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COEXISTING IRON AND VITAMIN D DEFICIENCY IN CHILDREN: CLINICAL SIGNIFICANCE, DIAGNOSTIC APPROACH AND MANAGEMENT

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Abstract: Iron deficiency and vitamin D deficiency are among the most common micronutrient disorders of childhood and may coexist because they share nutritional, developmental, socioeconomic, inflammatory, and lifestyle risk factors. Emerging evidence also suggests biological interaction: vitamin D may influence iron homeostasis through hepcidin and inflammatory pathways, while iron-dependent enzymes participate in vitamin D metabolism. This structured review evaluates the clinical significance of combined iron and vitamin D deficiency in children, emphasizing mechanisms, risk groups, laboratory assessment, and management. Current guidelines, systematic reviews, observational pediatric studies, and a recent randomized trial were synthesized. Studies consistently show a higher frequency of low vitamin D status among children with iron deficiency or iron-deficiency anemia, although causality is not fully established. Clinical manifestations overlap and are often nonspecific, including fatigue, pallor, reduced appetite, impaired exercise tolerance, muscle weakness, bone discomfort, irritability, and suboptimal growth. Laboratory diagnosis should evaluate hemoglobin and red-cell indices together with ferritin interpreted in the context of inflammation, and serum 25-hydroxyvitamin D when risk factors or compatible clinical findings are present. Management should correct each documented deficiency according to pediatric guidance rather than assume that treating one nutrient will automatically normalize the other. Recent trial data suggest that combined supplementation may improve iron stores in selected children with iron-deficiency anemia, but larger studies are required. Integrated nutritional assessment is particularly relevant in young children, adolescents, children with restricted diets, chronic inflammation, obesity, limited sun exposure, or growth faltering.

Keywords: iron deficiency; iron-deficiency anemia; vitamin D deficiency; children; ferritin; hepcidin; 25-hydroxyvitamin D; micronutrients

Introduction

Iron and vitamin D are essential micronutrients with distinct classical functions but potentially overlapping clinical consequences when deficient. Iron is required for hemoglobin synthesis, tissue oxygen delivery, mitochondrial function and neurodevelopment. Vitamin D is central to calcium-phosphate homeostasis and skeletal mineralization and also participates in immune and inflammatory regulation. In childhood, deficiency of either nutrient may impair growth, physical performance and wellbeing; when both occur simultaneously, symptoms can become more difficult to interpret because fatigue, poor appetite, weakness and reduced activity are nonspecific.

Iron deficiency remains the most common nutritional cause of anemia worldwide. The WHO updated hemoglobin cut-offs for defining anemia in 2024, reinforcing the need for age-appropriate interpretation and appropriate measurement methods (1). The American Academy of Pediatrics

issued an updated clinical report in 2026 covering prevention, screening, diagnosis and treatment of iron deficiency and iron-deficiency anemia across infancy, childhood and adolescence (2). These recommendations emphasize that iron deficiency may exist before hemoglobin falls and that laboratory evaluation should not rely on hemoglobin alone.

Vitamin D deficiency is also frequent, although prevalence varies according to latitude, season, skin pigmentation, diet, supplementation policy, clothing, obesity and chronic disease. Pediatric guidance commonly uses serum 25-hydroxyvitamin D [25(OH)D] as the best available marker of vitamin D status. The Indian Academy of Pediatrics guideline, for example, defines deficiency as 25(OH)D below 12 ng/mL and insufficiency as 12–20 ng/mL, while recognizing that thresholds and supplementation policies differ across professional bodies (3).

Interest in coexisting deficiency has increased because the relationship may be more than coincidental. Vitamin D can suppress hepcidin expression and modulate inflammatory cytokines, potentially increasing iron availability for erythropoiesis; conversely, iron is involved in enzymatic pathways relevant to vitamin D hydroxylation (4,5). Pediatric observational studies have repeatedly found lower vitamin D status among children with iron deficiency or iron-deficiency anemia (6–8). However, association does not prove causation, and both deficiencies may simply arise from the same diet, socioeconomic conditions, limited outdoor activity, chronic inflammation or growth-related nutritional demand.

