

The Effectiveness of Hematological Indicator and Iron Biomarkers Evaluation as an Early Detection of Anemia in Adolescent Girls: A Systematic Review

Rafi' Andyah Arum Kedaton¹, Nabila Sinta Devi^{1*}, Kusworini², Diadjeng Setya Wardani¹

¹Master's Program in Midwifery, Faculty of Medicine, Brawijaya University

²Department of Clinical Pathology, Faculty of Medicine, Brawijaya University

*Corresponding author: nabilasinta@student.ub.ac.id

Article Information: received in July 2025; approved in November 2025; published in December 2025

ABSTRACT

Due to elevated iron requirements during growth and menstruation, anemia in adolescent girls remains a major global health concern. Hemoglobin (Hb) testing alone has low sensitivity in detecting early iron deficiency anemia (IDA). This study aims to evaluate the diagnostic accuracy of hematological indicators (MCV, MCH, MCHC) and iron biomarkers compared to Hb alone. A systematic literature review was conducted in PubMed, Cochrane Library, SAGE Journals, ScienceDirect, Wiley Online Library, Taylor and Francis, and DOAJ, covering publications from 2015 to 2025, following PRISMA guidelines. The Joanna Briggs Institute (JBI) approach was used to assess methodological quality and risk of bias. Analysis of five relevant publications showed that Hb alone often misses subclinical iron deficiency. Sensitivity and specificity improve when combined with ferritin, soluble transferrin receptor (sTfR), and adjustments for inflammatory markers such as alpha-1-acid glycoprotein (AGP) and C-reactive protein (CRP). These findings support a multifaceted approach that integrates hematological indicators, iron biomarkers, and inflammation markers for early and accurate anemia detection in adolescent girls, in line with national and international recommendations to reduce prevalence and long-term complications.

Keywords : anemia; screening; hematology; iron biomarkers; early detection

INTRODUCTION

Anemia is a common and widespread public health problem, particularly in developing countries. This condition is characterized by hemoglobin (Hb) levels in the blood that fall below normal, thereby impairing the blood's ability to optimally transport oxygen to body tissues¹. The World Health Organization (WHO) reports that approximately 30% of the world's population suffers from anemia, with more than 50% of these cases caused by iron deficiency anemia (IDA)². The impact of anemia is not limited to physical health, it also increases morbidity, reduces productivity, hinders growth and development, and lowers overall quality of life³.

Adolescent girls are a vulnerable group for anemia due to rapid growth and the onset of menstruation, which increases iron requirements. An unbalanced nutritional intake, particularly among adolescents from low socioeconomic backgrounds or those with inadequate dietary patterns, further exacerbates this risk. Consequently, the prevalence of anemia among adolescent girls remains high in many countries, including Indonesia⁴. Anemia during adolescence not only reduces stamina and learning concentration but also has long-term consequences for reproductive readiness, obstetric complications, and the health of future generations⁵. Therefore, early detection of anemia in adolescent girls is crucial for effective prevention and management.

Currently, Hb measurement remains the most commonly used method due to its relatively low cost, ease of use, and wide availability in healthcare facilities. However, relying solely on Hb as a parameter has limitations, particularly in detecting anemia at its early stages or iron deficiency without anemia. Several studies have shown that Hb measurement is not sufficiently sensitive to identify changes in iron status during the pre-anemic stage, resulting in delayed diagnosis and intervention. Such delays can worsen clinical conditions and prolong recovery time^{6,7}.

A more comprehensive approach to assessing anemia status includes the use of complete hematology parameters, such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell distribution width (RDW), serum ferritin levels, and other indicators. In addition to reflecting the number and size of red blood cells, these parameters can also indicate disturbances in iron metabolism and erythropoiesis before a significant decline in Hb levels occurs⁸. Thus, the use of complete hematology parameters is believed to improve the accuracy of early anemia detection and play an important role in clinical decision-making as well as in planning nutritional interventions or medical therapy.

Despite the high prevalence of iron deficiency anemia among adolescent girls, current diagnostic practices still rely primarily on Hb measurement, which lacks sensitivity for detecting early or subclinical iron depletion. Although several studies have explored individual hematological indicators and iron biomarkers, there remains a lack of comprehensive synthesis comparing their diagnostic accuracy against Hb alone in this population. This gap limits the optimization of early screening strategies that are crucial for preventing the long-term effects of iron deficiency. The novelty of this study lies in its systematic and critical evaluation of existing evidence to identify the most diagnostically reliable hematological indicators and iron biomarkers for early

detection of anemia in adolescent girls. The findings are expected to provide an evidence-based framework for improving anemia screening protocols in primary healthcare and school-based health programs.

