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VITAMIN D DEFICIENCY IN CHILDREN: CLINICAL MANIFESTATIONS, DIAGNOSTIC DIFFICULTIES, AND CURRENT MANAGEMENT – A LITERATURE REVIEW

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ABSTRACT

Background: Vitamin D deficiency remains an important pediatric health problem because it can lead to nutritional rickets, impaired bone mineralization, delayed growth, muscle weakness, and severe hypocalcemic complications, especially in infants and other high-risk groups. Despite being preventable, it continues to present diagnostic and therapeutic challenges in everyday pediatric practice.

Objective: This review summarizes current evidence on the epidemiology, risk factors, clinical manifestations, diagnostic difficulties, treatment, and prevention of vitamin D deficiency in children.

Methods: A structured search of PubMed/MEDLINE and the Cochrane Library was conducted on March 28, 2026. Priority was given to pediatric guidelines, consensus statements, systematic reviews, meta-analyses, randomized trials, and observational studies.

Results: Available evidence shows that low circulating vitamin D levels are common worldwide, whereas overt rickets and hypocalcemic presentations are concentrated in identifiable vulnerable populations. Diagnostic difficulties arise from inconsistent biochemical thresholds, assay variability, and the need to distinguish nutritional rickets from genetic or renal disorders. Current management relies on risk-based assessment, appropriate vitamin D replacement, adequate calcium intake, and monitoring for adverse effects, while prevention centers on infant supplementation and public health measures that improve adherence.

Conclusions: Pediatric vitamin D deficiency is largely preventable, but improved diagnostic harmonization, laboratory standardization, and stronger implementation of prevention programs remain necessary to reduce avoidable morbidity.

KEYWORDS

Vitamin D Deficiency, Children, Nutritional Rickets, Supplementation, Hypocalcemia, Pediatric Review

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Introduction

Vitamin D plays a central role in calcium-phosphate balance and in the mineralization of the growing skeleton. In children, severe deficiency may lead to nutritional rickets, with impaired growth plate mineralization and characteristic skeletal deformities, and it may also present with hypocalcemia, seizures, or cardiomyopathy in susceptible infants (Munns et al., 2016; Uday & Högler, 2017; World Health Organization, 2019). Overt rickets is much less frequent than isolated biochemical deficiency, but it remains an important and preventable source of pediatric morbidity, especially in children with low ultraviolet B exposure, darker skin pigmentation, low calcium intake, or poor access to supplementation.

Clinical practice is made more difficult by the fact that vitamin D status is not defined uniformly across guidelines, recommendations have evolved over time, and laboratory assessment of 25-hydroxyvitamin D is still affected by inter-assay variability (Binkley & Carter, 2017; Herrmann et al., 2017; Sempos & Binkley, 2020). Recent guidance from the Endocrine Society places greater emphasis on vitamin D in the prevention setting and separates supplementation strategies from indications for laboratory testing, while international guidance on nutritional rickets continues to stress the combined importance of vitamin D and calcium (Demay et al., 2024; Munns et al., 2016). Even so, debate persists around optimal thresholds, whom to screen, and how strongly supplementation should be linked to extra-skeletal outcomes.

This review therefore brings together current evidence on pediatric vitamin D deficiency with a practical clinical focus. It addresses epidemiology, risk factors, clinical manifestations, diagnostic issues, management, prevention, and ongoing controversies, drawing primarily on pediatric guidelines and higher-level clinical studies.

Methodology

This paper is a narrative literature review supported by a structured and reproducible database search. PubMed/MEDLINE and the Cochrane Library were searched on March 28, 2026. Search terms covered vitamin D deficiency, 25-hydroxyvitamin D, cholecalciferol, ergocalciferol, infants, children, adolescents, rickets, osteomalacia, hypocalcemia, seizures, cardiomyopathy, supplementation, prevention, treatment, guidelines, randomized trials, systematic reviews, and meta-analyses.

Included sources comprised pediatric guidelines, consensus statements, systematic reviews, meta-analyses, randomized controlled trials, surveillance studies, cohort studies, and other observational reports focused on people aged 18 years or younger. Studies limited to adults were excluded unless they contributed essential background, and papers on genetic rickets were included only when relevant to differential diagnosis. Official publications from health agencies were considered when they informed public health policy or prevention practice. The evidence was synthesized qualitatively, and no meta-analysis was performed.

Results

Epidemiology

Large pooled datasets indicate that low 25-hydroxyvitamin D concentrations are common across many world regions (A systematic review and meta-analysis of circulating 25-hydroxyvitamin D concentration and vitamin D status worldwide, 2023; Cui et al., 2023). In a pooled analysis covering 2000 to 2022 and almost 7.95 million participants, the estimated global prevalence was 15.7% for serum 25-hydroxyvitamin D below 30 nmol/L and 47.9% for concentrations below 50 nmol/L (Cui et al., 2023). These figures are not limited to pediatric populations, but they help explain why vitamin D deficiency remains clinically relevant in children, particularly at higher latitudes and during winter and spring.

