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BEYOND HEMOGLOBIN: RISK-BASED AND NONINVASIVE SCREENING TO ENHANCE EARLY DETECTION OF IRON DEFICIENCY AMONG CHILDREN IN INDONESIA

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Abstract

Background: Iron deficiency anemia (IDA) remains the most common micronutrient deficiency globally and continues to represent a major public health concern among children younger than five years, particularly in low- and middle-income countries. Early identification of children at risk is essential to prevent adverse effects on growth, neurodevelopment, and long-term health outcomes. **Methods:** A narrative review was undertaken to synthesize evidence from observational studies indexed in Scopus and published between 2019 and 2026. The review focused on studies evaluating screening approaches beyond conventional hemoglobin measurement, with particular emphasis on risk-based and non-invasive strategies for improving the early detection of IDA among Indonesian children. **Results:** The available evidence indicates that, in settings where access to invasive laboratory investigations is constrained, validated risk-based screening instruments and non-invasive assessment methods may improve the identification of children at risk for IDA. These approaches contribute not only to more accurate estimation of disease burden but also to a broader understanding of the cognitive implications and nutritional determinants of iron deficiency, extending beyond reliance on biomarker-defined diagnostic thresholds. **Conclusion:** Incorporating a practical risk-based IDA screening tool into routine child growth monitoring has the potential to enhance the early identification of vulnerable children, facilitate appropriate referral for confirmatory testing and timely intervention, and support the integration of anemia prevention within Indonesia's existing child nutrition and growth promotion programs.

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Keywords: Iron deficiency anemia, Risk-based screening, Hemoglobin, Ferritin, Child growth

Introduction

Iron Deficiency Anemia (IDA) is recognized as the most prevalent micronutrient deficiency worldwide and disproportionately affects children under five years of age.[1] Young children are particularly vulnerable because their rapid somatic growth generates iron requirements that frequently outpace dietary intake, a relationship formalized in the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition's position paper on iron requirements in infancy and early childhood.[2] Global Burden of Disease estimates corroborate this vulnerability, identifying iron deficiency as the leading cause of anemia-related disability among children under five, with the World Health Organization further estimating that approximately 40% of children aged 6–59 months were affected by anemia in 2019, a burden concentrated most heavily in the African and South-East Asian regions.[1,3] The prevalence of anemia among children under five in Indonesia has exhibited a consistent upward trend, rising from 27.7% in 2007 to a slightly higher figure of 28.1% in 2013, before increasing sharply to 38.5% in 2018.[4] This indicates that IDA remains a significant but underrecognized challenge in child nutrition, both globally and within Indonesia specifically. The long-standing burden of anemia among Indonesian children under five is likely driven by multiple interacting determinants, including inadequate dietary iron intake and poor dietary diversity, low birth weight, low socioeconomic status, recurrent infections, food insecurity, inadequate sanitation, and limited access to healthcare.[2,3]

Iron depletion is not a single event but a graded, sequential process that begins with exhaustion of storage iron, progresses to iron-restricted erythropoiesis, and culminates in overt anemia only once compensatory erythropoietic mechanisms are exceeded.[5] Evidence from longitudinal cohorts and mechanistic studies indicates that the developing brain is especially sensitive during this earlier, pre-anemic phase, when regions governing memory, motor function, and socio-emotional regulation are undergoing iron-dependent maturation.[6,7] As a result, children can already sustain measurable deficits in cognitive and behavioral outcomes while hemoglobin concentrations remain within the ostensibly normal range.[7] These observations establish that the clinically meaningful consequences of IDA are neither confined to, nor reliably signaled by, the onset of anemia.

Hemoglobin (Hb) measurement remains the cornerstone of anemia screening in primary healthcare because it is inexpensive, rapid to perform, and does not require sophisticated laboratory infrastructure.[8,9] However, Hb is fundamentally a marker of anemia rather than of iron status, and physiological compensation means concentrations typically decline only after iron stores have been substantially, and often chronically, depleted.[7] Reliance on Hb as a stand-alone screening tool therefore risks both underestimating the true burden of iron deficiency and misattributing anemia of other etiologies to iron status, thereby delaying appropriate intervention. Serum ferritin, interpreted alongside inflammatory markers such as C-reactive protein, offers a considerably earlier and more specific window into declining iron stores than Hb.[10] Nevertheless, routine population-level use of such biomarkers remains constrained in Indonesia by reagent and co-testing costs, uneven laboratory capacity, and marked disparities in diagnostic access between urban centers and rural or remote primary care facilities.[11] A risk-based screening approach offers a pragmatic alternative by combining readily available clinical and nutritional information—such as age, birth history, dietary and complementary feeding practices, growth trajectory, recurrent infection, and maternal iron status—to identify children at elevated probability of iron deficiency.[12] This strategy parallels recent revisions to international pediatric screening guidance, which now explicitly incorporate age- and risk-factor-based criteria to prioritize confirmatory laboratory testing rather than applying a uniform protocol to all children.[13] In doing so, risk-based screening may enable earlier and more targeted identification of children who stand to benefit most from further evaluation and iron intervention.

