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Original Research Article

Clinical Usefulness of Reticulocyte Hemoglobin Equivalent in the Assessment of Iron Deficiency: A Cross-Sectional Study

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Abstract

Background: Reticulocyte Hemoglobin Equivalent (Ret-He) reflects the hemoglobin content of newly formed reticulocytes and may provide an early indicator of iron-restricted erythropoiesis. This study evaluated the diagnostic utility of Ret-He for detecting iron deficiency.

Materials & Methods: This hospital-based cross-sectional study included 140 patients aged >12 years with microcytic hypochromic or dimorphic anemia. Ret-He and hematological parameters were measured using the Sysmex XN-1000 analyzer. Serum iron, ferritin, TIBC, transferrin saturation, and soluble transferrin receptor (sTfR) were assessed. Iron deficiency was defined using sTfR-based classification. Data were analyzed using IBM SPSS Statistics version 27.0. Diagnostic performance was assessed using sensitivity, specificity, predictive values, accuracy, and ROC-AUC analysis.

Results: Iron deficiency was identified in 58.6%participants. Mean Ret-He was significantly lower in iron-deficient than non-iron-deficient participants (24.86 ± 3.21 vs. 29.74 ± 3.46 pg; $p<0.001$). Hemoglobin, MCV, MCH, and MCHC were lower, whereas RDW was higher in the iron-deficient group (all $p<0.001$). At a Ret-He cutoff of ≤27.0 pg, sensitivity was 85.4%, specificity 79.3%, PPV 85.4%, NPV 79.3%, and diagnostic accuracy 82.9%. Serum ferritin <30 ng/mL showed sensitivity of 82.9%, specificity of 75.9%, and accuracy of 80.0%. ROC analysis demonstrated an AUC of 0.884 (95% CI: 0.825–0.943; $p<0.001$) for Ret-He and 0.861 (95% CI: 0.796–0.926; $p<0.001$) for serum ferritin.

Conclusion: Ret-He demonstrated good diagnostic performance for sTfR-confirmed iron deficiency, with an AUC of 0.884 and a sensitivity of 85.4% at a cutoff of ≤27.0 pg. Ret-He may serve as a useful complementary parameter for assessing iron deficiency in patients with microcytic hypochromic or dimorphic anemia. Although its AUC was numerically higher than that of ferritin, statistical superiority cannot be concluded because the AUCs were not formally compared.

Keywords: Ret-He (reticulocy hemoglobin); Serum Iron; Iron Deficiency; Serum Ferritin; ROC-AUC.

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Introduction

Iron deficiency (ID) is one of the most common micronutrient deficiencies worldwide and remains an important cause of morbidity across different age groups. Although iron deficiency anemia (IDA) represents the clinically overt stage of iron depletion, iron deficiency may exist for a considerable period before the development of anemia. Recent evidence indicates that absolute iron deficiency affects approximately 2 billion people globally, while iron-deficiency anemia affects more than 1 billion individuals, highlighting the substantial clinical and public-health burden of this condition.[1] Iron is essential for hemoglobin synthesis, cellular metabolism, oxygen transport, DNA synthesis, and several enzymatic processes; therefore, inadequate iron availability can adversely affect physical performance, cognition, quality of life, and overall health even in the absence of overt anemia.[1,2] More recent investigations have provided additional evidence regarding the diagnostic value of Ret-He, although reported thresholds vary according to age, population

characteristics, analyzer platform, and diagnostic criteria. Poventud-Fuentes et al., in a large pediatric tertiary-care cohort of 3158 patients, demonstrated significant positive correlations between Ret-He, ferritin, and TSAT. A Ret-He cutoff of ≤30.0 pg showed an AUC of 0.88 for identification of iron deficiency, while diagnostic performance was stronger for iron-deficiency anemia than for isolated iron deficiency without anemia.[3]