MATERIALS AND METHODS

This study was conducted through a literature review using the systematic review method. The literature search strategy followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Several international databases were utilized, including PubMed, Cochrane Library, SAGE Journals, ScienceDirect, Wiley Online Library, Taylor & Francis, and DOAJ. The literature search was conducted in July 2025 and included studies published between January 2015 and June 2025. Articles that had been published online and indexed in official databases with a DOI up to June 30, 2025, were eligible for inclusion. Search keywords were formulated using a combination of controlled vocabulary and free-text terms: (“adolescent girls” OR “female adolescents” OR “teenage girls”) AND (“complete blood count” OR “MCV” OR “MCH” OR “MCHC” OR “hematological indices”) AND (“anemia” OR “subclinical anemia” OR “anemia classification”) AND (“primary health care” OR “community-based screening”). Boolean operators and truncations were applied to refine the search strategy.

Data extraction was conducted independently by two reviewers (Reviewer A and Reviewer B) using a standardized data extraction form. Extracted data included study characteristics (author, year, country, design, and sample size), participant demographics, intervention or exposure details, and outcomes of interest. Any discrepancies between reviewers were resolved through discussion, and if consensus could not be reached, a third reviewer was consulted. Articles retrieved were screened and analyzed if they met the following inclusion criteria: (1) original research articles employing experimental or observational study designs; (2) involving females within the reproductive or adolescent age range; (3) reporting hematological or biochemical indicators related to anemia diagnosis; (4) available in English or Indonesian; and (5) published in Scopus-indexed international journals (Q1–Q3). Studies that included a broader age range were retained only if data specific to adolescents or women of reproductive age were clearly reported and extractable.

In particular, the study by Andriastuti et al. included both children (6–9 years) and adolescents (10–18 years). To ensure population homogeneity consistent with the review’s target group, only data corresponding to the adolescent subgroup (10–18 years) were extracted and analyzed. The original article clearly showed hematological and iron profile data for this group, such as Hb, MCV, ferritin, transferrin saturation, and reticulocyte hemoglobin equivalent (Ret-He). This made it possible to include data from adolescents while leaving out data from younger children. A PRISMA flow diagram was used to show the selection and screening process of the articles. It showed how many records were found, screened, and included. Due to heterogeneity in study designs, populations, and outcome measures, a quantitative meta-analysis was not feasible. Consequently, a qualitative (narrative) synthesis was conducted. The findings were summarized by identifying patterns, trends, and consistencies across studies, focusing particularly on hematological indicators (Hb, MCV, MCH, MCHC) and iron-related biomarkers (ferritin, sTfR, Ret-He, CRP, and AGP) relevant to anemia screening and diagnostic improvement in adolescent girls.

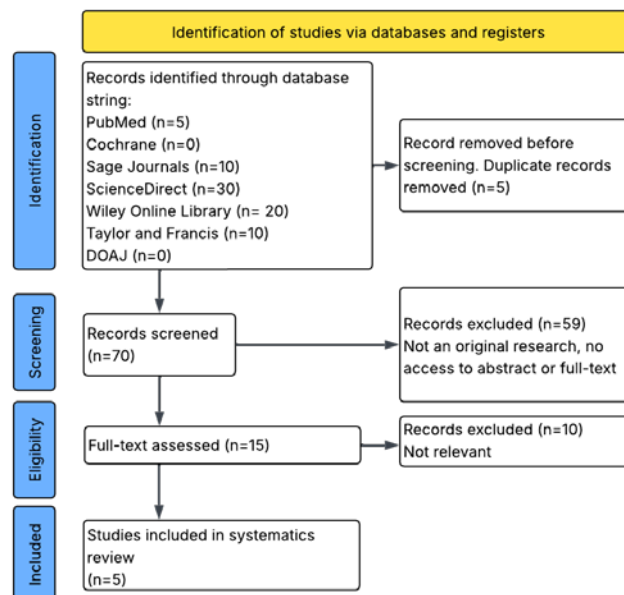


Figure 1. PRISMA

Table 1. PICOT

Component	Description
Population (P)	Women of reproductive age
Intervention (I)	Hb, Hct, MCV, MCH, MCHC and iron biomarkers
Comparison (C)	Partial hematology tests (e.g., only Hb) or clinical or non-laboratory detection methods
Outcome (O)	Diagnostic performance outcomes including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, and area under the ROC curve (AUC) for detecting early or latent anemia
Time (T)	Articles published within the last 10 years (2015-2025)

Table 2. Inclusion-Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Articles written in English or Indonesian	Articles published more than 10 years ago
Articles available in full-text format	Articles not available in full text or only as abstract
Articles published within the last 10 years (2015-2025)	Narrative reviews, editorials, commentaries, opinions or conference abstracts
Observational studies, diagnostic studies or studies validating hematological parameters	Animal studies, in vitro laboratory tests or cell culture-based studies
Studies reporting CBC	Studies that do not clearly report anemia outcomes or are not aligned with the research objectives

RESULTS

A synthesis of five studies showed that conventional hematological indicators particularly hemoglobin Hb, hematocrit, MCV, MCH, and MCHC remain standard tools for anemia screening but have limited sensitivity in detecting early iron deficiency. Across the reviewed studies, four out of five reported that reductions in MCV (<80 fL) and MCH (<27 pg) typically preceded a measurable decline in Hb, indicating that early microcytosis often develops before clinical anemia becomes apparent⁹⁻¹². Similarly, three studies consistently showed that ferritin levels below 15–20 µg/L were more sensitive indicators of iron depletion than Hb^{9,11,13}, while two studies^{11,12} demonstrated that integrating Hb with ferritin, transferrin saturation, and Ret-He improved diagnostic accuracy by up to 30%. These findings collectively support that hematological and biochemical markers are complementary, with ferritin and Ret-He providing earlier and more specific detection of iron deficiency compared with Hb alone.