Against this background, this review discusses the biological and clinical limitations of hemoglobin as a stand-alone screening tool for iron deficiency among children, examines the challenges of implementing alternative biomarkers within Indonesia's primary healthcare system, and proposes a pragmatic risk-based screening framework intended to support earlier detection of iron deficiency in resource-limited settings.

Methods

This review employed a narrative literature review design to synthesize current evidence on the early detection of iron deficiency among children, with particular consideration of its

relevance to Indonesia. A systematic search of the literature was undertaken using the Scopus database, which was selected because of its extensive indexing of peer-reviewed journals in medicine, nutrition, and public health. The search was limited to articles published between January 2019 and 2026 to capture recent developments in screening strategies, diagnostic biomarkers, and approaches to identifying iron deficiency in pediatric populations. The search strategy utilized Boolean operators as follows: (children) AND (iron deficiency anemia) AND (screen OR detect) AND (hemoglobin OR ferritin OR risk-based). The search was designed to retrieve studies examining children, iron deficiency or anemia, screening or diagnostic practices, and the use of laboratory biomarkers or risk-based approaches for early detection. All records identified through the search were imported for screening and eligibility assessment according to predefined selection criteria.

Eligible studies were restricted to original research articles, while conference abstracts, editorials, commentaries, letters to the editor, and publications without open-access full-text availability were excluded from the review. The remaining articles underwent full-text assessment to determine their relevance to the review objective, specifically their focus on pediatric iron deficiency, anemia screening, or diagnostic methods involving hemoglobin, ferritin, or other risk-based detection strategies. Following the selection process (Figure 1), the eligible studies were subsequently examined and synthesized narratively by comparing their findings, particularly within the Indonesian healthcare setting.

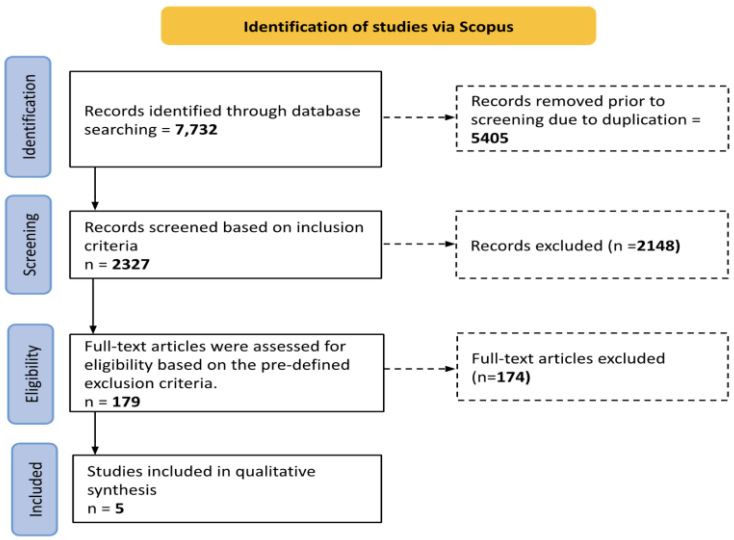


Figure 1. Flow chart of study selection

Results and Discussion

The five included studies were published between 2019 and 2026 and represent evidence from Southeast Asia and the United States, with 3 studies conducted in Indonesia, 1 in Malaysia, and 1 secondary analysis of a nationally representative United States dataset. The studies encompass diverse epidemiological designs, including three cross-sectional studies, one diagnostic validation study, and one secondary analysis of population-based survey data. Most studies focused on infants, toddlers, or school-aged children, reflecting the importance of iron deficiency (ID) and iron deficiency anemia (IDA) across different developmental stages. Collectively, these studies examined various aspects of iron deficiency, including risk-based screening tool validation, prevalence estimation, cognitive consequences, nutritional determinants, and biomarker-based diagnostic thresholds. This diversity provides complementary evidence for understanding both the epidemiology of iron deficiency and opportunities for improving early detection strategies in children.