Similarly, Bouzid et al. reported that Ret-He was significantly lower among individuals with latent iron deficiency and identified an AUC of 0.872, with a high negative predictive value, suggesting potential usefulness for excluding latent iron deficiency.[4] Several recent studies have demonstrated the diagnostic potential of Reticulocyte Hemoglobin Equivalent (Ret-He) in the assessment of iron deficiency and iron-deficiency anemia (IDA). Ret-He has been reported to provide a reliable estimate of the iron available for erythropoiesis and may serve as a useful marker for the early detection of iron-restricted erythropoiesis during routine hematological evaluation.[5] In pediatric populations, Ret-He has also shown significant associations with established biochemical indicators of iron status, supporting its potential utility as a screening parameter for both iron deficiency and IDA [6]. These findings suggest that Ret-He may complement conventional hematological and biochemical parameters and facilitate earlier recognition of iron deficiency, particularly before the development of overt anemia. [6] More recently, Rana et al. reported diagnostic utility of Ret-He in an Eastern Indian tertiary-care population, further supporting its potential application in the evaluation of iron-deficiency anemia in routine clinical practice.[7]

Aim & Objectives

Aim: To evaluate the clinical usefulness and diagnostic performance of Reticulocyte Hemoglobin Equivalent (Ret-He) for the assessment of iron deficiency among patients with microcytic hypochromic or dimorphic anemia, using sTfR-confirmed iron deficiency as the reference standard.

Objectives

- To compare Ret-He levels between patients with and without sTfR-confirmed iron deficiency.
- To compare Ret-He with conventional hematological parameters, including hemoglobin, MCV, MCH, MCHC, and RDW.
- To assess the association of Ret-He with biochemical iron-status markers, including serum iron, serum ferritin, TIBC, and transferrin saturation.
- To determine the diagnostic performance of Ret-He, including sensitivity, specificity, PPV, NPV, and diagnostic accuracy, for identifying iron deficiency.
- To determine the discriminatory ability of Ret-He using ROC curve analysis and AUC and compare its performance with serum ferritin.

Materials & Methods

Study Design: A hospital-based, cross-sectional observational study was conducted to evaluate the clinical utility of Reticulocyte Haemoglobin Equivalent (RET-He) in assessing iron deficiency among patients with microcytic hypochromic and dimorphic anemia.

Study Setting and Study Period: The study was conducted in the Department of Pathology, Bhagwan Mahavir Institute of Medical Sciences (BMIMS), Pawapuri, Nalanda, Bihar, India, over 12 months from May 2025 to April 2026.

Study Population and Sample Size: A total of 140 patients aged >12 years with laboratory evidence of microcytic hypochromic or dimorphic anemia were included. Patients were identified on the basis of complete blood count (CBC) and peripheral blood smear examination. Eligible participants were enrolled consecutively after application of the predefined inclusion and exclusion criteria.

Ethical Considerations: The study was initiated after approval from the Institutional Ethics Committee. Written informed consent was obtained from participants or their legally authorized representatives, as applicable. Patient confidentiality was maintained throughout the study, and data were analyzed anonymously. No surgical procedure or additional invasive intervention was performed solely for study purposes.

Inclusion Criteria: Patients were eligible if they:

- were aged >12 years;
- had microcytic hypochromic anemia or dimorphic anemia on peripheral blood smear/CBC evaluation; and
- had complete relevant laboratory investigations, including CBC, RET-He, serum iron, and serum ferritin.

Exclusion Criteria: Patients were excluded if they:

- were aged ≤12 years;
- had received a blood transfusion recently;
- had incomplete clinical or laboratory data; or
- had hemolyzed, clotted, inadequately collected, or improperly processed blood samples.

Methodology: Approximately 2–3 mL of venous blood was collected aseptically into EDTA-containing tubes for hematological analysis. An additional sample was collected according to standard laboratory protocols for biochemical investigations. Peripheral blood smears were examined using standard staining and microscopy procedures for morphological classification of anemia. Serum iron and serum ferritin were estimated using standardized automated laboratory methods.

