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Using complete blood counts to inform send-out ferritin testing in children with selective eating or poor appetite: a retrospective exploratory study

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Abstract

Background

Iron deficiency in children can be present before anemia develops. Where serum ferritin can be measured only on referred specimens, complete blood count (CBC) results that are already available may help clinicians decide which children need further testing. We examined the associations between CBC indices and serum ferritin in children presenting with selective eating or poor appetite, with the aim of informing iron-status assessment in primary care.

Methods

We retrospectively analyzed paired CBC and ferritin records of 192 children seen at 12 township health centers in a county medical consortium in China between January 2025 and May 2026. Iron deficiency was defined according to the World Health Organization (WHO) 2020 age-specific ferritin thresholds. Associations were assessed by Spearman correlation, both overall and stratified by anemia status, and were examined further in sensitivity analyses. Exploratory logistic regression models were evaluated by stratified five-fold cross-validation. Three ferritin testing strategies were simulated: testing all children, selection by WHO 2024 age-specific hemoglobin (Hb) thresholds, and CBC-assisted selection.

Results

By WHO criteria, 92 children were iron deficient and 100 were not; 90 children were anemic and 102 were not. Only two nonanemic children were iron deficient. The age-specific Hb rule selected 90 children for testing, detecting 90 deficient children and missing two. In staged pathways in which all anemic children were tested, both the Hb-only pathway and the combined Hb, mean corpuscular volume (MCV), and red cell distribution width coefficient of variation (RDW-CV) pathway selected 93 children at a probability threshold of 0.50 and detected all 92 deficient children (sensitivity 100.0%; 95% confidence interval 96.1–100.0%). The overall Spearman correlation between Hb and ferritin was 0.807. Under an alternative, age-based American Academy of Pediatrics (AAP) definition, 107 children were iron deficient; the combined pathway selected 96 children and missed 14 deficient children.

Conclusions

In children presenting with selective eating or poor appetite, Hb, MCV, mean corpuscular hemoglobin, and RDW-CV were strongly associated with serum ferritin overall, although correlations within anemia strata were much weaker. These routinely available indices provide complementary information for the initial assessment of iron status in primary care and can help inform decisions on further ferritin testing.

Background

Iron deficiency is a common nutritional problem in children. It can develop before hemoglobin (Hb) falls below the anemia threshold and has consequences for both hematopoiesis and neurodevelopment [1, 2, 3]. In adolescents, iron deficiency without anemia has recently been linked to lower brain-imaging estimates of basal ganglia iron content [4]. In a prospective cohort of young children, those with chronic iron deficiency had lower cognitive scores during follow-up than iron-sufficient peers, and the differences persisted after iron status had improved [5]. These observations argue for recognizing iron deficiency before anemia develops and for assessing iron status as part of the nutritional and developmental evaluation of children.

Serum ferritin is an important marker of iron stores, yet some rural primary care facilities cannot measure it and depend on higher-level hospitals. In the county medical consortium examined here, CBCs are performed at township health centers, whereas specimens for ferritin measurement are referred to Funan County People's Hospital. During outreach clinics at township facilities, the pediatric team of the county hospital found iron deficiency on further investigation in a number of children brought in for picky eating, selective eating, or poor appetite. Dietary studies have likewise reported lower mean iron intake among picky eaters [6]. This setting raises a practical question: how much can CBC indices, which are already available in primary care, reveal about a child's iron stores?

CBC indices, including Hb, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width coefficient of variation (RDW-CV), describe erythrocyte size, hemoglobin content, and variability in cell size. The ability of routine hematological parameters to identify iron deficiency has been examined before, but in heterogeneous populations, including children attending primary care, children undergoing health examinations, and adolescents, and with differing definitions of iron deficiency [7, 8, 9, 10]. Quantifying CBC–ferritin associations, and characterizing them separately in anemic and nonanemic children, would clarify what routine erythrocyte indices contribute to the assessment of children who present to primary care with selective eating or poor appetite.

We therefore conducted a retrospective analysis of paired CBC and serum ferritin records from 192 children who presented with selective eating or poor appetite at 12 township health centers within a county medical consortium. Overall and anemia-stratified correlations between CBC indices and ferritin were examined to provide clinical evidence for the initial assessment of iron status in pediatric primary care.

Methods

Study design and clinical setting

This retrospective cross-sectional study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [11]. Outpatient records from January 2025 to May 2026 were retrieved from 12 township health centers belonging to the Funan County

People's Hospital medical consortium: Lucheng, Tianji, Miaoji, Liugou, Zhuzhai, Jiaobei, Wangdianzi, Chaiji, Xincun, Huanggang, Zhangzhai, and Xutang. CBCs were performed at the township health centers, and ferritin was measured on referred specimens at Funan County People's Hospital. The study was carried out jointly by local clinicians and researchers at Shanghai Jiao Tong University School of Medicine. The primary analyses examined CBC–ferritin correlations in the whole sample and within anemia strata. Classification modeling and the comparison of ferritin testing strategies were secondary, exploratory analyses; the testing strategies were formulated after data collection and evaluated retrospectively against existing test results.

