RESEARCH PAPER

VITAMIN D DEFICIENCY IN CHILDREN: CLINICAL IMPLICATIONS AND MANAGEMENT

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ABSTRACT

Vitamin D deficiency remains one of the most prevalent nutritional disorders among children worldwide, affecting both developing and developed nations. Vitamin D plays a critical role in calcium and phosphorus homeostasis, skeletal growth, immune regulation, and overall child development. Deficiency can result from inadequate dietary intake, insufficient sunlight exposure, malabsorption syndromes, obesity, chronic illnesses, and genetic abnormalities affecting vitamin D metabolism. In children, vitamin D deficiency primarily manifests as rickets, delayed growth, skeletal deformities, hypocalcemic seizures, muscle weakness, and impaired bone mineralization. Emerging evidence also links vitamin D deficiency with respiratory infections, autoimmune diseases, allergic disorders, metabolic syndrome, and neurodevelopmental abnormalities. Early recognition through clinical assessment and measurement of serum 25-hydroxyvitamin D levels is essential for timely intervention. Management involves preventive strategies, nutritional counseling, adequate sun exposure, and supplementation tailored to age and severity of deficiency. Recent advances include high-dose intermittent supplementation, food fortification programs, novel vitamin D analogs, and personalized approaches based on genetic profiling. This narrative review discusses the causes, skeletal effects, diagnostic approaches, supplementation strategies, recent advances, future directions, and clinical implications of vitamin D deficiency in children.

Keywords: Vitamin D deficiency, Children, Rickets, Bone health, Supplementation, Calcium metabolism, Pediatrics, Cholecalciferol.

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INTRODUCTION

Introduction

Vitamin D is a prohormone essential for normal intestinal calcium absorption, and its deficiency is associated with rickets in growing children and osteomalacia in adults. Rickets represents a failure of mineralization of growing bone and cartilage. The earliest descriptions of rickets were provided by Daniel Whistler and Francis Glisson in England during the seventeenth century.[1] At the beginning of the twentieth century, the disease became highly prevalent with industrialization until it was demonstrated that both sunlight exposure and cod liver oil could prevent and treat rickets.[2] Following the identification of vitamin D and the development of effective food-fortification strategies, nutritional rickets virtually disappeared from most industrialized nations.[3] However, recent decades have witnessed a resurgence of vitamin D deficiency rickets due to multiple contributing factors.[4] Dark-skinned infants who are exclusively breastfed and infants born to mothers with vitamin D deficiency during pregnancy are particularly vulnerable, although increasing numbers of cases have also been reported among older children.[5] In North America and the United Kingdom, accurate prevalence estimates for vitamin D deficiency rickets remain unavailable because most recent data originate from hospital-based case reports and case series. Large studies have documented 126 cases over a ten-year period in Australia and 104 cases over two years in Canada.[4,5] Furthermore, reported cases in the United States increased from 65 cases between 1975 and 1985 to 166 cases between 1986 and 2003, with subsequent reports contributing an additional 62 cases.[6–8] Nutritional rickets also continues to represent a significant public health problem in many developing regions worldwide.[9]

In response to these concerns, the American Academy of Pediatrics (AAP) recommended vitamin D supplementation for breastfed infants who consume less than 500 mL/day of vitamin D–fortified formula or beverages and for non-breastfed infants whose intake of fortified beverages is similarly inadequate.[10] Supplementation should commence within the first two months of life and continue throughout childhood and adolescence. This recommendation is based on evidence that neonatal vitamin D stores acquired through transplacental transfer from vitamin D–sufficient mothers generally persist for approximately 8–12 weeks after birth, considering the 2–3 week half-life of serum 25-hydroxyvitamin D [25(OH)D] and storage of vitamin D in adipose tissue.[10] In the United States, infant formulas are mandated to contain 40–100 IU of vitamin D per 100 kcal, with commercially available products typically providing at least 400 IU/L, thereby ensuring adequate vitamin D intake when at least 500 mL is consumed daily.[10] Nevertheless, despite established supplementation guidelines, cases of nutritional rickets continue to be reported.

Biochemical Manifestations of Different Stages of Vitamin D Deficiency

Parameter	Early Deficiency	Moderate Deficiency	Severe Deficiency
Plasma Calcium (Ca^{2+})	Normal or ↓	Normal or ↓	↓↓
Plasma Phosphate (PO_4^{3-})	Normal or ↓	↓	↓↓
Alkaline Phosphatase (ALP)	↑	↑↑	↑↑↑
Parathyroid Hormone (PTH)	↑	↑↑	↑↑↑
25-Hydroxyvitamin D [25(OH)D]	↓	↓↓	↓↓↓
1,25-Dihydroxyvitamin D [$1,25(OH)_2D$]	Normal	↑	↑ / Normal / ↓
Radiographic Changes	Osteopenia	Mild rachitic changes (+)	Moderate to severe rachitic changes (++)

Abbreviations: Ca^{2+} = Calcium; PO_4^{3-} = Phosphate; ALP = Alkaline Phosphatase; PTH = Parathyroid Hormone; 25(OH)D = 25-Hydroxyvitamin D; $1,25(OH)_2D$ = 1,25-Dihydroxyvitamin D.

Interpretation: Normal = Within reference range; ↑ = Increased; ↓ = Decreased; + = Mild changes; ++ = Moderate to severe changes.