C-reactive protein (CRP) was assessed when clinically indicated to assist in interpretation of ferritin in patients with suspected inflammatory conditions. Soluble transferrin receptor (sTfR) testing was performed in selected cases where additional assessment of iron status was clinically required, particularly when concomitant hemoglobinopathy or inflammatory conditions could influence conventional iron parameters.

Laboratory Investigations: CBC parameters, including hemoglobin, red blood cell count, MCV, MCH, MCHC, RDW, platelet count, and reticulocyte parameters, were analyzed using the Sysmex XN-1000 automated hematology analyzer. RET-He was obtained as part of the automated reticulocyte analysis and was considered an indicator of the hemoglobin content of newly produced erythrocytes and functional iron availability for erythropoiesis.

Outcome Measures

Primary Outcome: The primary outcome was the association between RET-He and conventional iron-status parameters, particularly serum ferritin and serum iron, for the assessment of iron deficiency.

Secondary Outcomes: Secondary outcomes included:

- diagnostic sensitivity and specificity of RET-He for identifying iron deficiency;
- positive and negative predictive values of RET-He;
- correlation of RET-He with hemoglobin, MCV, MCH, RDW, serum iron, and ferritin;
- assessment of the ability of RET-He to identify iron-restricted erythropoiesis; and
- evaluation of RET-He performance in patients with suspected inflammatory conditions or coexisting hematological disorders.

Statistical Analysis: Data were entered into Microsoft Excel 365 and analyzed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for distribution using the Shapiro–Wilk test and expressed as mean ± standard deviation (SD) for normally distributed variables or median (interquartile range [IQR]) for non-normally distributed variables. Categorical variables were summarized as frequencies and percentages. Differences between groups were assessed using the independent-samples Student's t-test for normally distributed continuous variables or the Mann–Whitney U test for non-normally distributed variables.

Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, as appropriate. Associations between RET-He and continuous hematological or biochemical parameters were evaluated using Pearson's correlation coefficient (r) for normally distributed variables or Spearman's rank correlation coefficient (ρ) when distributional assumptions were not met. The diagnostic performance of RET-He for identifying iron deficiency was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. The optimal RET-He cutoff was determined using the Youden index, where appropriate. A two-sided p-value <0.05 was considered statistically significant, and 95% confidence intervals (CIs) were reported where applicable.

Results

Table 1: Comparison of Biochemical and Ret-He Parameters According to sTfR-Confirmed Iron-Deficiency Status

Parameter	Iron-deficient group (n=82), Mean ± SD	Non-iron-deficient group (n=58), Mean ± SD	t-value	p-value
Ret-He (pg)	24.86 ± 3.21	29.74 ± 3.46	8.68	<0.001*
Serum iron (µg/dL)	36.72 ± 15.84	72.58 ± 22.41	10.84	<0.001*
Serum ferritin (ng/mL)	14.68 ± 8.92	58.42 ± 31.76	10.03	<0.001*
sTfR (mg/L)	4.82 ± 1.34	2.36 ± 0.72	12.58	<0.001*
TIBC (µg/dL)	428.64 ± 56.82	352.38 ± 48.76	8.49	<0.001*
Transferrin saturation (%)	8.62 ± 3.74	20.74 ± 6.18	13.47	<0.001*

Table 1 show that among the 140 study participants, 82 (58.6%) were classified as iron deficient and 58 (41.4%) as non-iron deficient based on sTfR-confirmed iron status. The mean Ret-He was significantly lower in the iron-deficient group than in the non-iron-deficient group (24.86 ±

3.21 vs. 29.74 ± 3.46 pg; p<0.001). Similarly, serum iron, serum ferritin, and transferrin saturation were significantly lower in the iron-deficient group, whereas sTfR and TIBC were significantly higher (p<0.001 for all comparisons). These findings demonstrate a significant difference in Ret-He and biochemical iron-status parameters according to iron-deficiency status.