The aim of this article is to summarize current evidence on the coexistence of iron and vitamin D deficiency in children, clarify plausible biological links, describe clinical and laboratory patterns, and propose a practical evidence-based approach to screening and treatment.

Materials and Methods

A structured narrative review was undertaken using PubMed-indexed literature and international pediatric guidance. Search concepts included “iron deficiency,” “iron-deficiency anemia,” “vitamin D deficiency,” “children,” “25-hydroxyvitamin D,” “ferritin,” “hepcidin,” and “combined supplementation.” Priority was given to pediatric studies, systematic reviews, current diagnostic guidance, and studies that directly evaluated the relationship between iron indices and vitamin D status. Publications from 2016 through August 2026 were emphasized, with older sources used when they remained foundational.

Evidence was grouped into four domains: pathophysiological interaction, epidemiology and risk factors, clinical-laboratory features, and treatment implications. Because included studies differed in age, definitions of vitamin D deficiency, ferritin thresholds, inflammatory burden and study design, the evidence was synthesized qualitatively rather than pooled. Numerical results are presented only from cited studies. This review does not contain original patient data and therefore required no ethics approval.

Results

Biological interaction between vitamin D and iron

The most plausible mechanistic link involves hepcidin, the hepatic peptide that reduces intestinal iron absorption and limits iron release from macrophages by promoting degradation of ferroportin. Vitamin D has been shown in experimental and clinical literature to suppress hepcidin-related pathways and reduce inflammatory signalling, potentially increasing bioavailable iron (4).

In children with acute infectious disease, Moran-Lev et al. found that lower 25(OH)D, higher interleukin-6 and higher hepcidin clustered with anemia and hypoferremia; children with 25(OH)D below 20 ng/mL had increased odds of anemia compared with those above this level (9). These findings are particularly relevant when iron indices are interpreted during inflammation, because ferritin can rise as an acute-phase reactant even when functional iron availability is reduced.

The interaction may also operate in the opposite direction. Iron participates in cytochrome P450 enzyme systems involved in vitamin D metabolism, and iron deficiency may theoretically influence 25- and 1-alpha-hydroxylase activity. A systematic review by Azizi-Soleiman et al. found observational evidence of a positive relationship between iron status and vitamin D, while intervention trials available at the time did not consistently show that iron therapy alone corrected vitamin D status (5). Thus, the relationship is biologically credible but not sufficiently deterministic to justify using one nutrient as a surrogate marker for the other.

Frequency of coexistence and risk groups

Several pediatric studies demonstrate clinically relevant coexistence. In a multicountry study of 4,509 African children, Mogire et al. reported iron deficiency in 35.1% of participants; children with 25(OH)D below 50 nmol/L had approximately twice the odds of iron deficiency compared with those above 75 nmol/L (6). The study also showed that inflammation modified the relationship between vitamin D and ferritin, underlining the importance of context when interpreting biochemical results.

In a study of children aged six months to five years, Cihan and Korgali observed vitamin D deficiency in 49.3% of children with iron deficiency/iron-deficiency anemia compared with 20% of controls; child and maternal vitamin D status were both associated with iron-related outcomes (7). More recently, Razzaq et al. studied 236 children aged one to five years with iron-deficiency anemia and found coexisting vitamin D deficiency in 67.5% (8). Female sex, older preschool age, low weight or height centiles, urban residence, socioeconomic factors and larger sibship were associated with vitamin D deficiency in that cohort.

These percentages should not be generalized directly to every population because definitions, seasons, diets and supplementation practices differ. Nevertheless, the consistent direction of association supports combined nutritional assessment in high-risk groups. Such groups include infants after the period of rapid postnatal iron-store depletion, toddlers consuming excessive cow's milk or diets poor in iron-rich foods, children with restrictive eating, adolescents during rapid growth, menstruating adolescents, children with obesity or low outdoor activity, those with dark skin or limited sunlight exposure, and children with chronic inflammatory, gastrointestinal, renal or malabsorptive conditions.