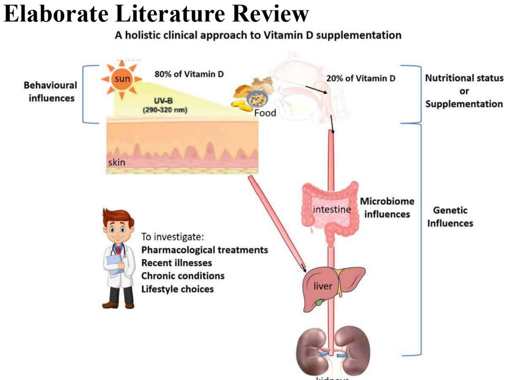
Vitamin D is synthesized predominantly in the skin following exposure to ultraviolet B (UVB) radiation, whereas less than 10% is obtained through dietary sources.[10] Contemporary lifestyles, extensive clothing coverage, indoor living habits, and recommendations aimed at reducing ultraviolet exposure to prevent skin cancer have significantly limited endogenous vitamin D production in many populations. Over the past two decades, substantial advances have enhanced understanding of vitamin D synthesis, metabolism, and its diverse physiological functions. These developments, together with increasing reports of vitamin D deficiency rickets, necessitate re-evaluation of traditional concepts regarding vitamin D requirements, sun exposure practices, and supplementation recommendations. Consequently, this review examines the causes of vitamin D deficiency, including the effects of natural and artificial sunblock use and maternal vitamin D status, and discusses current evidence regarding the prevention and treatment of vitamin D deficiency in children.

Methodology

This narrative review was conducted through a comprehensive literature search of electronic databases including **PubMed, Scopus, Google Scholar, Web of Science, Cochrane Library, and Embase**. Relevant articles published between 2005 and 2025 were identified using keywords such as "vitamin D deficiency," "children," "pediatric vitamin D," "rickets," "bone health," "calcium metabolism," "vitamin D supplementation," and "nutritional deficiency."

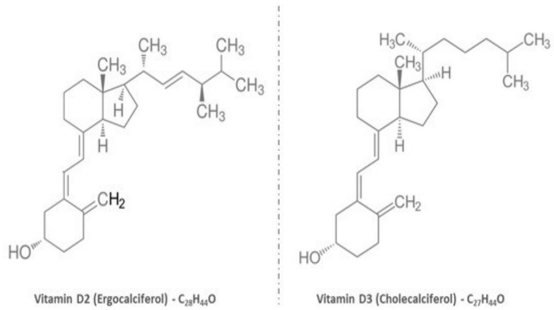
Eligible studies included systematic reviews, meta-analyses, randomized controlled trials, cohort studies, cross-sectional studies, clinical practice guidelines, and expert consensus statements addressing vitamin D deficiency in pediatric populations. Articles focusing on epidemiology, pathophysiology, skeletal manifestations, diagnosis, treatment, prevention, and recent advances were reviewed. Non-English studies and publications lacking pediatric relevance were excluded. Information was synthesized narratively to provide an updated overview of current evidence.

Elaborate Literature Review

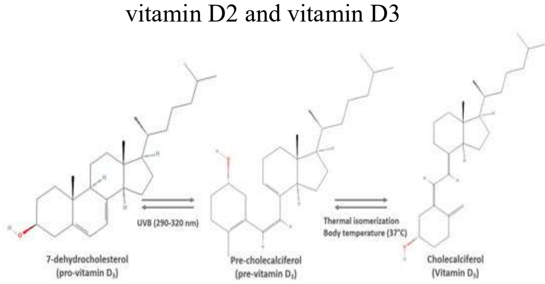


Physiology of Vitamin D

Vitamin D is a fat-soluble hormone that naturally occurs in two main forms: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Vitamin D2 is produced by plants, specifically produced by the ultraviolet irradiation of the yeast and fungi sterol, ergosterol, which is found in some types of mushrooms and yeasts[11]. Vitamin D3 (cholecalciferol) is synthesized in the skin epidermis through a series of chemical reactions that occur when 7-dehydrocholesterol, a type of cholesterol present in the skin, is exposed to sunlight UVB radiation. The UVB radiation transforms 7-dehydrocholesterol into pre-vitamin D3, which then undertakes a thermal isomerization process, converting it into cholecalciferol.

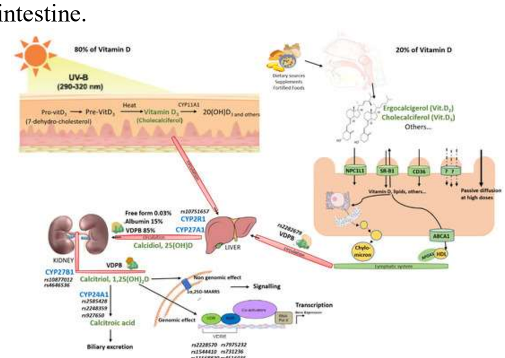


Chemical structure and molecular formula of vitamin D2 and vitamin D3



Conversion of 7–dehydrocholesterol to cholecalciferol in the skin

Vitamin D can be consumed through natural sources, such as fatty fish and egg yolks, or through fortified foods like UV-irradiated mushrooms and supplements like fish oil. When vitamin D is consumed in the diet, digestive enzymes such as trypsin and pepsin take part in vitamin D absorption by clearing vitamin D binding proteins that are present in food to allow its release. Moreover, in the duodenum, other digestive enzymes, like amylase, lipase, and protease, facilitate the release of vitamin D from the food matrix, favoring the absorption in the small intestine.