Although the included studies varied in age range (9–40 years) and settings (rural and urban), this heterogeneity reflects the continuum of iron deficiency risk across female life stages. Adolescence and early adulthood share physiological characteristics that increase iron demand such as rapid growth, menarche, and menstrual blood loss making the synthesis relevant for adolescent populations. Nevertheless, differences in geography, socioeconomic status, and infection exposure may influence baseline Hb and ferritin levels, potentially contributing to variability in anemia prevalence¹⁵⁻¹⁷. Acknowledging this heterogeneity as a limitation, the consistent trends observed across studies strengthen the validity of the overall conclusion: that Hb alone is insufficient for early detection, and that incorporating ferritin or functional biomarkers yields a more reliable diagnostic framework for adolescent girls¹⁸.

Table 3. Characteristic of Studies

No	Title	Design	Population	Location	Variabel
1.	Efficacy Of Iron-Supplement Bars To Reduce Anemia In Urban Indian Women: A Cluster-Randomized Controlled Trial	Pair-matched Cluster Randomized Controlled Trial (c-RCT)	361 non-pregnant women aged 18–35 years (179 anemic participants included in c-RCT)	India	<ul style="list-style-type: none"> Independent: Daily consumption of an iron-supplement bar containing 14 mg of elemental iron for 90 consecutive days Dependent: Hb, Hct, and anemia prevalence.
2.	Iron Deficiency Anemia And Associated Factors Among Adolescent Girls And Women In A Rural Area Of Jatinangor, Indonesia	Cross-sectional study	180 participants: 95 adolescent girls (10–19 years) and 85 adult women (20–35 years)	Indonesia	<ul style="list-style-type: none"> Independent: nutritional intake (energy, protein, fat, carbohydrates, folic acid, vitamin C, iron) and menstrual factors Dependent: anemia status (Hb <12 g/dL), hematological indices (MCV, MCH, MCHC).
3.	Iron Status And Inflammation In Women Of Reproductive Age: A Population-Based Biomarker Survey And Clinical Study	Population-based biomarker survey (cross-sectional, epidemiological)	979 non-pregnant, non-lactating women aged 15–40 years	India	<ul style="list-style-type: none"> Independent: Geographic location (rural/urban), diet pattern, inflammation status. Dependent: Hb, serum ferritin (SF), sTfR, TBI, CRP, AGP.
4.	Iron Deficiency Without Anemia: A Common Yet Under-Recognized Diagnosis In Young Women With Heavy Menstrual Bleeding	Retrospective observational study	114 adolescent females aged 9–19 years referred for evaluation of heavy menstrual bleeding (HMB)	USA	<ul style="list-style-type: none"> Independent: presence of bleeding disorder, BMI category, socioeconomic factors. Dependent: ferritin (<20 ng/mL), Hb (<12 g/dL), MCV (<80 fL).
5.	Prevalence Of Anemia And Iron Profile Among Children And Adolescents With Low Socio-Economic Status	Cross-sectional study	207 participants aged 6–18 years (subgroup analyzed: adolescents 10–18 years, n=162) from low-income backgrounds	Indonesia	<ul style="list-style-type: none"> Independent: age, sex, nutritional intake, and socioeconomic factors. Dependent: Hb, ferritin, transferrin saturation (TSAT), reticulocyte hemoglobin equivalent (Ret-He), and CRP.