Condition	Typical clinical pattern	Core laboratory assessment
Iron deficiency/IDA	Pallor, fatigue, irritability, pica, reduced attention, tachycardia in more severe cases	CBC, MCV/MCH, ferritin; consider CRP/inflammation, transferrin saturation or other iron markers as needed
Vitamin D	Often asymptomatic; muscle	Serum 25(OH)D; calcium,

Condition	Typical clinical pattern	Core laboratory assessment
deficiency	weakness, bone pain, delayed motor performance; rickets in severe/prolonged deficiency	phosphate, alkaline phosphatase and PTH if rickets/mineral disorder suspected
Combined deficiency	Greater nonspecific fatigue, low activity, poor diet/growth concerns; overlapping musculoskeletal and hematologic symptoms	Assess both nutrient pathways when clinical risk factors coexist; interpret ferritin with inflammation

Table 1. Practical clinical and laboratory differentiation of iron and vitamin D deficiency.

Clinical and laboratory significance

The clinical problem is that both deficiencies can be silent or produce nonspecific symptoms. Iron deficiency may initially present with fatigue, irritability, pica, reduced exercise tolerance or learning difficulties before frank anemia. Vitamin D deficiency may remain asymptomatic until biochemical abnormalities, muscle weakness, bone pain or rickets appear. When deficiencies coexist, attributing fatigue to “low vitamin D” alone can delay recognition of iron deficiency, while focusing only on hemoglobin can miss depleted iron stores or a clinically important mineral deficiency.

A stepwise laboratory strategy is therefore preferable. Hemoglobin should be interpreted with age-appropriate cut-offs (1). Mean corpuscular volume and mean corpuscular hemoglobin help characterize microcytosis and hypochromia but are not sufficiently sensitive for early iron deficiency. Ferritin is useful for iron stores but rises with inflammation; C-reactive protein or other clinical evidence of inflammation should be considered when ferritin appears normal in a symptomatic child. Transferrin saturation, soluble transferrin receptor, reticulocyte hemoglobin or other indices may be useful when diagnosis remains uncertain, depending on local availability (2).

Vitamin D status is assessed with serum 25(OH)D. Testing every healthy child is not universally recommended, but it is reasonable in children with rickets or bone symptoms, chronic diseases affecting absorption or metabolism, high-risk medication use, marked obesity, severe dietary restriction, or when coexisting micronutrient deficiency suggests a broader nutritional problem (3). When severe vitamin D deficiency or rickets is suspected, calcium, phosphate, alkaline phosphatase, parathyroid hormone and renal or liver parameters may be appropriate.

The evidence also has implications for inflammation. Vitamin D insufficiency has been associated with higher hepcidin and lower hemoglobin in pediatric inflammatory bowel disease and acute infection literature, providing a possible mechanism for reduced iron availability independent of depleted storage iron. Clinically, this means that anemia in a child with chronic inflammation may contain nutritional and inflammatory components simultaneously. Correct diagnosis is important because escalating oral iron without addressing inflammation, diet or vitamin D deficiency may not fully restore wellbeing.

Treatment implications

Management should correct each confirmed deficiency according to pediatric guidance. For iron deficiency and iron-deficiency anemia, oral elemental iron is the usual first-line therapy in uncomplicated cases, with dose, formulation and duration determined by age, severity, tolerance and local recommendations (2). Dietary counselling should address iron-rich foods, enhancers of non-heme iron absorption, excessive cow's milk in toddlers, and restrictive eating. Response should be monitored rather than assumed; refractory or recurrent deficiency warrants reassessment for adherence, ongoing blood loss, malabsorption, inflammation or an incorrect diagnosis.

Vitamin D deficiency should likewise be treated with an evidence-based pediatric regimen. The Indian Academy of Pediatrics guideline recommends preventive vitamin D during infancy and therapeutic cholecalciferol regimens for established deficiency or rickets, with dose varying by age and clinical context (3). Local or national pediatric guidance should take priority because recommended thresholds and treatment schedules differ. Calcium adequacy is important when treating rickets or severe deficiency.

The key question is whether combined supplementation produces benefits beyond correcting two separate deficiencies. Evidence is emerging but not definitive. In a 2025 randomized controlled trial, 67 children with iron-deficiency anemia received either iron alone or iron plus 400 IU vitamin D for four weeks. Both groups improved hematological parameters; the combined group showed a significantly greater mean increase in ferritin, although most between-group hematological outcomes were not significantly different (10). This finding is hypothesis-strengthening rather than practice-changing: children with documented vitamin D deficiency should receive vitamin D, but routine vitamin D solely to accelerate iron response in vitamin-D-sufficient children is not yet supported by robust evidence.