Clinical physiology of vitamin D and relevant SNPs

Causes of Vitamin D Deficiency in Children

Inadequate Sunlight Exposure

Sunlight exposure remains the most important natural source of vitamin D for children, as ultraviolet B (UVB) radiation stimulates the conversion of 7-dehydrocholesterol in the skin into vitamin D_3 (cholecalciferol).[12] In recent decades, substantial lifestyle changes have contributed to reduced sunlight exposure among children worldwide. Increased indoor activities, prolonged screen time, academic pressures, urbanization, and diminished outdoor recreation have significantly limited opportunities for adequate sun exposure.[13] Furthermore, the widespread use of sunscreens, although essential for preventing skin damage and skin cancer, can markedly reduce cutaneous vitamin D synthesis by blocking UVB radiation.[14] Environmental factors including air pollution, persistent cloud cover, and residence in densely populated urban settings further decrease UVB penetration and vitamin D production.[15] Geographic location also plays a significant role, as children living at higher latitudes receive less effective UVB radiation, particularly during winter months.[16] Cultural practices involving extensive body covering and avoidance of sun exposure because of climatic conditions may additionally restrict endogenous vitamin D synthesis in certain populations.[17] Consequently, inadequate sunlight exposure has emerged as one of the leading contributors to vitamin D deficiency among children globally.

Nutritional Deficiency

Dietary inadequacy represents another major cause of vitamin D deficiency during childhood. Unlike many micronutrients, vitamin D occurs naturally in only a limited number of foods. Rich dietary sources include fatty fish such as salmon, mackerel, sardines, and tuna, as well as fish liver oils, egg yolks, liver, and fortified dairy products.[18] However, these foods are often consumed infrequently because of dietary preferences, socioeconomic limitations, cultural practices, or restricted availability. In many low- and middle-income countries, food fortification programs remain inadequate or inconsistently implemented, thereby increasing the risk of deficiency.[19] Infants who are exclusively breastfed without vitamin D supplementation are particularly vulnerable because human breast milk contains relatively low concentrations of vitamin D, generally insufficient to meet the infant's physiological requirements.[20] Inadequate complementary feeding practices lacking vitamin D-rich foods can further aggravate deficiency during infancy and early childhood. Poor nutritional status, protein-energy malnutrition, and restrictive dietary habits may also contribute to insufficient vitamin D intake and subsequent deficiency.[21]

Maternal Vitamin D Deficiency

Maternal vitamin D status during pregnancy exerts a profound influence on neonatal and infant vitamin D stores. The fetus acquires vitamin D almost entirely through placental transfer from the mother, making maternal sufficiency essential for optimal fetal skeletal development and mineral homeostasis.[22] When pregnant women have inadequate vitamin D levels because of poor dietary intake, limited sunlight exposure, obesity, or underlying medical conditions, their infants are born with reduced vitamin D reserves.[23] Such neonates are particularly susceptible to developing vitamin D deficiency during the first few months of life, especially when exclusively breastfed without supplementation. Maternal deficiency has been associated with impaired fetal bone mineralization, neonatal hypocalcemia, congenital rickets, and delayed skeletal growth.[24] Moreover, vitamin D-deficient mothers may produce breast milk containing insufficient vitamin D concentrations, thereby perpetuating deficiency in the infant.[25] Consequently, maternal vitamin D deficiency represents an important intergenerational determinant of childhood vitamin D deficiency.

Dark Skin Pigmentation

Skin pigmentation significantly influences the efficiency of vitamin D synthesis. Melanin, the pigment responsible for skin coloration, acts as a natural sunscreen by absorbing ultraviolet radiation. While this mechanism provides protection against UV-induced skin damage, it simultaneously reduces the skin's capacity to synthesize vitamin D.[26] Children with darker skin pigmentation require considerably longer durations of sunlight exposure to generate amounts of vitamin D equivalent to those produced by children with lighter skin tones.[26] This physiological difference places darker-skinned populations at greater risk of deficiency, particularly in regions with limited sunlight exposure or among individuals who spend most of their time indoors. Studies consistently demonstrate lower serum 25-hydroxyvitamin D concentrations among children of African, South Asian, Middle Eastern, and other highly pigmented ethnic backgrounds.[27] The risk becomes even more pronounced when combined with factors such as urban residence, air pollution, extensive clothing practices, and inadequate dietary intake.[27]

Obesity

Childhood obesity has emerged as an increasingly recognized risk factor for vitamin D deficiency. Vitamin D is a fat-soluble vitamin that becomes sequestered within adipose tissue, thereby reducing its bioavailability in the circulation.[28] As body fat mass increases, a larger proportion of vitamin D is stored in adipose deposits, resulting in lower serum concentrations despite adequate dietary intake or sun exposure. Obese children frequently exhibit reduced bioavailability of vitamin D and may require higher supplementation doses to achieve optimal serum levels.[28] Additionally, obesity is commonly associated with sedentary lifestyles and reduced outdoor physical activity, further limiting sunlight exposure. Chronic low-grade inflammation characteristic of obesity may also alter vitamin D metabolism and contribute to reduced circulating concentrations. Numerous epidemiological studies have demonstrated an inverse relationship between body mass index (BMI) and serum vitamin D levels, highlighting obesity as an important determinant of vitamin D deficiency in pediatricpopulations.[29]