The burden of overt disease is distributed much less evenly. Reviews of nutritional rickets show that symptomatic cases occur mainly in infants and young children exposed to a combination of low vitamin D intake, limited sun exposure, and poor calcium intake, with especially high risk in migrant populations, dark-skinned children, and socially disadvantaged groups (Roth et al., 2018; Uday & Högler, 2017; World Health Organization, 2019). Surveillance data from high-income countries also make it clear that severe cases are less common than biochemical insufficiency but have not disappeared, and they continue to include preventable complications such as hypocalcemic seizures (Basatemur & Sutcliffe, 2015; Julies et al., 2020).

Risk Factors

Risk factors for pediatric vitamin D deficiency reflect an interplay between biology, environment, diet, and healthcare delivery. They include reduced cutaneous synthesis, low dietary intake, increased physiological demands, impaired absorption or metabolism, and social or program-level barriers to prevention. Common contributors are high latitude, seasonal reduction in ultraviolet B exposure, sun avoidance, extensive skin covering, darker skin pigmentation, exclusive breastfeeding without supplementation, maternal deficiency, inadequate calcium intake, obesity, and chronic illnesses such as inflammatory bowel disease.

Maternal status is particularly important during infancy because neonatal vitamin D stores depend largely on maternal supply, and breast milk usually contains only small amounts of vitamin D unless maternal concentrations are high (Tan et al., 2020; Thandrayen & Pettifor, 2010). Program delivery also matters. European data show wide differences in supplementation policies and in the factors that influence adherence, suggesting that prevention depends not only on biological efficacy but also on education, access, and the practical design of public health programs (Uday et al., 2017).

Clinical Manifestations

Pediatric vitamin D deficiency spans a wide clinical range. Many children with low 25-hydroxyvitamin D concentrations are asymptomatic or report only nonspecific complaints, and clinical consequences become more apparent as deficiency deepens or calcium deficiency coexists (Corsello et al., 2023; Fischer & Almasri, 2022; Munns et al., 2016).

When nutritional rickets is present, the physical findings in infants and young children may include craniotabes, frontal bossing, delayed fontanelle closure, a rachitic rosary, widening of the wrists and ankles, bowed legs, poor growth, and delayed motor development. Radiographs typically show metaphyseal cupping, fraying, and widening (Munns et al., 2016; World Health Organization, 2019). Severe hypocalcemia is a major complication, especially in infancy, and seizures, tetany, or dilated cardiomyopathy may precede obvious skeletal deformities (Basatemur & Sutcliffe, 2015; Uday et al., 2018; Uday & Högler, 2017).

Diagnostic Challenges

Most pediatric guidelines consider serum 25-hydroxyvitamin D the best available biochemical marker of vitamin D status. The difficulty is that the thresholds used to define deficiency and insufficiency vary across organizations, and the relationship between a given serum value and actual clinical risk is not straightforward, particularly in children, where the key outcome is prevention of rickets rather than adult skeletal endpoints (Corsello et al., 2023; Demay et al., 2024; Munns et al., 2016).

Recent research has tried to identify thresholds that are more clinically meaningful in childhood. An individual participant data meta-analysis examining the risk of rickets in young children reported very low mean 25-hydroxyvitamin D concentrations among those with radiologically confirmed disease and aimed to inform dietary requirements for early life (Rios-Leyvraz et al., 2024). In practice, suspected nutritional rickets must be evaluated by combining history, examination, laboratory testing, and radiography. Typical biochemical investigations include calcium, phosphate, alkaline phosphatase, parathyroid hormone, and 25-hydroxyvitamin D, while radiographs of fast-growing sites such as the wrist or knee help confirm the diagnosis. Differential diagnosis is essential when the pattern is atypical or response to therapy is poor, particularly to exclude renal phosphate-wasting conditions and genetic disorders (Munns et al., 2016; Uday & Högler, 2020).

Assay variability adds another layer of uncertainty. Differences between measurement methods and incomplete standardization can lead to misclassification near decision thresholds, which in turn complicates both research comparisons and the application of guidelines in daily practice (Herrmann et al., 2017; Sempos & Binkley, 2020).

Management

Management depends on the clinical problem being treated, whether that is isolated biochemical deficiency or established nutritional rickets with or without hypocalcemic disease. Across consensus documents, one message is consistent: treatment of nutritional rickets should combine vitamin D with adequate calcium intake, because calcium deficiency may coexist with or even dominate the clinical picture and can influence response to treatment (Chibuzor et al., 2020; Fischer & Almasri, 2022; Fischer et al., 2023; Munns et al., 2016).

