) females. Serum ferritin identified iron deficiency in 90 (54.5%) children, while the composite laboratory reference detected 74 (44.8%) cases. Serum ferritin showed sensitivity of 87.84%, specificity of 72.53%, positive predictive value of 72.22%, negative predictive value of 88.00% and overall diagnostic accuracy of 79.39%.

Conclusion: Serum ferritin was a useful and sensitive test for detecting iron deficiency in children with normal haemoglobin.

Key Words: Child, Diagnosis, Ferritin, Haemoglobin, Iron deficiency, Sensitivity and specificity

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INTRODUCTION

Iron Deficiency Anemia has been regarded as one of the most prevalent nutrient deficiencies in the world. This has been noticed in the case of children in both developing as well as developed countries.¹ Among the numerous markers used in the diagnosis as well as the determination of the severity of the situation of IDA, the role of serum ferritin has been found to be extremely important as it has the ability to identify the iron status in the body.¹ For a long time now, the diagnosis of Anemia has been greatly reliant upon the estimation of Hemoglobin levels.²

Current studies reveal that in the case of children, iron stores can become depleted even when Hemoglobin levels are found to be normal. This clearly goes on to identify the indispensable role of serum ferritin as a more specific marker.²

Children are at high risk of iron deficiency because of their high iron requirements during their rapid rates of growth. Iron has been shown to play a pivotal role in participating in important functions in the human body like oxygen transport, DNA synthesis, and enzymatic reactions.³ Thus, the lack of iron can generate reduced intellectual function, poor physical development, and immune dysfunction in the pediatric population.⁴ The clinical progression of iron deficiency has been shown to develop through sequential stages that include iron depletion leading to the involvement of the iron-recursive pathway. This finally culminates in the development of iron-deficiency anemia.⁵ Among the important markers used in the sequence of iron deficiency development has been the determination of serum ferritin. This has proven very important as it has given the clinician the opportunity to prevent the outcome of iron deficiency progressing towards the development of iron-deficiency anemia.⁵

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Ferritin in the serum is a intracellular protein that stores iron and releases it in a regulated fashion. This protein has a very important role to play in the iron regulatory functions of the body. When iron levels are sufficient in the body, the serum ferritin concentration ranges between 15-200 ng/ml in children.⁶ When the concentration is lower than that, the iron stores are depleted despite the fact that the patient may not have iron-deficiency anemia.⁷ However, serum ferritin levels must be interpreted cautiously, as they can be influenced by various factors, including inflammation, infection, and chronic disease. During acute or chronic inflammatory states, ferritin behaves as an acute-phase reactant, leading to elevated levels irrespective of iron stores.⁸ Therefore, concurrent assessment of other parameters, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), is recommended to differentiate between true iron deficiency and inflammation-induced changes.⁸

Thus, the proposed aim of the current researcher proposal has been set to examine the accuracy of the serum ferritin test in the detection of iron deficiency compared to the reference standard

METHODS

This cross-sectional validation study was carried out in the Department of Paediatrics, KRL Hospital, Islamabad, from 15th January 2026 to 15th July 2026. Ethical approval was obtained from the Institutional Ethical Review Committee of the hospital before starting the study. All study procedures were performed according to the institutional ethical guidelines. The sample size was calculated by using a diagnostic accuracy (sensitivity/specificity) calculator with expected sensitivity of 81.6%,⁹ specificity of 37.5%,⁹ prevalence of 44.8%,⁹ 95% confidence level and $\pm 10\%$ absolute precision for both sensitivity and specificity. The calculated sample size was 165 children.