Table 1. Summary of Findings

No	Author (Year)	Study Design	Population	Main Findings
1	Sjarif et al. (2025)[14]	Cross-sectional diagnostic validation study	Indonesian children aged 1–3 years	The modified NutricheQ questionnaire demonstrated acceptable psychometric performance for screening iron deficiency risk among Indonesian children aged 1–3 years. Moderate correlations were observed with dietary iron intake ($r = 0.39$, $p < 0.01$) and serum ferritin concentrations ($r = 0.29$, $p < 0.01$). The five-item version provided the best diagnostic performance at a cut-off score of 5, yielding 80.4% sensitivity, 48.3% specificity, and an AUC of 0.709 (95% CI: 0.648–0.770) for identifying children with inadequate iron intake.
2	Moeloek et al. (2026)[15]	Cross-sectional study	Indonesian elementary school children (6–12 years)	Children with impaired working memory had significantly lower mean hemoglobin levels than those with normal working memory (12.1 ± 1.1 vs. 12.4 ± 0.9 g/dL, $p = 0.035$). Additionally, stunted children were approximately three times more likely to have poor working memory performance than

No	Author (Year)	Study Design	Population	Main Findings
				their non-stunted peers (OR = 3.04, 95% CI: 1.15–8.01).
3	Sjarif et al. (2019)[16]	Cross-sectional study	Indonesian toddlers aged 1–3 years	The Ironcheq questionnaire is a validated screening tool for identifying toddlers at risk of iron deficiency. Given the established contribution of adequate iron intake to linear growth, the study further demonstrated that daily consumption of growing-up milk was independently associated with a lower prevalence of stunting. Toddlers who consumed growing-up milk daily had significantly reduced odds of stunting compared with non-daily consumers (adjusted OR = 0.28, 95% CI: 0.13–0.63).
4	Jalaludin et al. (2025)[17]	Cross-sectional study	Malaysian children aged <3 years	Approximately 30% of children (95% CI: 28–33) were identified as being at risk of anemia. The prevalence of anemia risk was significantly higher among children with lower weight-for-age Z-scores ($p < 0.05$). Multivariable analysis showed that higher weight-for-age was independently associated with a lower likelihood of anemia risk (adjusted OR = 0.88, 95% CI: 0.80–0.98).
5	Mei et al. (2023)[18]	Cross-sectional secondary analysis (NHANES III)	Healthy U.S. children aged 1–5 years and nonpregnant women aged 15–49 years	The application of physiologically derived serum ferritin thresholds (21.2 µg/L) identified substantially more children with iron deficiency than the current WHO hemoglobin-based criteria. Compared with the WHO cut-off, the serum ferritin threshold classified an additional 22.2% of apparently healthy U.S. children as iron deficient, indicating that reliance on hemoglobin alone may underestimate the true burden of iron deficiency.

Constructing a Locally Relevant Risk IDA Profile for Indonesian Children

A risk-based screening approach requires identification of locally validated risk factors. The modified NutricheQ Questionnaire, developed and validated specifically for the Indonesian pediatric population, identified five dietary risk factors: daily intake of growing-up

milk, chicken or beef liver, red meat, red-meat-based products, and eggs. Notably, the three-item subset comprising growing-up milk (GUM), liver, and red meat intake preserved these associations ($r = -0.527$ for iron intake, $r = -0.41$ for ferritin, both $p < 0.01$), and achieved an AUC of 0.768 for predicting inadequate iron intake (<7 mg/day) and 0.678 for predicting low serum ferritin levels, confirming that these three dietary dimensions capture the principal iron-deficiency risk drivers in the Indonesian toddler diet.[14]

Beyond iron-specific risk, the broader nutritional context showed compounded vulnerability. Among 335 elementary school children in urban Jakarta, 100% had inadequate protein and fat intake relative to the Indonesian Recommended Dietary Allowances, and anemic children had significantly lower protein intake (46.3% vs. 52.6% of the recommended allowance, $p = 0.010$).[15] This concurrent macronutrient deficit may be linked to direct growth implications: among 172 toddlers analysed for stunting, consumption of GUM of at least 300 mL/day was independently protective against stunting (adjusted OR 0.28, 95% CI 0.13–0.63, $p = 0.002$), whereas frequent consumption of processed red meat products (sausages, meatballs, nuggets) emerged as a risk factor (crude OR 3.70, 95% CI 1.17–11.74, $p = 0.026$).[16] These findings suggestthat the Indonesian toddler's risk profile is defined not merely by iron insufficiency but by a convergent pattern of low heme-iron intake, inadequate animal protein quality, and over-reliance on processed meat products that contribute little bioavailable iron or essential amino acids.[14,16]