Participants and data sources

Children were eligible if they were younger than 18 years and had presented during the study period with loss of appetite, poor appetite, picky eating, or selective eating. Inclusion further required paired CBC and serum ferritin results and complete data on age, sex, and the principal analytical variables. Outpatient medical and laboratory records were extracted retrospectively by the researchers and verified by clinicians. Each child contributed a single observation, giving a final sample of 192 children. Iron deficiency and anemia were classified independently, using age-specific ferritin and Hb thresholds, respectively.

Variables and operational definitions

Extracted variables comprised age, sex, height, weight, CBC indices, ferritin, C-reactive protein (CRP), and documentation of previous iron supplementation, transfusion, and relevant medical conditions. Data on the core analytical variables were complete, so no imputation was performed. Where age in months was recorded, age in years was obtained by dividing it by 12; otherwise, the recorded age in years was used. The interval between collection of the paired specimens was calculated in calendar days from the sampling dates.

The primary reference outcome was iron deficiency defined by the World Health Organization (WHO) 2020 age-specific ferritin thresholds for individuals without infection or inflammation: <12 μg/L in children younger than 5 years and < 15 μg/L in those aged 5 years or older [1]. All records had CRP ≤ 5 mg/L. Four records originally labeled as showing "elevated" inflammation were retained in the primary analysis and excluded in a sensitivity analysis. Anemia was defined according to the WHO 2024 age-specific Hb thresholds: <105 g/L at 6–23 months, < 110 g/L at 24–59 months, < 115 g/L at 5–11 years, and < 120 g/L at 12–14 years [12]; the oldest child in the sample was 14 years of age. This classification was applied in the anemia-stratified correlation analyses, the Hb-based testing rule, and the analyses of iron deficiency without anemia. Baseline characteristics are presented by WHO-defined iron status, and the cross-classification of iron deficiency and anemia is given in Supplementary Table S10.

CBC models and evaluation of testing strategies

For the classification models, the reference outcome was ferritin-defined iron deficiency, and only CBC indices were used as predictors. Three models were compared: Hb alone, a combined Hb + MCV + RDW-CV model, and an MCV + RDW-CV model. Age, sex, CRP, and ferritin were not entered as predictors; age was used only to define iron deficiency, the anemia thresholds, and the Hb-based comparator rule. To keep model complexity proportionate to the sample size, we fitted L2-penalized logistic regression with fixed parameters, without feature selection or hyperparameter tuning [13].

Models were evaluated by stratified five-fold cross-validation; standardization was fitted within each training fold, and predicted probabilities were generated for the corresponding validation fold. Three types of strategy were evaluated: ferritin testing for all children, selection based on the WHO 2024 age-specific Hb thresholds, and selection when the model-predicted probability was ≥ 0.50. The probability threshold was fixed at 0.50 throughout. In the staged, model-assisted pathway, all children meeting the anemia criterion were selected for testing, and nonanemic children were additionally selected if the model result was positive ("anemia rule or model positive"). Models were fitted to all children in each training fold. The principal descriptive comparisons were among the age-specific Hb rule, the Hb-only assisted pathway, and the combined-model assisted pathway.

In additional threshold analyses of the combined model, stratified four-fold inner cross-validation within each outer training set was used to select thresholds targeting a training sensitivity of 95% or 98%, and these thresholds were then applied to the outer validation fold. Discrimination of the predicted probabilities was quantified by the area under the receiver operating characteristic (ROC) curve (AUC). The staged pathways were evaluated in terms of testing volume and detection of iron deficiency.

For each strategy, testing decisions were cross-tabulated against ferritin-defined iron deficiency to obtain the numbers of children selected and not selected for testing, the number of deficient children detected, and the number of deficient children missed among those not selected. Sensitivity, specificity, and negative predictive value were calculated. The proportion of children not selected for testing used all 192 children as the denominator, and the proportion of missed cases used all children who were iron deficient under the corresponding definition. Strategies were compared descriptively within the same sample.

Correlation and sensitivity analyses

Analyses were performed in Python 3.12.14. Before analysis, variable types, units, missing values, and internal consistency among CBC parameters were checked. Inflammation labels, CRP values, and recorded ages were reviewed, and records with potential inconsistencies were flagged for sensitivity analyses. Continuous variables are summarized as medians (25th, 75th percentiles) and categorical variables as counts (within-group percentages). Spearman rank correlation was used to assess the associations of Hb, MCV, MCH, RDW-CV, the Mentzer index, and the red cell distribution width index (RDWI) with ferritin, in the whole sample and stratified by WHO 2024 anemia status. The primary overall association between Hb and ferritin is reported with an unadjusted P value. The remaining five overall

tests and the 12 within-stratum tests were treated as two separate families and adjusted using the Benjamini–Hochberg (BH) procedure [14].