Table 2: Comparison of Hematological Parameters According to Iron-Deficiency Status

Parameter	Iron-deficient group (n=82), Mean ± SD	Non-iron-deficient group (n=58), Mean ± SD	t-value	p-value
Hemoglobin (g/dL)	8.72 ± 1.34	10.14 ± 1.28	6.51	<0.001*
MCV (fL)	68.94 ± 7.26	75.82 ± 6.84	5.82	<0.001*
MCH (pg)	21.46 ± 2.84	24.18 ± 2.61	5.91	<0.001*
MCHC (g/dL)	29.86 ± 2.14	31.42 ± 1.86	4.54	<0.001*
RDW (%)	18.42 ± 3.26	15.76 ± 2.84	5.02	<0.001*

*Statistically significant.

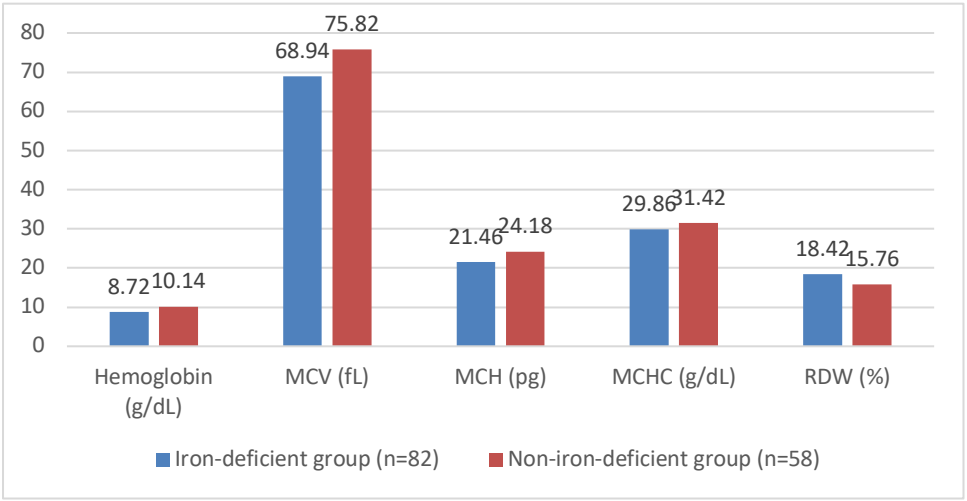

Figure 1: Comparison of Hematological Parameters According to Iron-Deficiency Status

Table 2 and figure I, present the iron-deficient group had significantly lower mean hemoglobin (8.72 ± 1.34 vs. 10.14 ± 1.28 g/dL), MCV (68.94 ± 7.26 vs. 75.82 ± 6.84 fL), MCH (21.46 ± 2.84 vs. 24.18 ± 2.61 pg), and MCHC (29.86 ± 2.14 vs. 31.42 ± 1.86 g/dL) compared with the non-iron-deficient group. In contrast, RDW was significantly higher in the iron-deficient group (18.42 ± 3.26 vs. 15.76 ± 2.84%). All between-group differences were statistically significant (p<0.001), indicating greater microcytosis, hypochromia, and anisocytosis among patients with iron deficiency.

Table 3: Diagnostic Classification of Ret-He According to sTfR-Confirmed Iron-Deficiency Status

Ret-He classification	sTfR-confirmed iron deficiency present (n=82)	sTfR-confirmed iron deficiency absent (n=58)
Ret-He ≤27.0 pg (positive)	70 (85.4%)	12 (20.7%)
Ret-He >27.0 pg (negative)	12 (14.6%)	46 (79.3%)
Total	82 (100.0%)	58 (100.0%)

Table 3 show that using a Ret-He cutoff of ≤27.0 pg as a positive test for iron deficiency, 70 of 82 sTfR-confirmed iron-deficient patients were correctly identified (true positives), while 12 were incorrectly classified as negative (false negatives). Among the 58 non-iron-deficient patients, 46 were correctly identified as negative (true negatives), whereas 12 were classified as positive (false positives). Thus, Ret-He ≤27.0 pg demonstrated good agreement with the sTfR-based reference classification.