Malabsorption Disorders

Several gastrointestinal disorders impair intestinal vitamin D absorption and can result in deficiency despite adequate dietary intake. Because vitamin D is fat-soluble, efficient absorption depends on normal digestion and assimilation of dietary lipids. Conditions such as celiac disease produce villous atrophy and intestinal mucosal damage, thereby reducing absorption of vitamin D and other nutrients.[30] Inflammatory bowel diseases, particularly Crohn's disease, may affect extensive portions of the gastrointestinal tract and interfere with fat absorption.[30] Children with cystic fibrosis commonly develop pancreatic insufficiency, resulting in inadequate secretion of digestive enzymes required for efficient fat digestion and absorption.[30] Similarly, short bowel syndrome, chronic pancreatitis, persistent diarrhea, cholestatic liver disease, and other malabsorptive conditions may compromise vitamin D uptake. These children frequently require higher supplementation doses or specialized formulations to maintain adequate vitamin D status.[30]

Chronic Liver and Kidney Diseases

The biological activation of vitamin D requires sequential hydroxylation reactions in the liver and kidneys. Vitamin D derived from sunlight exposure or dietary sources is initially converted in the liver to 25-hydroxyvitamin D [25(OH)D], the principal circulating form used to assess vitamin D status. Chronic liver diseases may impair this hydroxylation process, resulting in reduced production of 25(OH)D and subsequent deficiency.[30] Likewise, chronic kidney disease compromises renal conversion of 25(OH)D to the biologically active hormone 1,25-dihydroxyvitamin D [$1,25(OH)_2D$], leading to secondary hyperparathyroidism, hypocalcemia, and renal osteodystrophy.[30] Children with nephrotic syndrome may additionally lose vitamin D-binding proteins through urinary excretion, thereby reducing circulating vitamin D concentrations.[30] Consequently, hepatic and renal disorders significantly disrupt vitamin D metabolism and increase the risk of skeletal complications including rickets, osteomalacia, and impaired growth.

Medications

Several medications interfere with vitamin D metabolism and predispose children to deficiency during long-term therapy. Antiepileptic drugs such as phenytoin, phenobarbital, carbamazepine, and primidone induce hepatic cytochrome P450 enzymes, thereby accelerating vitamin D degradation and lowering serum concentrations.[30] Long-term glucocorticoid therapy impairs intestinal calcium absorption, inhibits vitamin D-mediated calcium transport, and adversely affects bone formation.[30] Rifampicin, commonly prescribed for tuberculosis treatment, increases hepatic enzyme activity and enhances vitamin D catabolism. Certain antiretroviral agents used in children with human immunodeficiency virus infection may similarly alter vitamin D metabolism.[30] Additional medications including cholestyramine, antifungal agents, and selected chemotherapeutic drugs have also been implicated in lowering vitamin D levels. Children receiving prolonged pharmacological therapy should therefore undergo regular monitoring of vitamin D status and may require preventive supplementation to minimize deficiency-related complications.[30]

Genetic Disorders

Although relatively uncommon, inherited disorders affecting vitamin D metabolism, transport, or receptor function represent important causes of severe vitamin D deficiency and rickets in children. Vitamin D–dependent rickets type I results from mutations in the gene encoding renal 1α-hydroxylase, leading to impaired conversion of 25(OH)D to its active hormonal form.[30] Affected children develop hypocalcemia, rickets, growth retardation, muscle weakness, and skeletal deformities despite adequate vitamin D intake. Vitamin D–dependent rickets type II arises from mutations in the vitamin D receptor gene, resulting in resistance to the biological actions of active vitamin D.[30] These patients often present with severe rickets, alopecia, and marked biochemical abnormalities. Hereditary hypophosphatemic rickets, the most common inherited form of rickets, involves abnormalities in phosphate regulation and renal phosphate wasting, producing defective bone mineralization despite normal vitamin D levels.[30] Advances in molecular genetics have enhanced understanding of these rare disorders, facilitating earlier diagnosis and targeted therapeutic interventions to prevent long-term skeletal complications.

Skeletal Effects of Vitamin D Deficiency

Nutritional Rickets

Nutritional rickets is the most severe and classical skeletal manifestation of vitamin D deficiency in children. It develops as a consequence of defective mineralization of growth plate cartilage and newly formed osteoid tissue resulting from inadequate calcium and phosphate availability.[31] During periods of rapid growth, particularly in infancy and early childhood, insufficient vitamin D disrupts normal endochondral ossification, leading to characteristic skeletal abnormalities and compromised bone strength.[32] Clinically, affected children may present with delayed motor development, irritability, poor growth, bone pain, and generalized muscle weakness.[33] Characteristic skeletal deformities include frontal bossing caused by expansion of cranial bones, craniotabes producing soft skull bones, delayed closure of fontanels, and enlargement of the costochondral junctions known as the rachitic rosary.[31,33] A horizontal depression along the lower chest wall, referred to as Harrison sulcus, develops secondary to diaphragmatic traction on weakened ribs.[32] Progressive deformity of weight-bearing bones results in genu varum (bow legs) or genu valgum (knock knees), while widening of the wrists and ankles occurs because of metaphyseal overgrowth. Radiographic findings typically demonstrate metaphyseal cupping, fraying, and widening of growth plates.[31] If left untreated, nutritional rickets may lead to permanent skeletal deformities, impaired physical development, and long-term functional disability.[32]

Delayed Growth

Vitamin D plays a fundamental role in skeletal growth and longitudinal bone development throughout childhood. Adequate vitamin D status facilitates intestinal calcium absorption and supports normal mineralization at the growth plate. Deficiency disrupts these processes, resulting in delayed bone maturation and impaired linear growth.[34] Children with chronic vitamin D deficiency frequently exhibit growth retardation, reduced height velocity, and failure to achieve expected developmental growth milestones.[34] Inadequate mineral deposition within developing bones compromises normal epiphyseal maturation and may result in delayed skeletal age relative to chronological age.[35] The severity of growth impairment depends on the duration of deficiency, nutritional status, genetic factors, and the coexistence of calcium deficiency. Early diagnosis and correction of vitamin D deficiency are therefore essential to support optimal skeletal growth and maximize adult height potential.[34]