Percentile 95% confidence intervals (CIs) were obtained from 5,000 bootstrap resamples drawn at the child level. Two-sided P values were derived from 99,999 permutations with an add-one correction. Statistical significance was set at $P < 0.05$ for the relevant unadjusted or BH-adjusted P value; CIs were not adjusted for multiplicity. Associations adjusted for age, sex, and CRP were estimated by rank-based partial correlation. Sensitivity analyses addressed CBC consistency flags, discordance between inflammation labels and CRP values, and uncertainty in age classification near threshold boundaries. The stratified analyses were also repeated using the Hb thresholds of the 2023 Chinese expert consensus [2]. Detailed procedures are given in the supplementary methods.

In the exploratory classification analyses, fixed-parameter L2-penalized logistic regression was used to compare the Hb, Hb + MCV + RDW-CV, and MCV + RDW-CV models [13]. Standardization and model fitting were confined to the training folds of the stratified five-fold cross-validation. AUC, sensitivity, specificity, and negative predictive value were estimated from out-of-fold predictions, and the cross-validation was repeated 20 times. The models were refitted under an alternative, age-based American Academy of Pediatrics (AAP) definition of iron deficiency [3], followed by threshold analyses and post hoc comparisons of testing strategies. Interval estimation, model parameters, and threshold-selection procedures are described in the supplementary methods, and the corresponding results are provided in Supplementary Tables S3, S4, and S12 and in the accompanying code.

AI assistance

OpenAI Codex was used to assist with code development and manuscript preparation under the supervision of the authors. The authors reviewed all analyses and the manuscript and take full responsibility for the work.

Results

Participant characteristics and outcome distribution

A total of 192 children were included, 115 (59.9%) of whom were boys. The median age was 8.00 years (25th–75th percentiles, 5.75–11.00), ranging from approximately 8 months to 14 years. According to the WHO ferritin thresholds, 92 children were iron deficient and 100 were not. Median Hb in these two groups was 103.0 and 131.0 g/L, and median ferritin was 5.92 and 40.03 μg/L, respectively (Table 1; Fig. 1). Paired specimens were collected on the same calendar day for 190 children; for the remaining two, the intervals were 1 and 2 days.

Table 1
Participant characteristics

Variable	Overall (n = 192)	WHO iron deficiency (n = 92)	No WHO iron deficiency (n = 100)
Demographic and anthropometric characteristics			
Male, n (%)	115 (59.9)	50 (54.3)	65 (65.0)
Female, n (%)	77 (40.1)	42 (45.7)	35 (35.0)
Age (years)	8.00 (5.75, 11.00)	8.00 (5.00, 11.00)	8.00 (6.00, 10.00)
Height (cm)	130.0 (113.5, 145.0)	129.0 (107.2, 145.2)	130.5 (117.0, 144.0)
Weight (kg)	25.0 (18.9, 31.0)	25.5 (16.4, 32.0)	25.0 (20.0, 29.0)
CBC and iron-status measures			
Hb (g/L)	118.0 (104.0, 131.0)	103.0 (98.0, 107.0)	131.0 (125.0, 136.2)
RBC (10^{12}/L)	4.64 (4.46, 4.87)	4.62 (4.38, 4.83)	4.67 (4.51, 4.90)
HCT (%)	37.6 (34.4, 40.3)	34.3 (32.0, 36.3)	40.2 (38.4, 42.0)
MCV (fL)	81.4 (75.6, 85.1)	75.2 (71.8, 78.1)	84.9 (82.7, 87.4)
MCH (pg)	26.4 (22.1, 27.7)	22.0 (20.6, 23.8)	27.7 (27.1, 28.7)
MCHC (g/L)	323.0 (305.2, 331.0)	302.5 (278.8, 316.0)	328.0 (323.8, 333.0)
RDW-CV (%)	14.0 (12.9, 18.0)	18.1 (17.4, 19.1)	13.0 (12.6, 13.3)
RDW-SD (fL)	40.65 (39.30, 42.32)	41.00 (39.20, 42.23)	40.50 (39.40, 42.40)
WBC (10^9/L)	6.49 (5.28, 7.70)	6.36 (5.39, 7.77)	6.57 (5.27, 7.55)
PLT (10^9/L)	278.0 (231.0, 324.0)	273.5 (225.0, 329.0)	279.5 (253.0, 315.0)
Ferritin (µg/L)	18.43 (6.38, 41.22)	5.92 (4.01, 8.38)	40.03 (27.62, 50.23)
CRP (mg/L)	3.15 (2.27, 4.14)	3.05 (1.50, 4.35)	3.20 (2.50, 4.03)
Mentzer index	17.14 (15.77, 18.64)	16.27 (15.24, 17.13)	18.15 (17.10, 19.05)

Values are medians (25th–75th percentiles) or numbers (within-group percentages). Groups are defined by WHO ferritin thresholds; anemia is classified using WHO 2024 age-specific Hb thresholds. 1 ng/mL = 1 µg/L. Mentzer index = MCV/RBC; RDWI = MCV × RDW-CV/RBC.