Children aged 6 months to 5 years of either gender, presenting with normal haemoglobin and having clinical suspicion of iron deficiency based on history of fatigue, poor growth or developmental delay were included in the study. Normal haemoglobin was considered as haemoglobin level >10.5 g/dl for children aged 6 months to 2 years and >11.5 g/dl for children aged more than 2 years up to 5 years. Children having history of chronic inflammatory diseases including juvenile rheumatoid arthritis or chronic infections, blood transfusion during the previous 4 weeks, overt anaemia with pallor and fatigue, liver disease, renal dysfunction, severe malnutrition or underweight according to WHO growth standards, coeliac disease, inflammatory bowel disease, or use of iron supplementation within the last 3 months were excluded. Baseline demographic information including age, gender, weight, area of residence and family socioeconomic background was recorded. A detailed

physical examination was performed to identify signs of overt anaemia, nutritional status, and other clinical findings relevant to the study.

A total of 10 ml of venous blood was collected by trained phlebotomists under aseptic conditions. Five ml of blood was placed in an EDTA tube for complete blood count analysis, while another 5 ml was collected in a yellow-top vacutainer for biochemical investigations. All specimens were immediately transported to the hospital laboratory for analysis. Laboratory investigations included serum ferritin adjusted for inflammation using C-reactive protein, soluble transferrin receptor (sTfR), transferrin saturation (TSAT), and reticulocyte haemoglobin content (Ret-He). The results of serum ferritin and composite non-invasive laboratory reference were documented on the study proforma for every participant. Iron deficiency by serum ferritin was considered when serum ferritin level was <30 $\mu\text{g/L}$. Iron deficiency by composite non-invasive laboratory reference was considered when at least 2 iron parameters were abnormal, including adjusted serum ferritin <12 $\mu\text{g/L}$ or <30 $\mu\text{g/L}$ in the presence of inflammation, soluble transferrin receptor-log ferritin index >5.6 , transferrin saturation $<20\%$ or reticulocyte haemoglobin <27 pg.

The collected data were entered and analysed using IBM SPSS version 26. Quantitative variables including age and weight were presented as mean $\pm$ standard deviation. Qualitative variables including gender, area of residence, socioeconomic background, serum ferritin results and composite non-invasive laboratory reference were expressed as frequencies and percentages.

RESULTS

The mean age of children was 2.86 ± 1.29 years and mean weight was 16.52 ± 3.93 kg, with serum ferritin level recorded as 35.03 ± 22.99 $\mu\text{g/L}$.

Table No. 1: Patient Demographics.

Demographics	Mean $\pm$ SD
Age (years)	2.86 ± 1.29
Weight (kg)	16.52 ± 3.93
Serum Ferritin Level ($\mu\text{g/L}$)	35.03 ± 22.99
Gender	
Male n (%)	91 (55.2%)
Female n (%)	74 (44.8%)
Residential Status	
Rural n (%)	90 (54.5%)
Urban n (%)	75 (45.5%)
Family Socioeconomic Status	
Low n (%)	58 (35.2%)
Middle n (%)	90 (54.5%)
High n (%)	17 (10.3%)

Among the participants, male was 91(55.2%) and female were 74(44.8%). Regarding residential status, majority were belonged to rural area 90(54.5%) while 75(45.5%) were from urban area. Concerning family socioeconomic status, low status was found in 58(35.2%), middle status in 90(54.5%) and high status in 17(10.3%) of children (Table-I).

On comparing iron deficiency diagnosis, serum ferritin detected positive result in 90(54.5%) and negative in 75(45.5%) of cases, whereas composite laboratory reference showed positive in 74(44.8%) and negative in 91(55.2%) cases, total sample being 165(100%) for both parameter (Table-2).

Table No.2: Overall results of Serum Ferritin and Composite Laboratory Reference in diagnosis of Iron Deficiency.

Iron Deficiency	Serum Ferritin	Composite Laboratory Reference
Positive	90(54.5%)	74(44.8%)
Negative	75(45.5%)	91(55.2%)
Total	165 (100%)	165 (100%)

When serum ferritin was compared against composite laboratory reference, true positive were found in 65 cases, false positive in 25 cases, false negative in 9 cases and true negative in 66 cases, with total positive on composite reference being 74 and total negative being 91 (Table-3).