A parallel assessment in 1,201 Malaysian children aged 6–36 months using noninvasive haemoglobin screening provided further evidence that age and nutritional status may be important modifiable risk factors across the region. Children aged 6–12 months had 1.73-fold higher odds of being at risk of anaemia compared with those aged 12–36 months (95% CI 1.34–2.24, $p < 0.001$), and each one-unit increase in weight-for-age Z-score was associated with 12% reduced odds (adjusted OR 0.88, 95% CI 0.80–0.98, $p = 0.020$).[17] These convergent data from Indonesia and Malaysia support the construction of a regionally anchored risk profile that prioritises GUM adequacy, age-specific vulnerability, and growth status as the entry points for screening.

Diagnostic Yield of a Risk-Based versus Universal Hb-Only Strategy

The case for moving beyond a haemoglobin-only threshold is further supported by evidence on ferritin cut-points. The current WHO serum ferritin threshold for iron deficiency in children (less than 12 µg/L) was derived from expert opinion, last revised in 1993, and has not been updated on the basis of published physiological data. Analysis of NHANES III data using restricted cubic spline regression suggested that iron-deficient erythropoiesis begins at serum ferritin concentrations of 21.2 µg/L (95% CI 18.5–26.5) as indicated by the haemoglobin plateau inflection. Adopting these physiologically based thresholds would classify an additional 22.2% of apparently healthy US children as iron-deficient compared with the WHO criterion.[18] When applied conceptually to the Indonesian setting, where the prevalence of iron deficiency without anaemia is high, the implication is that universal Hb-only screening at the conventional cut-off of 11.0 g/dL detects only the most severe stage of deficiency while missing the substantial proportion of children with depleted iron stores but preserved haemoglobin.

Evidence from Indonesian studies consistently impliesthat reliance on Hb alone is insufficient for identifying IDA, particularly during the early stages of iron depletion. Juffrie et al. highlighted that Hb lacks sensitivity and specificity because its concentration may be influenced by inflammation, infection, and other nutritional deficiencies, resulting in delayed diagnosis after iron stores have already been depleted. Providing a more reliable approach for accurate diagnosis and appropriate management of IDA is beyond necessary.[19]

A risk-based screening strategy, in contrast, directs confirmatory laboratory testing to those flagged by the item questionnaire. The original NutricheQ comprised 18 questions, whereas the modified NutricheQ was evaluated as a risk stratification tool against two physiological benchmarks: inadequate dietary iron intake (below 7 mg/day) and low serum ferritin. The five-question version demonstrated moderate discriminatory performance, with an AUC of 0.709 for inadequate iron intake and 0.598 for low serum ferritin.[14] A similar principle was demonstrated in the Malaysian cross-sectional study, where noninvasive screening using the Masimo Rad-67 Pulse CO-Oximeter identified 30% (95% CI 28–33%) of 1,201 children as being at risk of anaemia, warranting targeted confirmatory assessment rather than universal invasive testing. The high response rate of 97.9% in the Malaysian study

further indicated that noninvasive or questionnaire-based first-tier screening enhances parental acceptance and reduces the practical barriers to population-level screening.[17] Sekartini et al. further discussed that delayed diagnosis contributes substantially to the persistence of IDA in Indonesia and advocated for strengthening standardized screening protocols, laboratory capacity, and wider access to appropriate biochemical testing across primary healthcare settings.[20]

Feasibility of a Screen-and-Confirm Workflow at Posyandu/Puskesmas Level

The operational feasibility of implementing a two-tier screening workflow was evaluated across multiple dimensions. First, the modified NutricheQ questionnaire demonstrated acceptable inter-rater reliability, with Cohen's kappa scores ranging from 0.40 (fair agreement) to 1.00 (perfect agreement) across five question items when administered by different trained interviewers at the same Posyandu.[14] These inter-rater metrics indicate that the questionnaire can be administered reliably by community health workers after brief training, a prerequisite for integration into the Posyandu system where cadres rather than physicians conduct routine screenings. Rahayu et al. proposed that midwives should play a central role in risk-based screening through routine assessment of maternal and child risk factors, nutritional counseling, timely referral, and utilization of evidence-based screening algorithms, thereby expanding opportunities for earlier detection within primary healthcare services.[21]

Second, the time and resource burden of the screening process was modest. In the Malaysian counterpart study, the combined interviewer-led assessment, including anthropometric measurement and the noninvasive haemoglobin reading, required approximately 30 to 40 minutes per child. The Masimo Rad-67 Pulse CO-Oximeter reading itself took approximately 30 seconds and required only a finger or toe clip, with no blood draw, no consumable reagents, and no cold-chain requirements.[17] Children identified at risk by either method are then referred for confirmatory venous blood analysis at the Puskesmas, completing the screen-and-confirm circuit.