Variable	Overall (n = 192)	WHO iron deficiency (n = 92)	No WHO iron deficiency (n = 100)
Demographic and anthropometric characteristics			
RDWI	257.90 (231.06, 291.25)	291.31 (268.73, 314.42)	233.84 (222.22, 252.35)
Status defined by numerical thresholds			
WHO 2024 anemia, n (%)	90 (46.9)	90 (97.8)	0 (0.0)
Iron deficiency under the AAP age-based definition, n (%)	107 (55.7)	92 (100.0)	15 (15.0)

Values are medians (25th–75th percentiles) or numbers (within-group percentages). Groups are defined by WHO ferritin thresholds; anemia is classified using WHO 2024 age-specific Hb thresholds. 1 ng/mL = 1 µg/L. Mentzer index = MCV/RBC; RDWI = MCV × RDW-CV/RBC.

[Table 1 and Fig. 1 near here]

Based on the WHO 2024 age-specific Hb thresholds, 90 children were anemic and 102 were not. All 90 anemic children were iron deficient, as were two of the 102 nonanemic children. Both of these nonanemic, iron-deficient children were younger than 2 years and had an Hb concentration of 106 g/L, 1 g/L above the applicable anemia threshold (Supplementary Table S10).

Screening performance of ferritin testing strategies

Under the WHO definition of iron deficiency, the out-of-fold AUC was 0.9995 for Hb alone, 0.9995 for the combined Hb + MCV + RDW-CV model, and 0.9925 for the MCV + RDW-CV model. At the fixed threshold of 0.50, the Hb-only model selected 92 children for testing, detecting 91 deficient children and missing one, whereas the combined model selected 91 children, detecting 90 and missing two (Fig. 2; Supplementary Tables S2 and S3).

[Fig. 2 near here]

Taking ferritin testing of all 192 children as the reference, the WHO 2024 age-specific Hb rule selected 90 children for testing; it detected 90 deficient children and missed two, giving a sensitivity of 97.8% and a specificity of 100.0%. In the staged pathways, in which all anemic children were tested and nonanemic children were further screened with a model, both the Hb-only and the combined-model pathways selected 93 children at the 0.50 threshold and detected all 92 deficient children. Compared with the Hb rule alone, each pathway required three additional simulated tests and identified the two nonanemic deficient children.

For the combined-model assisted pathway, sensitivity was 100.0% (95% CI 96.1–100.0%), specificity 99.0% (94.6–100.0%), and negative predictive value 100.0% (96.3–100.0%). Both nonanemic deficient children were detected, although the 95% CI for the detection proportion in this subgroup was wide (15.8–100.0%) (Supplementary Table S13; Supplementary Fig. S1).

When thresholds targeted training sensitivities of 95% and 98%, the combined-model staged pathways selected 92 and 93 children, respectively, and missed no cases. In each of the 20 repeated cross-validation runs, the combined-model assisted pathway at the fixed 0.50 threshold selected 93 children and missed no deficient children. Repeated-validation results for the models alone and for the staged pathways are presented in Supplementary Tables S4 and S12, respectively.

Associations between CBC indices and ferritin

Overall, Hb was positively correlated with ferritin (ρ = 0.807; 95% CI 0.765–0.842; P < 0.0001). The corresponding correlation coefficients were 0.783 for MCV, 0.769 for MCH, − 0.762 for RDW-CV, 0.460 for the Mentzer index, and − 0.567 for RDWI; all five secondary overall associations had BH-adjusted P values < 0.0001.

After stratification by WHO 2024 anemia status, the Hb–ferritin correlation was 0.218 in anemic children (95% CI 0.005–0.414; BH-adjusted P = 0.0700) and 0.284 in nonanemic children (0.081–0.469; BH-adjusted P = 0.0238). Among anemic children, the correlation between MCV and ferritin was 0.396 (0.185–0.584; BH-adjusted P = 0.0012). Of the 12 within-stratum tests, only MCV in the anemic stratum and Hb in the nonanemic stratum remained statistically significant after BH adjustment (Table 2; Supplementary Figs. S3 and S4).