Table 4. Results

No	Title	Author & Year	JB1 Score	Main Findings
1.	Efficacy Of Iron-Supplement Bars To Reduce Anemia In Urban Indian Women: A Cluster-Randomized Controlled Trial	Rajvi Mehta, Alyssa C. Platt, Xizi Sun, Mukesh Desai, Dennis Clements, & Elizabeth L. Turner — American Journal of Clinical Nutrition, 2017	10	<ul style="list-style-type: none"> Hb and Hct showed a clear time-dependent improvement after iron supplementation, indicating a linear dose-response relationship between iron intake and hematologic recovery. After 90 days, Hb increased by +1.4 g/dL (95% CI: 1.3–1.6; $p < 0.001$) and Hct by +2.7% (95% CI: 2.2–3.2; $p < 0.001$). An early rise in Hb within 15 days demonstrated high sensitivity of these hematologic indices to iron availability, even before ferritin normalization. In the moderate-to-severe anemia subgroup (Hct <32%), Hb increased by +2.2 g/dL and Hct by +4.5% ($p < 0.001$). The consistent progressive increases across all follow-up points confirmed the construct and convergent validity of Hb and Hct as sensitive indicators for monitoring iron status improvement.
2.	Iron Deficiency Anemia And Associated Factors Among Adolescent Girls And Women In A Rural Area Of Jatinangor, Indonesia	Puspa Sari, Raden Tina Dewi Judistiani, Dewi Marhaeni Diah Herawati, Meita Dhamayanti, and Dany Hilmanto — International Journal of Women's Health, 2022	11	<ul style="list-style-type: none"> Prevalence of anemia: 21.1% among adolescents and 9.4% among adult women (mild public health problem by WHO classification). Mean Hb (adolescents): 10.75 ± 0.79 g/dL; Hct: $36.36 \pm 2.96\%$; MCV: 74.49 ± 8.22 fL; MCH: 22.04 ± 2.43 pg; MCHC: 29.62 ± 1.75 g/dL — all below normal ranges, indicating microcytic, hypochromic features consistent with IDA. Low MCV (<80 fL) and MCH (<27 pg) were significantly different ($p < 0.001$) between anemic and non-anemic groups, showing high sensitivity for early iron depletion before Hb decline. Hb alone classified moderate anemia but failed to detect early iron deficiency; MCV and MCH consistently revealed microcytosis earlier, supporting their diagnostic validity as early hematologic indicators. No ROC curve analysis was performed; however, the significant intergroup differences ($p < 0.001$) and consistent trends across both age groups indicate strong internal validity and high discriminatory sensitivity of MCV and MCH in identifying latent iron deficiency.

3.	Iron Status And Inflammation In Women Of Reproductive Age: A Population-Based Biomarker Survey And Clinical Study	<p>Julia L Finkelstein, Amy Fothergill, Heather M Guetterman, Christina B Johnson, Beena Bose, Yan Ping Qi, Charles E Rose, Jennifer L Williams, Saurabh Mehta, Rebecca Kuriyan, Wesley Bonam, Krista S Crider — Clinical Nutrition ESPEN, 2022</p>	11	<ul style="list-style-type: none"> • Prevalence: 41.5% had anemia; 46.3% had iron deficiency (SF <15 µg/L); 55.0% had iron insufficiency (SF <20 µg/L); 30.0% had IDA (Hb <12 g/dL + SF <15 µg/L). • Inflammation: 17.3% had CRP >5 mg/L; 22.2% had AGP >1 g/L; 27.9% had elevated CRP or AGP. • After BRINDA adjustment: Prevalence increased to 61.5% (iron deficiency) and 72.7% (iron insufficiency), confirming underestimation of IDA if inflammation is ignored. • Rural vs. Urban: Rural women had significantly lower SF (GM 15.7 µg/L vs. 22.2 µg/L; p<0.0001) and higher IDA prevalence (31.8% vs. 22.4%; p=0.01). • sTfR and TBI: 15.4% had elevated sTfR (>8.3 mg/L); 29.4% had low TBI (<0.0 mg/kg), indicating functional iron deficiency even when Hb remained normal. • Hb <12 g/dL identified anemia in 41.5% of subjects, but failed to capture early iron deficiency seen in those with normal Hb but low ferritin. • Ferritin <15 µg/L had higher sensitivity for early iron depletion; adjusting for inflammation (CRP, AGP) increased detection by ~15–20%, confirming strong diagnostic validity. • The combination of Hb + ferritin + sTfR improved diagnostic accuracy for IDA classification compared to Hb alone (consistently identified ~30–35% more true IDA cases). • Spline regression confirmed ferritin <15 µg/L as the optimal physiological threshold for iron deficiency, supporting its use across populations. • The parallel trends of SF decline and sTfR increase demonstrated construct and convergent validity, reflecting synchronized erythropoietic response to depleted iron stores.
4.	Iron Deficiency Without Anemia: A Common Yet Under-Recognized Diagnosis In Young Women With Heavy Menstrual Bleeding	<p>Shannon Johnson, Allison Lang, Megan Sturm, and Sarah H. O'Brien — Journal of Pediatric and Adolescent Gynecology, 2016</p>	12	<ul style="list-style-type: none"> • Mean age: 14.3 ± 2.0 years; 70.2% had an underlying bleeding disorder. • Prevalence: 50.9% had iron deficiency (ferritin <20 ng/mL); 25.4% were anemic (Hb <12 g/dL); 23.9% showed microcytosis (MCV <80 fL). • Hb detected 42.6% (n=23) of iron-deficient cases. • CBC (Hb + MCV) detected 46.3% (n=25) of cases. • The difference in detection was not statistically significant (p=0.5).