Follow-up should be clinically integrated. Improvement in hemoglobin does not necessarily mean iron stores are replete, and correction of 25(OH)D does not ensure adequate dietary quality. Growth, diet, adherence, physical activity, musculoskeletal symptoms and developmental or school performance should be reviewed. Where socioeconomic constraints contribute to both deficiencies, counselling must be realistic and linked to affordable food sources and preventive supplementation programs.

Discussion

The reviewed evidence indicates that iron and vitamin D deficiencies frequently coexist in children and that the relationship is supported by plausible biology. Vitamin D may influence iron availability through hepcidin and inflammatory pathways, while iron participates in enzymes relevant to vitamin D metabolism (4,5,9). However, the current evidence does not establish a simple causal chain in which deficiency of one nutrient inevitably produces deficiency of the other. Shared determinants—poor diet, limited sunlight, rapid growth, chronic inflammation, obesity, socioeconomic disadvantage and chronic disease—remain powerful alternative explanations.

This distinction matters clinically. The value of recognizing coexistence is not to create a new diagnostic label, but to avoid fragmented assessment. A child with iron-deficiency anemia may also have low vitamin D because the same dietary or lifestyle pattern affects both nutrients. Conversely, a child with vitamin D deficiency and fatigue should not be presumed to have symptoms from vitamin D alone if pallor, pica, rapid growth, menstruation, restrictive diet or low ferritin suggest iron deficiency. Integrated screening is especially useful when multiple risk factors are present.

The most important limitation in the literature is heterogeneity. Studies use different 25(OH)D thresholds, ferritin cut-offs and definitions of anemia; some adjust ferritin for inflammation and others do not. Season and latitude alter vitamin D levels, while infections alter ferritin and hepcidin. Cross-sectional associations cannot demonstrate directionality. These factors explain why observational studies show consistent coexistence but intervention studies provide less certain evidence of nutrient-to-nutrient therapeutic effects.

Recent guidelines improve the clinical framework. The 2024 WHO hemoglobin guidance and 2026 AAP clinical report support careful, age-specific evaluation of anemia and iron deficiency (1,2), while pediatric vitamin D recommendations emphasize risk-based assessment and treatment of established deficiency (3). The 2025 randomized trial adds early interventional evidence that combined iron and vitamin D supplementation may improve ferritin in children with iron-deficiency anemia (10). Larger randomized studies should stratify participants by baseline 25(OH)D status and inflammation so that the effect of vitamin D replacement on iron recovery can be separated from the effect of correcting true vitamin D deficiency.

For pediatric practice, the evidence supports a pragmatic approach: screen iron status when clinical or dietary risk is present; assess vitamin D status when there are specific risk factors or signs; consider combined testing when one deficiency coexists with broader nutritional risk; treat each confirmed deficiency with guideline-based dosing; and investigate persistent abnormalities rather than repeatedly supplementing without diagnosis. This strategy is clinically safe, avoids overtesting, and acknowledges that micronutrient deficiencies often reflect whole-child nutritional and social context.

Conclusion

Coexisting iron and vitamin D deficiency is clinically relevant in pediatrics because the two conditions are common, share risk factors, produce overlapping nonspecific symptoms, and may interact through hepcidin, inflammation and metabolic pathways. Pediatric studies consistently demonstrate a higher frequency of low vitamin D status in children with iron deficiency or iron-deficiency anemia, but causality remains incompletely established. Diagnosis should combine age-appropriate hematologic assessment with inflammation-aware interpretation of ferritin and targeted measurement of 25(OH)D in at-risk children. Treatment should correct each documented deficiency according to pediatric guidelines and address diet, growth, sun exposure, chronic disease and adherence. Early randomized evidence suggests a possible benefit of combined supplementation for iron stores in selected children, but larger trials are needed before routine combined therapy can be recommended for all patients with iron-deficiency anemia.

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