Table 2
Overall and anemia-stratified correlations using WHO 2024 criteria

Variable	Spearman ρ (95% CI)	P value	BH-adjusted P
Overall (n = 192)			
Hb	0.807 (0.765, 0.842)	<0.0001	—
MCV	0.783 (0.725, 0.829)	<0.0001	<0.0001
MCH	0.769 (0.719, 0.806)	<0.0001	<0.0001
RDW-CV	-0.762 (-0.807, -0.702)	<0.0001	<0.0001
Mentzer index	0.460 (0.339, 0.575)	<0.0001	<0.0001
RDWI	-0.567 (-0.659, -0.466)	<0.0001	<0.0001
WHO 2024 anemia (n = 90)			
Hb	0.218 (0.005, 0.414)	0.0389	0.0700
MCV	0.396 (0.185, 0.584)	0.0001	0.0012
MCH	0.127 (-0.095, 0.336)	0.2324	0.2789
RDW-CV	-0.098 (-0.301, 0.114)	0.3574	0.3899
Mentzer index	0.217 (-0.017, 0.438)	0.0408	0.0700
RDWI	0.226 (0.003, 0.430)	0.0323	0.0700
No WHO 2024 anemia (n = 102)			
Hb	0.284 (0.081, 0.469)	0.0040	0.0238
MCV	0.175 (-0.032, 0.366)	0.0795	0.1192
MCH	0.208 (0.011, 0.394)	0.0368	0.0700
RDW-CV	-0.214 (-0.415, -0.007)	0.0308	0.0700
Mentzer index	0.044 (-0.152, 0.243)	0.6574	0.6574
RDWI	-0.145 (-0.340, 0.062)	0.1445	0.1926

Spearman ρ and 95% CIs from 5,000 paired bootstrap resamples at the child level are shown. P values were calculated using 99,999 two-sided permutations. BH adjustment was applied separately to the five secondary overall tests and the 12 within-stratum tests. The primary overall Hb association was not adjusted for multiplicity. CIs were not adjusted for multiplicity. Anemia was determined using age-specific Hb thresholds.

[Table 2 near here]

After adjustment for age, sex, and CRP, the rank-based partial correlation between Hb and ferritin was 0.812 (95% CI 0.767–0.845). The association remained strong in a sensitivity analysis of 185 children (ρ

= 0.802; 95% CI 0.757–0.837; Supplementary Table S1). Results of the other adjusted and sensitivity analyses are reported in Supplementary Tables S1 and S9.

Alternative iron-deficiency definition and internal validation

The alternative, age-based AAP definition classified 107 of the same 192 children as iron deficient, 17 of whom were not anemic. Fifteen children classified as nondeficient under the WHO definition were reclassified as deficient (Supplementary Tables S8 and S10).

At the fixed 0.50 threshold, the combined-model assisted staged pathway selected 96 children, detecting 93 deficient children and missing 14, and detected three of the 17 nonanemic deficient children. The Hb-only assisted pathway selected 100 children, detecting 95 deficient children and missing 12. With thresholds targeting training sensitivities of 95% and 98%, the combined-model pathway selected 141 and 185 children and missed five cases and one case, respectively. Under the latter strategy, 96.4% of the sample was selected for testing, and one of the seven children not selected was iron deficient (Supplementary Tables S6 and S11; Supplementary Fig. S2).

Repeated-validation and exclusion-based sensitivity analyses for the models alone are presented in Supplementary Tables S4 and S5, respectively, and repeated-validation results for the staged pathways in Supplementary Table S12.

Discussion

Principal findings and the clinical question

This study suggests that CBC indices already available in primary care can help identify children with low ferritin. Among children presenting with picky eating, selective eating, or poor appetite, Hb, MCV, and MCH were positively correlated with ferritin, and RDW-CV was negatively correlated. The overall association between Hb and ferritin was essentially unchanged after covariate adjustment and in sensitivity analyses, and the exploratory classification models discriminated well in internal evaluation when iron deficiency was defined by ferritin. These results provide preliminary support for using routine primary care tests to inform the assessment of iron stores and the decision to request ferritin testing. Within anemia strata, however, the Hb correlation coefficients were much smaller than the overall estimate, indicating that the pooled association does not adequately describe the relationship within each stratum. At the fixed 0.50 threshold, the combined-model staged pathway detected no more iron-deficient children than the Hb-only pathway, and screening performance shifted when an alternative definition of iron deficiency was applied. These secondary findings indicate that the value of CBC-assisted assessment depends on the outpatient population, anemia status, and ferritin reference threshold under consideration.

Relation to previous research

Earlier studies support the use of CBC parameters as indicators of iron status, although their ability to identify low ferritin differs between populations. Among 1,735 children aged 1–3 years attending well-child visits, Oatley et al. found that Hb < 110 g/L had a sensitivity of only 25% for ferritin < 12 μg/L [7]. Zhan et al. reported an AUC of 0.73 for MCV in identifying iron deficiency in children undergoing health examinations, and Alsafi et al. reported AUCs of 0.71 for Hb and 0.73 for RDW in adolescents [8, 9]. Comparisons of classification performance across these studies need to take account of differences in age distribution, clinical setting, and reference thresholds.