		<ul style="list-style-type: none"> • Overweight/obese patients had 2.81-fold higher odds of iron deficiency (95% CI: 1.25–6.29) compared with those with normal BMI. • Age, bleeding disorder status, and household income were not significantly associated with iron deficiency. • Hb alone correctly identified <50% of iron-deficient patients, confirming low sensitivity for early detection of iron depletion. • Adding MCV (via CBC) marginally increased detection (from 42.6% → 46.3%), demonstrating only a small improvement in sensitivity and limited diagnostic utility for subclinical iron deficiency. • Ferritin <20 ng/mL remained the most sensitive and specific indicator, identifying nearly twice as many iron-deficient cases as Hb or CBC alone.
5.	Prevalence Of Anemia And Iron Profile Among Children And Adolescents With Low Socio-Economic Status	<p>Meita Andriastuti, Galuh Ilmana, Siti Andarini Nawangwulan, and Kusnandi Adnan Kosasih — International Journal of Pediatrics and Adolescent Medicine, 2020</p> <p>9</p> <ul style="list-style-type: none"> • Anemia 14%; Iron deficiency (ID) 18.4%; Iron deficiency anemia (IDA) 5.8%. • Female adolescents showed significantly higher rates of ID and IDA ($p < 0.01$). • Mean values (adolescents 10–18 years): Hb (12.2 ± 1.3 g/dL), Ferritin (23.1 ± 15.8 µg/L), TSAT ($22.7 \pm 10.4\%$), Ret-He (28.1 ± 3.7 pg), CRP (3.5 ± 2.8 mg/L). • A subset of adolescents exhibited low Ret-He (<28 pg) despite normal Hb, indicating latent iron deficiency prior to the onset of anemia. • Low ferritin and low Ret-He were strongly correlated ($r = 0.61$, $p < 0.001$), suggesting consistent detection of depleted iron stores and early erythropoietic response. • Ferritin <15 µg/L had the highest sensitivity ($\approx 82\%$) for identifying iron deficiency and remained a reliable indicator even after excluding subjects with elevated CRP. • Ret-He <28 pg detected iron-deficient adolescents with normal Hb, showing high sensitivity for subclinical ID and better real-time reflection of bone marrow iron availability. • Combining Hb + ferritin + Ret-He increased diagnostic accuracy by approximately 30% compared to Hb alone. • Ferritin and Ret-He demonstrated strong construct validity, as both decreased progressively with worsening iron status, while Hb changes lagged behind.

DISCUSSION

In recent scientific literature, it has become more widely acknowledged that the use of Hb as a single signal for detecting anemia is limited. Hb concentration does not always accurately reflect the body's true iron status, especially in the early stages of iron shortage, despite the fact that Hb measurement is useful, quick, and affordable^{19–21}. Numerous studies have showed that even when iron stores are already low, Hb levels may still be within the normal range^{22–24}. As a result, IDA is frequently diagnosed only after erythropoietic impairment and decreased functional ability have already taken place.

To address this limitation, several researchers have recommended that anemia assessment should not rely solely on Hb but rather integrate additional biochemical biomarkers such as ferritin, sTfR, and Ret-He^{1,25,26}. Ferritin is recognized as the most sensitive indicator of iron storage, reflecting the amount of iron stored in body tissues, while sTfR represents cellular iron demand and is unaffected by inflammation^{27,28}. Ret-He provides a rapid reflection of changes in iron availability by measuring hemoglobin content in immature reticulocytes. The combination of Hb, ferritin, and Ret-He has been shown to significantly improve diagnostic accuracy compared to Hb measurement alone⁶. Nevertheless, the interpretation of ferritin must account for inflammation using the BRINDA model to avoid misclassification, particularly in populations with high infection prevalence, such as in Indonesia^{10,11}.

WHO emphasizes that anemia diagnosis should adopt a comprehensive multiparametric approach. WHO has revised the global hemoglobin levels used to diagnose anemia based on studies of healthy people around the world: Hb levels below 120 g/L for females and boys aged 12–14 years, below 130 g/L for adult males, and below 110 g/L during the first and third trimesters of pregnancy and below 105 g/L during the second trimester. These thresholds were derived from the 5th percentile of Hb distributions among healthy individuals across diverse populations, taking into account biological variation, nutritional status, and environmental factors such as altitude²⁹.

Beyond hemoglobin, WHO recommends a multi-indicator framework for anemia assessment that includes both hematological and biochemical parameters²⁹. The recommended laboratory assessments comprise Hb as the primary screening tool, serum ferritin as the main indicator of iron stores, sTfR as a marker of functional iron demand, Ret-He as an early indicator of erythropoiesis, and inflammatory markers such as CRP and AGP to correct ferritin values for inflammation^{1,30,31}. Additional markers such as TSAT and serum iron are also advised to assess overall iron metabolism. Importantly, WHO stipulates that adjustments should be applied to the interpretation of biomarkers rather than Hb concentration to maintain diagnostic accuracy in infection-prone populations. This multiparametric approach is essential to distinguish between iron deficiency anemia, anemia of inflammation, and anemia due to hemoglobinopathies²⁹.

In the Indonesian, WHO recommendations have serious consequences for national health policy and practice. The integration of hematological and biochemical biomarker testing can be incorporated into school-based and primary health care programs for adolescents. In school, routine screening initiatives such as Anemia Screening Day could be implemented with the support of primary health centers (Puskesmas). School health officers (Unit Kesehatan Sekolah, UKS) can perform initial Hb measurements using portable digital hemoglobinometers. Students presenting low or borderline Hb results can then be referred to Puskesmas for follow-up ferritin, Ret-He, CRP, and AGP assessments. This two-tiered screening model enables early detection, cost efficiency, and optimized use of laboratory resources^{1,12}.