Table 4: Diagnostic Performance of Ret-He and Serum Ferritin for the Detection of Iron Deficiency

Diagnostic parameter	Ret-He ≤27.0 pg	Serum ferritin <30 ng/mL
True positive (TP), n	70	68
False positive (FP), n	12	14
True negative (TN), n	46	44
False negative (FN), n	12	14
Sensitivity (%)	85.4	82.9
Specificity (%)	79.3	75.9
Positive predictive value (PPV, %)	85.4	82.9
Negative predictive value (NPV, %)	79.3	75.9
Diagnostic accuracy (%)	82.9	80.0

Table 4 demonstrate that Ret-He at a cutoff of ≤27.0 pg demonstrated a sensitivity of 85.4%, specificity of 79.3%, PPV of 85.4%, NPV of 79.3%, and diagnostic accuracy of 82.9%.

In comparison, serum ferritin <30 ng/mL showed a sensitivity of 82.9%, specificity of 75.9%, PPV of 82.9%, NPV of 75.9%, and diagnostic accuracy of 80.0%.

Thus, Ret-He showed slightly higher sensitivity, specificity, predictive values, and overall diagnostic accuracy than serum ferritin in this study.

Table 5: Receiver Operating Characteristic (ROC) Curve Analysis of Ret-He and Serum Ferritin for Detection of Iron Deficiency

Test variable	AUC	Std. Error	Asymptotic Sig. (p-value)	95% CI for AUC – Lower Bound	95% CI for AUC – Upper Bound
Ret-He	0.884	0.030	<0.001*	0.825	0.943
Serum ferritin	0.861	0.033	<0.001*	0.796	0.926

AUC, area under the curve; CI, confidence interval. *Statistically significant (<0.05).

Table 5 shows that Ret-He had an area under the ROC curve (AUC) of 0.884 (95% CI: 0.825–0.943; p<0.001), while serum ferritin had an AUC of 0.861 (95% CI: 0.796–0.926; p<0.001). The AUC of Ret-He was numerically higher than that of serum ferritin (0.884 vs. 0.861), indicating slightly better discriminatory performance in the present study. However, the difference between the two AUCs was not formally tested; therefore, statistical superiority of Ret-He over serum ferritin cannot be concluded from the present analysis.

Discussion

The present study demonstrated a significant reduction in Ret-He among participants with sTfR-confirmed iron deficiency compared with non-deficient participants. Because reticulocytes represent newly produced erythrocytes, their hemoglobin content reflects iron availability during recent erythropoiesis. Thus, reduced Ret-He may provide a functional indication of iron-restricted erythropoiesis. The present finding is consistent with the concept emphasized by Qiao and Mathur (2025), who described reticulocyte hemoglobin as a practical hematological marker capable of identifying iron-restricted erythropoiesis and highlighted its potential role in patient blood management. They noted that reticulocyte hemoglobin provides information on recent iron availability for erythropoiesis and may complement conventional biochemical parameters.[8] The biochemical findings in the present study further support the classification based on sTfR. Serum iron was significantly lower in the iron-deficient group, while serum ferritin was markedly reduced. Conversely, sTfR was substantially higher in the iron-deficient group. The increase in sTfR is consistent with enhanced cellular demand for iron and increased expression of transferrin receptors under conditions of tissue iron depletion. TIBC was also significantly higher in iron-deficient participants, while transferrin saturation was markedly lower. Choorapoikayil et al. (2025), in a retrospective study of 2,966 patients undergoing major surgery, evaluated Ret-He as a marker of iron deficiency in both anemic and non-anemic individuals. They demonstrated that Ret-He could identify iron deficiency, although diagnostic performance varied according to the clinical subgroup. This observation is important because it indicates that Ret-He is sensitive to the biological state of iron availability but that the optimal threshold may differ according to population and clinical context.[9]