In our sample, all 90 children with anemia met the WHO ferritin criteria for iron deficiency, and only two children had iron deficiency without anemia; iron deficiency and low Hb therefore overlapped almost completely. Because the age-specific Hb rule alone identified most iron-deficient children, the high sensitivity, specificity, and AUC of the models may partly reflect this case mix. Likewise, the contrast between the strong pooled Hb–ferritin correlation and the much weaker within-stratum correlations suggests that differences in distribution between the anemic and nonanemic groups contributed to the overall association. The narrower Hb range within each stratum may also have attenuated the stratum-specific estimates. Spectrum effects of this kind on test performance have been described previously [15]. The internal validation results support the discriminative ability of CBC parameters in this sample, but their transportability needs to be established in independent populations.

The effect of changing the ferritin reference threshold further shows that the value of CBC parameters depends on how the target condition is defined. Physiologically based studies and AAP recommendations adopt higher ferritin thresholds than the conventional WHO cut-offs and thus broaden the definition of iron deficiency [3, 16, 17]. Under the alternative age-based AAP definition, the number of children with iron deficiency without anemia rose from two to 17, and more cases were missed at the fixed classification threshold. This shift may reflect the fact that iron stores decline before hematological changes become apparent, and it suggests that CBC parameters have limited ability to identify low ferritin in children without anemia. Additional markers of iron status and follow-up data are required to characterize the iron metabolism and clinical significance of the reclassified cases.

When thresholds were selected to achieve 98% sensitivity in the training data, the combined-model staged pathway assigned 96.4% of children to send-out testing in the simulation. Only seven children screened negative, one of whom met the definition of iron deficiency. The high detection rate thus came at the cost of a heavy testing load, and the small number of screen-negative children made the estimate of negative predictive value imprecise. The clinical value of CBC-assisted ferritin testing should therefore be judged by weighing detection, negative predictive value, and testing demand together. Independent validation in consecutively enrolled children with similar outpatient presentations is needed to define the population to which this adjunctive approach applies and to establish its value.

Implications for send-out testing pathways

CBC-assisted iron-status assessment could be evaluated within the existing laboratory referral pathway of the county medical consortium. Future studies should examine the incremental value of combined

indices over Hb alone, together with ferritin testing completion, turnaround time, burden on families, and subsequent clinical outcomes. Because the reference outcome in this study was ferritin-defined iron deficiency, the analyses addressed the ability of CBC parameters to identify low ferritin. Ferritin testing also contributes to establishing the cause of anemia, and its results should be interpreted in light of inflammatory status and other clinical information. In practice, decisions on send-out testing must also take into account dietary history, risk of blood loss, previous treatment, and other indications. Within this broader assessment, CBC indices can provide supplementary clues that help direct further evaluation of iron status.

Strengths and limitations

This study drew on real-world outpatient records from 12 township health centers, verified by clinicians, and applied explicit ferritin-based reference definitions. Both correlation analyses and exploratory classification analyses were used to evaluate the adjunctive value of CBC parameters. De-identified data, analysis code, out-of-fold predictions, and model parameters are provided to allow independent scrutiny of the results.

The principal limitations relate to sample selection and case mix. All included children had already undergone both CBC and ferritin testing, and only records with complete data were analyzed. Because the total number of records screened, the reasons for noninclusion, and the original indications for send-out testing were not available, the influence of case selection on the findings could not be quantified. Anemia and iron deficiency overlapped extensively, and only two children had iron deficiency without anemia, which limited evaluation of this clinically important subgroup. The study was confined to a single county medical consortium and included no children aged 15–17 years, and standardized dietary and developmental assessments were not available. The generalizability of the findings therefore requires further evaluation.

Ferritin concentrations are affected by infection and inflammation, and a low CRP level does not fully exclude these effects [1, 18]. Data on α_1-acid glycoprotein and on overall clinical inflammatory status were lacking, so inflammation-related bias cannot be ruled out. Information on CBC analyzers, ferritin assay methods, reagents, and quality control during the study period was incomplete, which limited assessment of measurement consistency. Some ages were recorded only in completed years, and data on pubertal status and menstruation were unavailable, which complicates the interpretation of age-based classifications. Finally, the available records did not allow actual turnaround times for send-out ferritin testing to be assessed.

The exploratory classification analyses and the post hoc send-out testing strategies were evaluated internally only. Performance intervals were derived from fixed out-of-fold predictions or sample counts and therefore do not fully capture the uncertainty arising from model development and strategy selection. Formal comparison of strategies, comprehensive assessment of calibration, clinical net benefit, and cost-effectiveness remain to be investigated.

Building on the existing collaboration between the medical consortium and Shanghai Jiao Tong University, neighboring counties and township health institutions could gradually be brought into a clinical research network. Harmonized core variables, data collection procedures, and laboratory quality-control standards would allow consecutive enrollment of children with similar presenting complaints and systematic collection of paired test results, and data from new centers could then be used to test the stability of CBC–ferritin associations. The exploratory classification models should be externally validated with models and thresholds locked in advance. Concurrent evaluation of testing completion, turnaround time, family burden, and subsequent clinical outcomes would help establish the external validity and clinical utility of this adjunctive approach.