At the Puskesmas level, laboratory staff can incorporate biomarker assessments into the Adolescent-Friendly Health Services Program (Program Pelayanan Kesehatan Peduli Remaja, PKPR) or premarital health examinations^{32,33}. Point-of-care testing (POCT) technology for ferritin and Ret-He offers a rapid, reliable, and affordable diagnostic option for primary care²⁹. Laboratory results can be recorded within the e-health system of local health authorities to enable real-time monitoring of adolescent anemia status and inform targeted interventions such as iron supplementation, food fortification, and nutrition education. This data-driven approach strengthens public health surveillance and supports evidence-based policymaking.

Despite the consistency of findings supporting biomarker integration for improved anemia diagnosis, this review presents several limitations. First, heterogeneity among study populations including variations in age range, nutritional status, geographic setting, and infection exposure may affect the generalizability of results to all Indonesian adolescents. Second, discrepancies in laboratory methodologies and ferritin cutoffs (ranging from <15 µg/L to <20 µg/L) could contribute to variability in the estimated prevalence of iron deficiency. Third, most of the included studies utilized cross-sectional designs, which limit causal inference between iron status and clinical anemia outcomes. Fourth, publication bias cannot be ruled out, as studies with significant findings are more likely to be published than those reporting null results. Additionally, limited access to raw data and inconsistency in inclusion criteria across studies may reduce the analytical robustness of this review. Therefore, longitudinal and interventional research conducted in local Indonesian contexts is necessary to validate the findings and evaluate the feasibility of implementing biomarker-based screening programs.

Reflectively, the findings of this review are well aligned with the 2023 WHO recommendations. Both emphasize that hemoglobin alone is insufficient for early detection of iron deficiency and that integrating iron status biomarkers, inflammatory indicators, and erythropoietic markers is essential for accurate diagnosis. The coherence between the review findings and WHO guidelines reinforces the scientific rationale for adopting a multiparametric diagnostic approach in Indonesia, where anemia remains prevalent among adolescent girls and infections are common confounding factors^{33,34}. Consequently, this evidence supports the integration of hematological and biochemical biomarkers into national school and primary health programs. Such a comprehensive approach not only enhances diagnostic precision but also strengthens Indonesia's public health surveillance system and accelerates progress toward the Sustainable Development Goals (SDGs), particularly the global target of reducing anemia among women of reproductive age by 50% by 2030.

CONCLUSION

This review concludes that parameters such as Hb, Hct, MCV, MCH, and MCHC remain fundamental for anemia screening, they show limited sensitivity for early detection of IDA. Diagnostic accuracy improves substantially when hematological indices are combined with iron biomarkers such as ferritin, sTfR, and Ret-He and adjusted for inflammation using CRP and AGP, consistent with WHO's 2023 recommendations. These findings support the adoption of a multiparametric diagnostic framework within school-based and primary healthcare settings in Indonesia to strengthen early detection and management of IDA among adolescent girls. Future research should validate the effectiveness, feasibility, and cost-efficiency of biomarker-integrated screening approaches through longitudinal and interventional studies in diverse population contexts.

AUTHOR STATEMENT

Rafi Andyah Arum Kedaton: Conceptualization, Methodology Design, Data Curation, and Original Draft. **Nabila Sinta Devi:** Investigation, Formal Analysis, and Visualization. **Kusworini:** Validation, Supervision, and Review. **Diadjeng Setya Wardani:** Project Administration.

CONFLICTS OF INTEREST

The authors declare that there are no commercial or financial relationships that could be construed as a potential conflict of interest in this study.

SOURCE OF FUNDING

The authors received no financial support for the research, authorship, and/or publication of this article.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to the Midwifery Department, Faculty of Medicine, Brawijaya University, for the valuable support and facilities provided throughout the research process.