Third, the approach addresses the specific infrastructure constraints of the Indonesian primary healthcare system. The Indonesian Pediatric Society currently recommends iron

supplementation for all children aged 0–5 years without prior screening, a policy reflecting the practical difficulty of laboratory-based diagnosis at the community level. Effective IDA prevention requires comprehensive strategies integrating dietary improvement, micronutrient interventions, and health system strengthening rather than relying solely on iron supplementation.[22,23]

Policy Translation: Embedding Risk-Based IDA Screening into Indonesia's Stunting Agenda

The intersection of iron deficiency anemia and stunting creates a compelling rationale for integrating IDA screening into Indonesia's national stunting reduction programme. Zulfikar et al. concluded that sustainable IDA prevention in Indonesia requires multisectoral approaches, including nutrition education, food fortification, iron supplementation for high-risk populations, strengthened maternal and child health services, and improved public awareness to address the multifactorial causes of iron deficiency.[24] Iron deficiency and stunting share overlapping dietary determinants, particularly inadequate intake of animal-source protein and micronutrient-fortified foods. Putri et al. demonstrated that anemia is related to poor nutritional status and unfavorable anthropometric characteristics among Indonesian adolescent girls, emphasizing the need for preventive strategies targeting nutritional improvement before pregnancy to interrupt the intergenerational cycle of iron deficiency.[25]

A systematic review and meta-analysis by Oktarina et al. suggested that children with IDA had significantly greater odds of being stunted than their non-anemic peers, supporting the biological and epidemiological link between chronic iron deficiency and impaired linear growth. This association may be mediated through multiple mechanisms, including reduced cellular energy production, impaired immune function, decreased appetite, and disruption of growth-regulating pathways, suggesting that failure to detect and manage iron deficiency early may compromise child growth even before severe anemia develops.[26] The dual burden was further evidenced among school-age children, where iron-deficiency anaemia was associated with working memory deficits (mean haemoglobin 12.1 ± 1.1 g/dL in affected children versus 12.4 ± 0.9 g/dL in unaffected peers, $p = 0.035$), and children with short stature had threefold higher odds of compromised working memory (OR = 3.04, 95% CI 1.15–8.01).[15]

These data establish that iron deficiency, undernutrition, and cognitive impairment form a self-reinforcing triad that undermines the developmental objectives of the stunting agenda.

Adopting a life-course approach may provide a practical framework for translating this evidence into national policy. Sungkar et al. implied that iron deficiency develops across multiple stages of life, from adolescence and pregnancy to infancy and early childhood, and may require coordinated interventions throughout the continuum of care rather than isolated supplementation programs. Integrating routine nutritional risk assessment, timely screening, nutrition education, iron supplementation for high-risk populations, food fortification, and strengthened maternal and child health services into existing primary healthcare platforms might offer greater potential to reduce the burden of both IDA and stunting than single-component interventions.[27]

Limitations

This review highlights the potential of risk-based and non-invasive approaches to improve early identification of iron deficiency among Indonesian children and integrates evidence on dietary, growth, cognitive, and screening-related factors. The focus on applicability within Posyandu and Puskesmas settings also provides practical relevance for Indonesia's primary healthcare system. However, the review has several limitations. The number of eligible studies was small and heterogeneous in terms of population, study design, and outcome measures, while some evidence was derived from Malaysia and the United States and may not be fully generalizable to Indonesian children. As a narrative review based primarily on Scopus-indexed literature, publication and database selection bias cannot be excluded. Most included studies were cross-sectional, limiting causal inference, and the proposed risk-based approaches should therefore be considered as screening or triage tools rather than replacements for biochemical confirmation. Further prospective studies in diverse Indonesian populations are needed to validate their diagnostic performance and implementation feasibility.

Conclusion

Embedding a simple risk-based IDA screening tool within routine growth monitoring

may facilitate early identification of at-risk children, help prioritize confirmatory assessment and intervention for those most likely to benefit, and support the integration of anemia prevention into the country's broader child growth and nutrition policies.

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Conflict of Interest

The author declares that there are no conflicts of interest related to the publication of this manuscript.

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