Conclusions

In children presenting with selective eating or poor appetite, CBC indices were strongly associated with serum ferritin overall, although correlations within anemia strata were much weaker. These indices provide complementary information for the initial assessment of iron status and can help inform decisions on further ferritin testing. The exploratory classification findings require independent validation in the intended clinical population.

Abbreviations

AAP
American Academy of Pediatrics
AUC
area under the receiver operating characteristic curve
BH
Benjamini–Hochberg
CBC
complete blood count
CI
confidence interval
CRP
C-reactive protein
Hb
hemoglobin
HCT
hematocrit
MCH
mean corpuscular hemoglobin
MCHC
mean corpuscular hemoglobin concentration
MCV

mean corpuscular volume
NPV
negative predictive value
RBC
red blood cell count
RDW-CV/SD
red cell distribution width coefficient of variation/standard deviation
RDWI
red cell distribution width index
ROC
receiver operating characteristic
WHO
World Health Organization.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Funan County People's Hospital approved this retrospective study and the use of existing clinical records for research (approval no. FNLL20261007143), and waived the requirement for informed consent from guardians and, where applicable, assent from the children. Direct identifiers, including names and outpatient registration numbers, were removed before analysis.

Consent for publication

Not applicable. Neither the manuscript nor the supplementary materials contain directly identifiable personal information or images of individuals.

Availability of data and materials

Summary results are presented in the main manuscript and Additional file 1. With the authorization of the hospital, the de-identified analytical dataset for all 192 children is provided in Additional file 2, together with label definitions and revision notes, a data dictionary, Python code, a dependency lock file, out-of-fold predictions, and instructions for reproducing the analyses. Study identifiers allow records to be cross-checked across analysis files; the linkage key is held separately by the hospital and is not included in the shared materials. The shared data contain no direct identifiers, exact visit dates, or original Excel row numbers.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

Jiaojiao Wang contributed to discussions of the study design, laboratory data extraction, and quality control. Xuequn Huang contributed to protocol discussions, data quality control, and data verification. Lei Zang contributed to discussions of the pediatric clinical question. Tienan Feng contributed to the study design and protocol development, performed and verified the statistical analyses, and drafted the manuscript. Lei Dong formulated the clinical research question and contributed to protocol discussions, review of the study, and preparation of the manuscript. All authors read and approved the final manuscript and are accountable for their contributions and for the accuracy and integrity of the work as a whole.