Osteomalacia

In older children and adolescents, prolonged vitamin D deficiency may result in osteomalacia, a disorder characterized by defective mineralization of mature bone matrix. Unlike rickets, which primarily affects growing bones and epiphyseal growth plates, osteomalacia involves impaired mineralization of existing bone tissue.[36] Affected individuals commonly experience diffuse bone pain, skeletal tenderness, fatigue, and difficulty performing routine physical activities. The weakened bone structure predisposes patients to microfractures and stress fractures, particularly in weight-bearing regions such as the lower extremities and pelvis.[36] Histopathological examination reveals excessive accumulation of unmineralized osteoid within the bone matrix, leading to reduced mechanical strength and increased susceptibility to skeletal deformity.[36] Adolescents with osteomalacia may additionally experience diminished exercise tolerance and chronic musculoskeletal discomfort, adversely affecting quality of life and physical functioning.[37]

Reduced Bone Mineral Density

Adequate vitamin D concentrations are essential for achieving optimal bone mineralization and peak bone mass during childhood and adolescence. Vitamin D deficiency impairs intestinal calcium absorption, resulting in inadequate incorporation of minerals into the developing skeleton. Consequently, affected children frequently demonstrate reduced bone mineral density (BMD), which can be detected using dual-energy X-ray absorptiometry (DEXA) scanning.[38] Failure to attain optimal peak bone mass during critical growth periods may have significant long-term consequences, including an increased risk of osteopenia and osteoporosis later in life.[38] Studies have demonstrated that childhood vitamin D insufficiency is associated with lower bone mineral accrual and impaired skeletal development.[39] Furthermore, reduced BMD may persist despite subsequent correction of vitamin D deficiency if inadequate mineralization occurs during key developmental stages, emphasizing the importance of early prevention and intervention.[38]

Increased Fracture Risk

Vitamin D deficiency contributes substantially to skeletal fragility and increased susceptibility to fractures in children. Poor mineralization weakens both cortical and trabecular bone architecture, diminishing the ability of bones to withstand normal mechanical stresses.[39] Consequently, fractures may occur following minimal trauma or routine physical activities that would not ordinarily result in injury. Recurrent fractures, stress fractures, and delayed fracture healing have all been documented in children with severe vitamin D deficiency.[40] Epidemiological investigations have demonstrated significant associations between low serum 25-hydroxyvitamin D concentrations and an increased incidence of pediatricfractures.[39] Maintaining adequate vitamin D status is therefore essential for preserving skeletal strength and minimizing fracture risk throughout childhood and adolescence.[40]

Dental Manifestations

Vitamin D is indispensable for normal odontogenesis, enamel mineralization, and maintenance of oral health. Deficiency during critical periods of tooth development can adversely affect both primary and permanent dentition.[37] Delayed tooth eruption is commonly observed in affected children owing to impaired mineralization and delayed skeletal maturation.[37] Enamel hypoplasia, characterized by defective enamel formation and increased enamel fragility, predisposes children to dental caries, tooth sensitivity, and structural dental abnormalities.[37] Inadequate dentin mineralization further compromises tooth integrity and increases susceptibility to developmental defects. Emerging evidence also suggests an association between vitamin D deficiency and a higher prevalence of periodontal disease and gingival inflammation through mechanisms involving immune modulation and bone metabolism.[37] These oral manifestations may serve as early clinical indicators of underlying vitamin D deficiency and warrant further evaluation.

Muscle Weakness

Musculoskeletal manifestations frequently accompany vitamin D deficiency and contribute significantly to morbidity in affected children. Vitamin D receptors are widely expressed in skeletal muscle tissue, where they regulate muscle protein synthesis, cellular proliferation, and neuromuscular function.[35] Deficiency results in proximal muscle weakness, hypotonia, decreased muscle strength, and impaired coordination. Infants may present with delayed attainment of developmental motor milestones such as sitting, crawling, and walking, whereas older children may experience difficulty climbing stairs, running, or rising from a seated position.[35] Reduced muscle strength also increases the likelihood of falls and subsequent fractures. Moreover, vitamin D deficiency has been associated with impaired balance, reduced physical performance, and diminished endurance. Prompt correction of deficiency generally leads to substantial improvement in muscle function, motor performance, and overall physical activity.[35]

Extra-Skeletal Clinical Implications of Vitamin D Deficiency

Immune Function

Beyond its well-established skeletal functions, vitamin D plays a critical role in regulating both innate and adaptive immune responses. Immune cells, including macrophages, dendritic cells, T lymphocytes, and B lymphocytes, express vitamin D receptors (VDRs) and possess the enzymatic machinery necessary for local activation of vitamin D.[41] Active vitamin D enhances the synthesis of antimicrobial peptides such as cathelicidin and β-defensins, thereby strengthening host defense against bacterial, viral, and fungal pathogens.[42] Furthermore, vitamin D modulates cytokine production, suppresses excessive inflammatory responses, promotes differentiation of regulatory T cells, and contributes to the maintenance of immune tolerance.[41,42] Consequently, vitamin D deficiency may impair immune competence, increase susceptibility to infectious diseases, and contribute to the development of inflammatory disorders.[43]