Table No.3: Comparison of Serum Ferritin versus Composite Laboratory Reference in diagnosis of Iron Deficiency.

Serum Ferritin	Composite Laboratory Reference	Total
	Positive	Negative
Positive	65 (TP)	25 (FP)
Negative	9 (FN)	66 (TN)
Total	74	91

Key: TP = True positive, FP = False positive, FN = False negative, TN = True negative

The diagnostic performance of serum ferritin in diagnosing iron deficiency showed sensitivity of

87.84%, specificity of 72.53%, diagnostic accuracy of 79.39%, positive predictive value of 72.22% and negative predictive value of 88% (Table-4).

Table No.4: Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of Serum Ferritin in diagnosis of Iron Deficiency.

Diagnostic Parameter	Result
Sensitivity	87.84%
Specificity	72.53%
Diagnostic Accuracy	79.39%
PPV	72.22%
NPV	88%

Diagnostic accuracy was best in high socioeconomic group (94.12%) and least in middle socioeconomic group (74.44%). Negative predictive value was notably high across most subgroup, particularly in high socioeconomic group (100%) and urban residents (95.74%), whereas positive predictive value were comparatively low in urban (50%), weight >15kg (50%) and middle socioeconomic (48.78%) subgroup (Table-5).

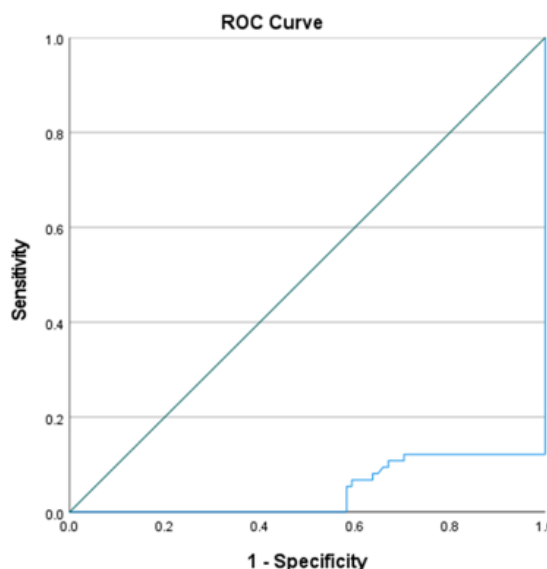


Figure No.1: ROC Curve

Table No.5: Stratified analysis of Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of Serum Ferritin in diagnosis of Iron Deficiency with demographics.

Variables	Groups	Diagnostic Parameter	Result
Age (years)	≤3	Sen	88.33%
		Spec	68%
		DA	82.35%
		PPV	86.89%
		NPV	70.83%
	>3	Sen	85.71%
		Spec	74.24%
		DA	76.25%

Gender	Male	PPV	41.38%
		NPV	96.08%
		Sen	92.50%
		Spec	72.55%
		DA	81.32%
	Female	PPV	72.55%
		NPV	92.50%
		Sen	82.35%
		Spec	72.50%
		DA	77.03%
Weight (kg)	≤15	PPV	71.79%
		NPV	82.86%
		Sen	93.75%
		Spec	54.55%
		DA	86.44%
	>15	PPV	90%
		NPV	66.67%
		Sen	76.92%
		Spec	75%
		DA	75.47%
Residential Status	Rural	PPV	50%
		NPV	90.91%
		Sen	87.93%
		Spec	65.63%
		DA	80%
	Urban	PPV	82.26%
		NPV	75%
		Sen	87.50%
		Spec	76.27%
		DA	78.67%
Family Socioeconomic Status	Low	PPV	50%
		NPV	95.74%
		Sen	84.09%
		Spec	78.57%
		DA	82.76%
	Middle	PPV	92.50%
		NPV	61.11%
		Sen	90.91%
		Spec	69.12%
		DA	74.44%
	High	PPV	48.78%
		NPV	95.92%
		Sen	100%
		Spec	88.89%
		DA	94.12%
		PPV	88.89%
		NPV	100%