The use of sTfR in the present study is particularly relevant because ferritin may be elevated by inflammation despite inadequate iron availability. De la Cruz-Garcinuño et al. (2025), studying critically ill patients, similarly emphasized the limitations of conventional iron markers in inflammatory and intensive-care settings and investigated Ret-He as an alternative hematimetric parameter.[10] In present study, mean hemoglobin

was significantly lower in the iron-deficient group than in the non-iron-deficient group. Similarly, MCV, MCH and MCHC were significantly lower in iron-deficient participants. In contrast, RDW was significantly higher in the iron-deficient group. This pattern reflects impaired hemoglobin synthesis, microcytosis, hypochromia, and increasing red-cell size heterogeneity associated with iron-restricted erythropoiesis. The present findings are consistent with the observations of Choorapoikayil et al. (2025), who demonstrated differences in Ret-He and conventional hematological parameters across iron-status categories in a large surgical cohort. Their findings emphasized that Ret-He provides information related to current erythropoietic iron availability, whereas conventional red-cell indices represent the cumulative effects of iron availability over the lifespan of circulating erythrocytes.[9]

A particularly important aspect of the present results is the significantly lower Ret-He observed in parallel with lower MCV, MCH, and MCHC. Ret-He may therefore provide an additional functional indicator of iron restriction before substantial changes in mature erythrocyte indices become apparent. Qiao and Mathur (2025) similarly emphasized that reticulocyte hemoglobin complements traditional red-cell indices because reticulocytes provide a more recent representation of erythropoietic iron availability.[8]

The recent study by Otiv et al. (2026) is particularly relevant because it evaluated Ret-He among acutely ill hospitalized children and compared its diagnostic utility with serum ferritin. Their work further supports the clinical relevance of Ret-He across different patient populations, although the population-specific nature of Ret-He thresholds remains important.[11]

At a Ret-He cutoff of ≤27.0 pg, 85.4%) sTfR-confirmed iron-deficient participants were correctly identified, while 14.6%) were classified as negative. Among non-deficient participants, 79.3% were correctly classified as negative and 20.7% as positive. Thus, the selected threshold identified most iron-deficient individuals while maintaining reasonable specificity. The resulting classification indicates that a Ret-He threshold of ≤27.0 pg successfully identified the majority of individuals with sTfR-confirmed iron deficiency while maintaining a relatively low proportion of false-positive classifications. Divya et al. (2025), in a study of regular female blood donors with latent iron deficiency, reported a Ret-He cutoff of ≤26.7 pg and found that Ret-He had high sensitivity, specificity, positive predictive value, and negative predictive value for identifying latent iron deficiency. Their cutoff is remarkably close to the ≤27.0 pg threshold identified in the present study. [12] The study by Choorapoikayil et al. (2025) further illustrates the variability of Ret-He thresholds across clinical settings. In their major surgical cohort, the optimal threshold for identifying iron deficiency was higher than the cutoff observed in the present study, reinforcing the principle that Ret-He values should not be interpreted using a universal threshold without considering patient characteristics, disease status, and analyzer methodology.[9]