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Figures

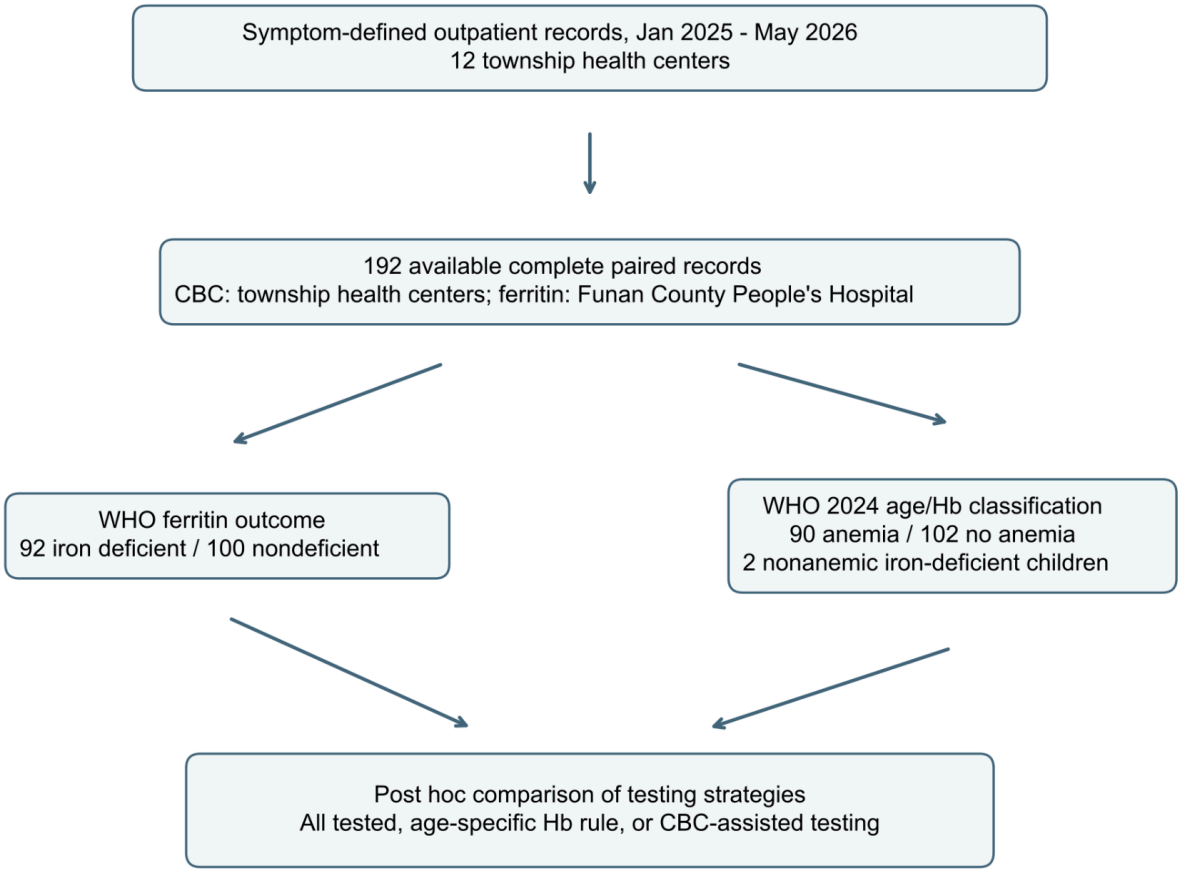

Figure 1

Study data and analysis flow

Existing paired outpatient records from 192 children were analyzed. WHO ferritin thresholds identified 92 deficient and 100 nondeficient children; WHO 2024 age-specific Hb thresholds identified 90 anemic and 102 nonanemic children. Testing strategies were compared post hoc using existing laboratory results.

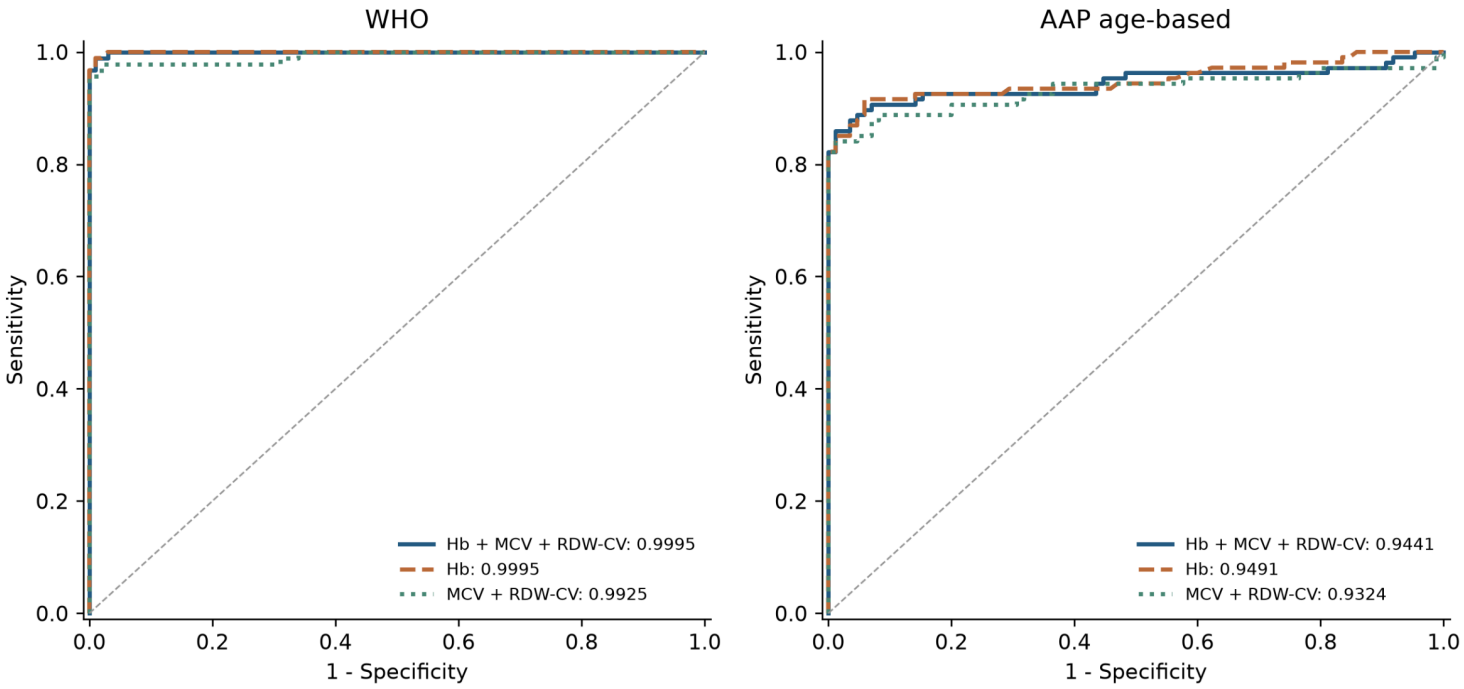

Figure 2

Out-of-fold ROC curves for CBC models

Out-of-fold predictions of ferritin-defined iron deficiency from the models alone are shown. These curves do not represent staged pathways incorporating the anemia rule. WHO and AAP define different reference outcomes. Code and out-of-fold predictions are provided in Additional file 2.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFile1SupplementaryMaterialEnglish20261108.docx