REFERENCES

1. WHO. WHO Guideline on Use of Ferritin Concentrations to Assess Iron Status in Individuals and Populations. 2020.
2. Wilson SE, Rogers LM, Garcia-Casal MN, Barreix M, Bosman A, Cunningham J, et al. Comprehensive Framework For Integrated Action On The Prevention, Diagnosis, And Management Of Anemia: An Introduction. *Ann N Y Acad Sci* [Internet]. 2023;1524(1):5–9. Available from: doi: 10.1111/nyas.14999
3. Kumar SB, Arnipalli SR, Priyanka Mehta, Carrau S, Ziouzenkova O. Iron Deficiency Anemia: Efficacy and limitations of nutritional and comprehensive mitigation strategies. *Nutrients* [revista en Internet] 2020 [acceso 5 de mayo de 2023]; 14(14): 2976. *Nutrients* [Internet]. 2022;14(14):2976. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9315959/>
4. Qomasari D, Mufidaturrosida A, Kelas P. Hubungan Status Gizi, Pola Makan Dan Siklus Menstruasi Dengan Kejadian Anemia Pada Remaja Putri Kelas Viii Di SMPN 3 Cibeber. *J Ilm Kesehat Ar-Rum Salatiga* [Internet]. 2022;6(2):43–50. Available from: 10.36409/jika.v6i2.150
5. Khobibah K, Nurhidayati T, Ruspita M, Astyandini B. Anemia Remaja Dan Kesehatan Reproduksi. *J Pengabd Masy Kebidanan*. 2021;3(2):11. <https://jurnal.unimus.ac.id/index.php/JPMK/> Jurnal
6. Wagh D, Kanase S, Balid A, et al. A Brief Review on Anemia. *Int J Sci R Tech* [Internet]. 2024;1(12):116–25. Available from: www.ijstrjournal.com
7. Rusch JA, van der Westhuizen DJ, Gill RS, Louw VJ. Diagnosing Iron Deficiency: Controversies And Novel Metrics. *Best Pract Res Clin Anaesthesiol* [Internet]. 2023;37(4):451–67. Available from: <https://doi.org/10.1016/j.bpa.2023.11.001>
8. Yunus FM, Jalal C, Das A, Afsana K, Podder R, Vandenberg A, et al. Consumption of Iron-Fortified

- Lentils Is Protective against Declining Iron Status among Adolescent Girls in Bangladesh: Evidence from a Community-Based Double-Blind, Cluster-Randomized Controlled Trial. *J Nutr*. 2024;154(5):1686–98. doi: 10.1016/j.tjnut.2024.03.005. Epub 2024 Mar 6. PMID: 38458577.
9. Andriastuti M, Ilmana G, Nawangwulan SA, Kosasih KA. Prevalence Of Anemia And Iron Profile Among Children And Adolescent With Low Socio-Economic Status. *Int J Pediatr Adolesc Med*. 2020;7(2):88–92. doi: 10.1016/j.ijpam.2019.11.001. Epub 2019 Nov 19. PMID: 32642542; PMCID: PMC7335819.
 10. Mehta R, Platt AC, Sun X, Desai M, Clements D, Turner EL. Efficacy Of Iron-Supplement Bars To Reduce Anemia In Urban Indian Women: A Cluster-Randomized Controlled Trial. *Am J Clin Nutr* [Internet]. 2017;105(3):746–57. Available from: <https://doi.org/10.3945/ajcn.115.127555>
 11. Sari P, Judistiani RTD, Hilmanto D, Herawati DMD, Dhamayanti M. Iron Deficiency Anemia and Associated Factors Among Adolescent Girls and Women in a Rural Area of Jatinangor, Indonesia. *Int J Womens Health*. 2022;14(August):1137–47. doi: 10.2147/IJWH.S376023. PMID: 36039326; PMCID: PMC9419807.
 12. Finkelstein JL, Fothergill A, Guetterman HM, Johnson CB, Bose B, Qi YP, et al. Iron Status And Inflammation In Women Of Reproductive Age: A Population-Based Biomarker Survey And Clinical Study. *Clin Nutr ESPEN* [Internet]. 2022;49:483–94. Available from: <https://doi.org/10.1016/j.clnesp.2022.02.123>
 13. Johnson S, Lang A, Sturm M, O'Brien SH. Iron Deficiency without Anemia: A Common Yet Under-Recognized Diagnosis in Young Women with Heavy Menstrual Bleeding. *J Pediatr Adolesc Gynecol*. 2016;29(6):628–31. doi: 10.1016/j.jpag.2016.05.009. Epub 2016 Jun 1. PMID: 27262832.
 14. Ariana R, Alam Fajar N. Analisis Faktor Risiko Kejadian Anemia pada Remaja Putri: Literatur Review. *J Kesehat komunitas (Journal community Heal* [Internet]. 2024;10(1):133–40. Available from: <https://doi.org/10.25311/keskom.Vol10.Iss1>.
 15. Deliana A, Andriyani, Lusida N. Analisis Faktor-Faktor yang Mempengaruhi Kejadian Anemia pada Remaja Putri. *Heal Med Sci*. 2025;2(3):14.
 16. Słota M, Wąsik M, Stołtny T, Machoń-Grecka A, Kasperczyk A, Bellanti F, et al. Relationship Between Lead Absorption And Iron Status And Its Association With Oxidative Stress Markers In Lead-Exposed Workers. *J Trace Elem Med Biol*. 2021;68. <https://doi.org/10.1016/j.jtemb.2021.126841>. (<https://www.sciencedirect.com/science/article/pii/S0946672X21001310>)
 17. Aynalem M, Shiferaw E, Adane T, Gelaw Y, Enawgaw B. Anemia In African Malnourished Pre-School Children: A Systematic Review And Meta-Analysis. *SAGE Open Med*. 2022;10. doi: 10.1177/20503121221088433. PMID: 35371481; PMCID: PMC8968978.
 18. Garcia-Casal MN, Dary O, Jefferds ME, Pasricha SR. Diagnosing Anemia: Challenges Selecting Methods, Addressing Underlying Causes, And Implementing Actions At The Public Health Level. *Ann N Y Acad Sci*. 2023;1524(1):37–50. doi: 10.1111/nyas.14996. Epub 2023 Apr 15. PMID: 37061792; PMCID: PMC10880862.
 19. Karakochuk CD, Hess SY, Moorthy D, Namaste S, Parker ME, Rappaport AI, et al. Measurement And Interpretation Of Hemoglobin Concentration In Clinical And Field Settings: A Narrative Review. *Ann N Y Acad Sci*. 2019;1450(1):126–46.
 20. Meiriska I putri, Anggraini D. Pendekatan Laboratorium Dalam Identifikasi Dini Anemia Pada Ibu Hamil. *J Public Heal Sci*. 2025;2(2):144–52.
 21. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron Deficiency Anaemia: Pathophysiology, Assessment, Practical Management. *BMJ Open Gastroenterol*. 2022;9(1).
 22. Garcia-Casal MN, Pasricha SR, Sharma AJ, Peña-Rosas JP. Use And Interpretation Of Hemoglobin Concentrations For Assessing Anemia Status In Individuals And Populations: Results From A WHO Technical Meeting. *Ann N Y Acad Sci*. 2019;1450(1):5–14. doi: 10.1111/nyas.14003. Epub 2019 Jan 16. PMID: 30652320.
 23. Saito H. Nature of storage iron turnover. *Nagoya J Med Sci*. 2024;86(3):361–9. doi: 10.18999/nagjms.86.3.361. PMID: 39355366; PMCID: PMC11439605.
 24. Gosdin L, Sharma AJ, Suchdev PS, Jefferds ME, Young MF. Limits of Detection in Acute-Phase Protein Biomarkers Affect Inflammation Correction of Serum Ferritin for Quantifying Iron Status among School-Age and Preschool-Age Children and Reproductive-Age Women. *J Nutr* [Internet]. 2022;152(5):1370–7. Available from: <https://doi.org/10.1093/jn/nxac035>
 25. Tomasz G, Ewa W, Jolanta M. Biomarkers Of Iron Metabolism In Chronic Kidney Disease. *Int Urol Nephrol* [Internet]. 2021;53(5):935–44. Available from: <https://doi.org/10.1007/s11255-020-02663-z>
 26. Yu L, Xu J, Que T, Miao Z, Zhou Y, Que S, et al. Role of Iron Metabolic Disturbances and Inflammatory Iron Biomarkers in Liver Transplant Prognosis. *Int J Med Sci*. 2025;22(13):3202–19. doi: 10.7150/ijms.113479
 27. Jefferds ME, Mei Z, Addo OY, Sharma AJ, Flores-Ayala RC, Brittenham GM. Under-Recognition Of