Ret-He at ≤27.0 pg showed a sensitivity of 85.4%, specificity of 79.3%, PPV of 85.4%, NPV of 79.3%, and diagnostic accuracy of 82.9%. Serum ferritin <30 ng/mL showed corresponding values of 82.9%, 75.9%, 82.9%, 75.9%, and 80.0%, respectively. Ret-He therefore demonstrated numerically higher performance across all evaluated diagnostic measures. The slightly higher performance of Ret-He compared with serum ferritin is an important finding. Ferritin reflects iron storage, whereas Ret-He reflects the functional availability of iron for erythropoiesis. Therefore, Ret-He may provide complementary information, particularly in situations where storage iron and functional iron availability do not correspond. This finding is supported by Choorapoikayil et al. (2025), whose large surgical cohort demonstrated clinically useful diagnostic information from Ret-He but also showed that its performance differed according to the presence or absence of anemia.[9]

Similarly, Otiv et al. (2026) evaluated Ret-He against serum ferritin in acutely ill hospitalized children and highlighted its potential usefulness in clinical settings in which conventional iron markers may be difficult to interpret. Their study provides contemporary evidence that Ret-He remains clinically relevant across different age groups and disease settings. [11]

Divya et al. (2025) also reported that Ret-He performed better than serum ferritin for identifying latent iron deficiency in regular female blood donors, with a cutoff of ≤26.7 pg.[12] This observation closely parallels the present findings, in which Ret-He demonstrated slightly better sensitivity, specificity, predictive values, and diagnostic accuracy than ferritin.

In present study, Ret-He and serum ferritin showed good discriminatory ability for detecting iron deficiency. Ret-He had an AUC of 0.884 (95% CI: 0.825–0.943; p<0.001), indicating strong diagnostic performance. Serum ferritin showed an AUC of 0.861 (95% CI: 0.796–0.926; p<0.001), also demonstrating good discrimination. The AUC of Ret-He was numerically higher than that of serum ferritin (0.884 vs. 0.861), suggesting better discriminatory performance in the present study; however, this difference was not statistically tested and therefore superiority of Ret-He cannot be concluded.

The present finding is consistent with Lundgren (2022), who reported good diagnostic performance of reticulocyte hemoglobin parameters for identifying iron deficiency, with an AUC of approximately 0.889.[13] Zuther et al. (2023) reported an AUC of 0.847 for Ret-He in critically ill patients, demonstrating that Ret-He may retain diagnostic value even in complex clinical settings where conventional iron markers can be difficult to interpret.[14] Ding et al. (2024) also demonstrated significant diagnostic utility of reticulocyte hemoglobin measurements for identifying iron deficiency, further supporting their role as indicators of functional iron availability.[15] Rana et al. (2026) reported AUCs of 0.839 for Ret-He and 0.728 for serum ferritin, with Ret-He showing significantly better performance after formal comparison of the ROC curves.[16] Although the present study similarly showed a higher AUC for Ret-He than ferritin, the difference was not formally compared and therefore cannot be considered statistically significant.

Limitations of the Study

- This study was limited by its single-centre, cross-sectional design and relatively small sample size (n=140), which may restrict generalizability and preclude assessment of temporal relationships or treatment response.
- Ret-He values may vary with analyzer platform, laboratory methodology, and population characteristics, limiting the universal applicability of the identified cutoff (≤27.0 pg).
- Ferritin may also be affected by inflammatory conditions despite the use of sTfR as the reference criterion.
- As the study included patients with established microcytic hypochromic or dimorphic anemia, the findings may not be generalizable to early or isolated iron deficiency without anemia.
- Finally, the Ret-He cutoff and diagnostic performance were not externally validated in an independent population.

Conclusion

In present study, Ret-He demonstrated a significant association with sTfR-confirmed iron deficiency and was significantly lower among iron-deficient patients. It showed significant differences and correlations with conventional hematological and biochemical indicators of iron status. Its diagnostic performance was slightly better than that of serum ferritin in the present study. These findings suggest that Ret-He may serve as a useful, readily available hematological indicator of iron-restricted erythropoiesis and may complement conventional iron-status assessment, particularly in patients with microcytic hypochromic or dimorphic anemia. Further multicentre studies with larger populations and external validation are warranted to establish standardized Ret-He cutoffs for routine clinical use.

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