Respiratory Infections

Numerous epidemiological and clinical studies have demonstrated an association between vitamin D deficiency and an increased risk of respiratory tract infections in children.[43] Low vitamin D concentrations compromise innate immune defenses within the respiratory epithelium and reduce production of antimicrobial peptides essential for pathogen clearance.[42] Children with vitamin D deficiency are more likely to experience recurrent upper respiratory tract infections, bronchiolitis, pneumonia, and other lower respiratory tract infections.[44] Several investigations have also identified a relationship between low vitamin D status and increased susceptibility to tuberculosis, particularly in populations where both conditions are highly prevalent.[45] Although the precise causal mechanisms continue to be investigated, maintaining adequate vitamin D levels appears important for supporting respiratory immune function and reducing the burden of infectious respiratory diseases during childhood.[44]

Allergic Diseases

Emerging evidence suggests that vitamin D influences allergic sensitization and immune tolerance through its immunomodulatory properties. Vitamin D regulates T-helper cell differentiation, suppresses excessive inflammatory cytokine production, and promotes the development of regulatory T lymphocytes responsible for maintaining immune homeostasis.[46] Deficiency has been associated with an increased prevalence and severity of allergic conditions including asthma, allergic rhinitis, and atopic dermatitis.[46] Children with low vitamin D levels may exhibit enhanced airway inflammation, greater bronchial hyperresponsiveness, and increased frequency of asthma exacerbations.[47] Although some studies have produced conflicting results, accumulating evidence supports a contributory role of vitamin D in the pathogenesis, progression, and clinical control of allergic diseases.[46,47]

Autoimmune Disorders

Vitamin D exerts significant immunoregulatory effects that may influence the development and progression of autoimmune diseases. By modulating antigen presentation, cytokine secretion, lymphocyte proliferation, and regulatory T-cell activity, vitamin D helps preserve immune tolerance and prevents inappropriate immune responses directed against self-antigens.[41] Epidemiological studies have demonstrated associations between vitamin D deficiency and several autoimmune conditions, including type 1 diabetes mellitus, multiple sclerosis, and juvenile idiopathic arthritis.[48] Deficiency may increase disease susceptibility in genetically predisposed individuals by promoting pro-inflammatory immune pathways and impairing immune regulatory mechanisms.[48] Although vitamin D supplementation alone is insufficient to prevent autoimmune diseases, maintaining adequate vitamin D status may contribute to lowering disease risk and modulating disease activity.[48]

Neurodevelopment

Vitamin D receptors and vitamin D-metabolizing enzymes are widely distributed throughout the developing central nervous system, suggesting an important role in neurodevelopment.[49] Vitamin D influences neuronal differentiation, neurotransmitter synthesis, neurotrophic factor expression, synaptic plasticity, and neuroprotection during critical stages of brain maturation.[49] Childhood vitamin D deficiency has been associated with alterations in cognitive performance, language acquisition, behavioral regulation, and educational achievement. Some studies have also suggested possible associations between low vitamin D concentrations and neurodevelopmental disorders, although definitive causal relationships remain uncertain.[49] Ensuring adequate vitamin D status during early life may therefore support optimal neurological development, cognitive function, and long-term brain health.[49]

Metabolic Disorders

Vitamin D deficiency has increasingly been implicated in the pathogenesis of several metabolic disorders affecting children and adolescents. Low vitamin D levels are commonly observed among obese children and may contribute to insulin resistance through effects on pancreatic β-cell function, insulin secretion, glucose metabolism, and systemic inflammation.[50] Associations have also been reported between vitamin D deficiency and metabolic syndrome, a cluster of abnormalities characterized by central obesity, hypertension, dyslipidemia, and impaired glucose tolerance.[50] Furthermore, vitamin D deficiency has been linked to endothelial dysfunction, elevated inflammatory biomarkers, and other cardiovascular risk factors that may predispose individuals to future cardiometabolic disease.[50] Although causality remains under investigation, maintenance of adequate vitamin D status is considered an important component of overall metabolic health during childhood and adolescence.

Diagnosis of Vitamin D Deficiency

Laboratory Assessment

Laboratory evaluation remains the cornerstone for diagnosing vitamin D deficiency in children. The most reliable and widely accepted biomarker is serum 25-hydroxyvitamin D [25(OH)D], which reflects vitamin D derived from both cutaneous synthesis and dietary intake.[43] Owing to its relatively long half-life of approximately two to three weeks, serum 25(OH)D provides an accurate assessment of overall vitamin D status. Various professional organizations have proposed classification systems based on serum concentrations, with severe deficiency generally defined as levels below 10 ng/mL, deficiency as levels below 20 ng/mL, insufficiency as levels between 20 and 29 ng/mL, and sufficiency as levels of 30 ng/mL or higher.[43] The interpretation of serum vitamin D concentrations should always be considered within the broader clinical context, including age, nutritional status, growth patterns, and associated medical conditions.