- Measurement And Management Of Serum Ferritin Among Populations At High Risk Of Iron Deficiency – Authors’ reply. *Lancet Haematol.* 2021;8(11):e787–8. [https://doi.org/10.1016/S2352-3026\(21\)00299-4](https://doi.org/10.1016/S2352-3026(21)00299-4)
28. WHO. Guideline on Haemoglobin Cutoffs to Define Anaemia in Individuals and Population [Internet]. Geneva; 2024. Available from: <https://iris.who.int/>
29. Bries AE, Wang C, Agbemaflle I, Wels B, Reddy MB. Assessment of Acute Serum Iron, Non-Transferrin-Bound Iron, and Gastrointestinal Symptoms with 3-Week Consumption of Iron-Enriched *Aspergillus oryzae* Compared with Ferrous Sulfate. *Curr Dev Nutr.* 2019;3(12):nzz127. doi: 10.1093/cdn/nzz127. PMID: 32154497; PMCID: PMC7053575.
30. Fonseca Ó, Ramos AS, Gomes LTS, Gomes MS, Moreira AC. New Perspectives on Circulating Ferritin: Its Role in Health and Disease. *Molecules.* 2023;28(23). doi: 10.3390/molecules28237707. PMID: 38067440; PMCID: PMC10708148.
31. Anisa Yulianti, Siti Aisyah, Sri Handayani. Faktor-Faktor yang Berhubungan dengan Anemia pada Remaja Putri. *Lentera Perawat.* 2024;5(1):10–7.
32. Priliani L, Harahap AR, Satyagraha AW, Noviyanti R, Apriyana I, Nanine IS, et al. Mapping Anemia Prevalence Across Indonesia. *Asia Pac J Clin Nutr.* 2025;34(3):430–9. doi: 10.6133/apjcn.202506_34(3).0017. PMID: 40419403; PMCID: PMC12126302.
33. Nasruddin H, Faisal Syamsu R, Permatasari D. Angka Kejadian Anemia Pada Remaja di Indonesia. *Cerdika J Ilm Indones.* 2021;1(4):357–64. <http://cerdika.publikasiindonesia.id/index.php/cerdika/index>