Randomized pediatric studies indicate that both daily and intermittent regimens can improve biochemical status. Choice of regimen should be tailored to expected adherence, the risk of excessive post-dose 25-hydroxyvitamin D concentrations, and the feasibility of monitoring. Trials comparing high single oral doses, such as 300,000 IU and 600,000 IU, demonstrated biochemical and radiographic improvement but also documented clinically relevant rates of hypercalcemia, underscoring the need for cautious dosing and follow-up (Mittal et al., 2014; Mondal et al., 2014). In settings where adherence is poor, depot strategies may be useful, although some evidence suggests that daily dosing maintains serum concentrations more steadily over time (Wadia et al., 2018).

Children with comorbid conditions, including inflammatory bowel disease, may need individualized dosing and closer surveillance because absorption, inflammation, and concomitant medications can alter treatment response (Pappa et al., 2012). Safety remains a central issue. High-dose vitamin D can be effective, but excessive dosing may produce hypercalcemia and other adverse effects, especially with repeated bolus regimens (Brustad et al., 2022).

Prevention

Prevention policies consistently place routine infant supplementation at the center of rickets prevention. The global rickets consensus recommends preventive supplementation throughout infancy and emphasizes adequate calcium intake (Munns et al., 2016).

Evidence syntheses in breastfed infants show that vitamin D supplementation, most often 400 IU daily, raises infant 25-hydroxyvitamin D concentrations and lowers the risk of insufficiency, although the certainty of evidence for harder skeletal outcomes is lower, and maternal supplementation strategies may also have a role (Lerch & Meissner, 2007; Tan et al., 2020). Implementation, however, remains uneven. Cross-national analyses describe major differences in policies and adherence, highlighting that the success of prevention programs depends as much on delivery systems, health literacy, and equity as on the biological effect of supplementation itself (Uday et al., 2017; World Health Organization, 2019).

Controversies

Several questions remain unresolved, including the most appropriate pediatric target for 25-hydroxyvitamin D, the usefulness of routine screening outside high-risk groups, and the extent to which supplementation influences extra-skeletal outcomes in children. The 2024 Endocrine Society guideline reframes vitamin D primarily in terms of disease prevention and separates supplementation decisions from indications for laboratory testing, whereas earlier debates about intake targets and deficiency thresholds continue to shape clinical interpretation (Demay et al., 2024; Rosen et al., 2012; Ross et al., 2011).

Extra-skeletal outcomes remain especially controversial. Large meta-analyses examining respiratory infections include pediatric data, but they are heterogeneous with respect to baseline vitamin D status, dosing schedules, and measured outcomes, limiting straightforward translation into pediatric policy (Aglipay et al., 2017; Jolliffe et al., 2021; Martineau et al., 2017). Another area of debate is the differentiation of nutritional rickets from child abuse on imaging. Reviews in pediatric radiology emphasize that careful integration of clinical, biochemical, and radiographic findings is essential to avoid misclassification (Aldana Sierra & Christian, 2021).

Discussion

One of the clearest lessons from the literature is that biochemical deficiency and clinical disease do not overlap perfectly. Low vitamin D status is common at a population level, but severe manifestations are concentrated in recognizable groups, particularly infants with poor stores and inadequate supplementation, children with darker skin living at higher latitudes, and those with chronically low calcium intake. For clinicians, this means that thoughtful risk-based assessment is usually more useful than indiscriminate screening.

The diagnostic problem is not purely technical. It also reflects the fact that different thresholds are designed around different goals, such as preventing rickets, identifying broader deficiency states, or guiding supplementation strategies. Assay variability further blurs the picture. In practical terms, decisions are strongest when laboratory results are interpreted alongside clinical risk, physical findings, biochemical patterns, and radiographic evidence rather than in isolation.

Treatment evidence allows some flexibility in dosing strategy, but the overall direction is clear. Therapy should be safe, feasible, and accompanied by sufficient calcium intake. The most consistent message across guidelines and reviews is that nutritional rickets should not be approached as a vitamin D-only disorder. In many children, a combined vitamin D and calcium strategy is more appropriate both physiologically and clinically.

Conclusions

Vitamin D deficiency in children remains clinically important because serious but preventable complications, especially nutritional rickets and hypocalcemic events, continue to occur in vulnerable groups. Current best practice centers on routine infant supplementation, focused risk assessment, integrated evaluation of suspected rickets, and treatment that combines vitamin D with adequate calcium alongside appropriate monitoring. Future progress will depend on better pediatric outcome-based thresholds, improved assay standardization, and stronger implementation of prevention strategies.

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