Vitamin D Status	Serum 25(OH)D Level
Severe deficiency	<10 ng/mL
Deficiency	<20 ng/mL
Insufficiency	20–29 ng/mL
Sufficiency	≥30 ng/mL

In addition to serum 25(OH)D measurement, several biochemical investigations help determine the severity of deficiency and its physiological consequences. Serum calcium concentrations may remain normal during mild deficiency owing to compensatory hormonal mechanisms; however, severe deficiency can lead to hypocalcemia.[43] Serum phosphorus levels are often reduced because secondary hyperparathyroidism promotes renal phosphate excretion. Elevated serum alkaline phosphatase represents one of the most sensitive biochemical indicators of active rickets and reflects increased osteoblastic activity associated with defective mineralization.[33] Measurement of parathyroid hormone (PTH) is particularly valuable because vitamin D deficiency commonly induces secondary hyperparathyroidism, resulting in increased bone turnover and mineral mobilization.[43] Renal function assessment is also important, especially in children with chronic kidney disease, where impaired renal activation of vitamin D contributes to metabolic bone disease. Additional investigations such as serum magnesium levels, urinary calcium excretion, and liver function tests may be indicated in selected patients to identify underlying etiologies or associated metabolic abnormalities.[43]

Radiological Findings

Radiological evaluation plays a pivotal role in confirming the diagnosis of vitamin D deficiency–related bone disease, particularly nutritional rickets. Plain radiographs of rapidly growing bones, especially the wrists and knees, are routinely obtained because these regions exhibit characteristic abnormalities early in the disease process.[31] One of the hallmark radiographic features is metaphyseal cupping, resulting from defective mineralization at the growth plate.[31] Metaphyseal fraying appears as irregular and poorly defined metaphyseal margins due to disorganized cartilage maturation and impaired mineral deposition.[31] Widening of the growth plates occurs because of accumulation of unmineralized cartilage and osteoid tissue, producing the classic radiographic appearance of active rickets.[33] Generalized osteopenia, characterized by reduced bone density and cortical thinning, may also be evident.[36] In advanced disease, bowing deformities of long bones, pathological fractures, and delayed skeletal maturation may be observed.[32] Radiological findings not only facilitate diagnosis but also provide valuable information regarding disease severity and response to therapy during follow-up assessments.[31]

Supplementation and Management

Prevention Strategies

Prevention of vitamin D deficiency is substantially more effective and cost-efficient than treating established disease. Public health interventions focus on ensuring adequate vitamin D intake through supplementation, appropriate sunlight exposure, and optimization of dietary practices.[51] Because infants are particularly vulnerable owing to limited vitamin D reserves and rapid skeletal growth, routine supplementation is recommended from birth.[51] Preventive strategies should additionally emphasize maintenance of maternal vitamin D sufficiency during pregnancy and lactation, encouragement of regular outdoor physical activity, and increased consumption of vitamin D-rich or fortified foods.[52] Educational initiatives directed toward parents, caregivers, and healthcare professionals are equally important for improving awareness, adherence to supplementation guidelines, and early recognition of deficiency.[51]

Infants

For infants, daily supplementation with 400 IU of vitamin D is recommended shortly after birth and should continue throughout infancy regardless of feeding method.[51] This recommendation is especially important for exclusively breastfed infants because human breast milk generally contains insufficient vitamin D to satisfy physiological requirements.[53] Adequate supplementation helps maintain optimal serum vitamin D concentrations, supports normal skeletal development, and effectively prevents nutritional rickets.[51] Premature infants, low-birth-weight neonates, and infants born to mothers with vitamin D deficiency require closer surveillance and may need individualized supplementation strategies.[54] Consistent adherence to supplementation during the first year of life significantly reduces the incidence of vitamin D deficiency and its associated complications.[53]

Children and Adolescents

Children and adolescents require sufficient vitamin D intake to support ongoing skeletal growth, bone mineralization, and attainment of peak bone mass. Current recommendations generally advocate a daily intake of 600 IU of vitamin D for healthy children and adolescents.[55] Adequate dietary calcium intake should accompany vitamin D supplementation because both nutrients act synergistically to maintain optimal skeletal health.[55] Regular consumption of fortified dairy products, fatty fish, eggs, and other vitamin D-containing foods should be encouraged. Participation in outdoor recreational activities that facilitate safe sunlight exposure also contributes substantially to maintaining adequate vitamin D status.[52] High-risk groups, including obese children, individuals with chronic illnesses, patients with malabsorption syndromes, and children receiving medications that alter vitamin D metabolism, may require additional monitoring and individualized supplementation regimens.[55]

Treatment of Deficiency

The principal objectives of treatment are to replenish vitamin D stores, correct biochemical abnormalities, promote healing of rickets or osteomalacia, alleviate clinical symptoms, and prevent recurrence.[56] Treatment regimens vary according to age, severity of deficiency, underlying etiology, and the presence of clinical manifestations. Oral vitamin D therapy remains the preferred treatment modality because of its safety, efficacy, affordability, and widespread availability.[56] Clinical improvement, including reduction of bone pain, enhanced muscle strength, and improved physical activity, is often evident within several weeks of initiating therapy, whereas complete radiological recovery may require several months.[56]

Infants (<1 year)

Infants diagnosed with vitamin D deficiency are generally treated with 2000 IU of vitamin D daily for 6–12 weeks.[56] This therapeutic approach effectively replenishes depleted vitamin D stores and promotes normalization of calcium and phosphate metabolism. During treatment, monitoring of serum calcium and vitamin D concentrations may be necessary, particularly in infants with severe deficiency, hypocalcemia, or associated metabolic disturbances.[56] Following biochemical and clinical recovery, maintenance supplementation of 400 IU/day should be continued to prevent recurrence.[51] Early intervention is especially important because infancy represents a critical period for rapid skeletal growth, brain development, and neuromuscular maturation.[54]

Children (1–18 years)