The optimal cutoff value of serum ferritin for diagnosis of iron deficiency was determined as $\leq 21.90 \mu\text{g/L}$, at which sensitivity was 87.80%, specificity was 100% and area under curve was 0.954 (Fig-1)

DISCUSSION

The present study was conducted to evaluate role of serum ferritin as indicator of iron deficiency in children

having normal hemoglobin level. Total of 165 children were enrolled, among them serum ferritin detected iron deficiency in 90(54.5%) of cases as compared to composite laboratory reference which detected 74(44.8%) cases, suggesting that serum ferritin alone may overestimate the burden of iron deficiency when used without another supportive parameter. Serum ferritin showed sensitivity of 87.84% and specificity of

72.53% in detecting iron deficiency, with diagnostic accuracy of 79.39%. The high sensitivity of this parameter implies that serum ferritin test is quite dependable in diagnosing iron deficiency, and this could be due to the fact that the serum ferritin levels represent the level of iron content within the body, hence falling when there is an iron shortage, even before any effect is experienced on the hemoglobin levels. Relatively low specificity on the other hand implies that it is not always dependable in ruling out iron deficiency because serum ferritin levels are sometimes influenced by conditions unrelated to iron such as infections.

The present study found serum ferritin positive for iron deficiency in 90(54.5%) of children while composite laboratory reference detected only 74(44.8%) cases, with sensitivity of 87.84% and specificity of 72.53%. This is comparable to findings of Khan and Shah¹⁰ who also reported serum ferritin as most sensitive marker among iron indices, with sensitivity of 85%, though their specificity was markedly lower at 15%, possibly because their sample comprised already anemic children where overlap of inflammatory and depletion state is more common, reducing specificity of test further than seen in present study.

Findings of present study, where 39 children had no overt anaemia yet abnormal ferritin reflecting subclinical iron deficiency, are in line with study by Ibrahim and Habeeb¹¹ who studied 150 children with normal haemoglobin but low MCV and MCH and found mean ferritin of 86.5 ± 7 ng/mL, supporting that ferritin can detect deficiency even before haemoglobin become affected, similar principle being demonstrated in present cohort where iron deficiency was identified despite normal Hb status.

Zaman et al.¹² reported sensitivity of anaemia for predicting depleted iron store as only 33.8%, much lower than sensitivity of serum ferritin (87.84%) observed in present study, indicating that ferritin is far superior marker compared to haemoglobin alone for detecting iron deficiency, this difference likely arise because anaemia is late manifestation of iron depletion whereas ferritin decline early in course of negative iron balance.^{13,14}

Khan et al.¹⁵ reported higher ferritin in rural compared to urban children and positive correlation with hygienic condition, somewhat differing from present study where diagnostic accuracy was comparatively better in urban children, this discrepancy may be due to difference in nutritional and healthcare access pattern across different population, with urban setting in present cohort possibly having better access to balanced diet reducing confounding inflammatory influence on ferritin.

The variation observed across socioeconomic group in present study, with best diagnostic accuracy in high socioeconomic class, is consistent with epidemiological

pattern described by Animasahun et al¹⁶ highlighting that nutritional deprivation and lower socioeconomic status increase burden and diagnostic complexity of iron deficiency, particularly in non-industrialised setting, reinforcing that socioeconomic factor remain important determinant of both prevalence and diagnostic performance of ferritin based testing.

CONCLUSION

The current study found out that serum ferritin acts as an accurate and sensitive marker in assessing iron deficiency in children with normal hemoglobin status. It can accurately diagnose subclinical iron deficiency prior to hemoglobin being affected.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hafsa Hashmi, Sughra Wahid
Drafting or Revising Critically:	Hafsa Hashmi, Maliha Akhtar Qureshi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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