For children and adolescents aged 1–18 years, treatment generally involves vitamin D supplementation ranging from 2000 to 6000 IU daily for 6–12 weeks depending on the severity of deficiency and individual clinical circumstances.[56] Higher therapeutic doses may be necessary in obese children, patients with malabsorption disorders, or those receiving medications that accelerate vitamin D catabolism.[56] Successful treatment is accompanied by normalization of serum alkaline phosphatase levels, improvement of radiological abnormalities, resolution of symptoms, and restoration of normal growth trajectories.[56] Following correction of deficiency, patients should transition to age-appropriate maintenance doses to sustain adequate vitamin D status over the long term.[55]

Alternative High-Dose Regimens

Alternative treatment strategies have been developed to improve adherence, particularly in settings where daily supplementation is difficult to maintain. High-dose intermittent regimens administer larger quantities of vitamin D at less frequent intervals while achieving biochemical outcomes comparable to conventional daily therapy.[57] These approaches may be useful in selected clinical circumstances; however, careful supervision and individualized patient selection remain necessary to ensure safety and effectiveness.[57]

Stoss Therapy

Stoss therapy involves administration of a single large oral dose of vitamin D, generally ranging from 100,000 to 600,000 IU under medical supervision.[58] The term *stoss*, derived from German, signifies a “push” or rapid replenishment of vitamin D stores. This strategy offers the advantage of improved compliance because treatment can often be completed during a single healthcare encounter.[58] Clinical studies have demonstrated effectiveness in correcting vitamin D deficiency and facilitating healing of nutritional rickets. Nevertheless, concerns regarding transient hypercalcemia, hypercalciuria, nephrocalcinosis, and potential vitamin D toxicity necessitate careful monitoring and appropriate patient selection.[58] Consequently, this regimen is generally reserved for circumstances in which adherence to conventional daily therapy is expected to be poor.

Calcium Supplementation

Adequate calcium intake is fundamental to the successful management of vitamin D deficiency because vitamin D-mediated calcium absorption is essential for proper skeletal mineralization.[59] In many children with nutritional rickets, concurrent dietary calcium deficiency coexists and contributes substantially to disease severity. Correction of vitamin D deficiency alone may therefore be insufficient if calcium intake remains inadequate.[59] Combined supplementation with calcium enhances treatment efficacy, accelerates healing of rickets, improves bone mineralization, and promotes normalization of biochemical parameters.[59] Recommended elemental calcium intake generally ranges from 500 to 1000 mg/day depending on age, dietary habits, and severity of deficiency. Dietary counseling should accompany supplementation to encourage sustained consumption of calcium-rich foods and support long-term bone health.[59]

Monitoring

Continuous monitoring is essential to evaluate treatment response, ensure biochemical normalization, and prevent recurrence. Clinical assessment includes documentation of symptom resolution, improvement in muscle strength, correction of skeletal abnormalities, and restoration of normal physical activity.[56] Regular measurement of height, weight, and growth velocity provides valuable information regarding recovery and overall nutritional status. Repeat assessment of serum 25-hydroxyvitamin D concentrations is typically performed several weeks after treatment initiation to confirm adequate replenishment of vitamin D stores.[56] Additional biochemical markers including serum calcium, phosphorus, alkaline phosphatase, and parathyroid hormone may be monitored to document metabolic recovery.[56] In children with rickets, follow-up radiographs may demonstrate progressive healing characterized by restoration of normal metaphyseal architecture, reappearance of the zone of provisional calcification, and improved bone mineralization.[56]

Recent Advances in Management

High-Dose Intermittent Supplementation

Recent research has focused on the development of high-dose intermittent vitamin D supplementation schedules as alternatives to traditional daily regimens. Weekly and monthly dosing protocols have demonstrated promising results in maintaining adequate serum vitamin D concentrations while improving treatment adherence, particularly among adolescents and populations with poor compliance.[57] Several clinical trials have shown that intermittent regimens can achieve biochemical outcomes comparable to daily supplementation when equivalent cumulative doses are administered.[57] These strategies offer practical advantages by reducing treatment burden and simplifying administration schedules. Nevertheless, individualized dosing and ongoing monitoring remain essential to ensure safety and therapeutic effectiveness.[57]

Food Fortification Programs

Food fortification has emerged as one of the most effective population-level interventions for addressing widespread vitamin D deficiency. By enriching commonly consumed foods such as milk, yogurt, cereals, infant formulas, edible oils, and flour products with vitamin D, public health authorities can improve nutrient intake across diverse populations.[60] Countries implementing mandatory fortification policies have reported substantial reductions in vitamin D deficiency prevalence, incidence of nutritional rickets, and associated healthcare expenditures.[60] Fortification strategies are particularly valuable in regions where sunlight exposure is limited or dietary intake is inadequate. Ongoing initiatives focus on optimizing fortification levels, ensuring safety, and expanding access to fortified foods among underserved communities.[60]

Novel Vitamin D Analogs

Advances in pharmaceutical research have facilitated the development of novel vitamin D analogs possessing enhanced therapeutic properties and a lower risk of hypercalcemia. These compounds selectively target vitamin D receptors while minimizing adverse effects associated with excessive calcium absorption. Such analogs are being investigated for use in inherited disorders of vitamin D metabolism, chronic kidney disease, hypoparathyroidism, and other complex metabolic bone disorders. Early studies suggest potential benefits in improving bone health, regulating mineral metabolism, and reducing treatment-related complications. Continued research is required to establish long-term safety and efficacy in pediatricpopulations.[60]

Point-of-Care Vitamin D Testing

Technological innovations have enabled the development of portable point-of-care devices capable of rapidly measuring vitamin D concentrations using small blood samples. These platforms provide results within minutes, facilitating prompt diagnosis and therapeutic decision-making in outpatient clinics, community health programs, and resource-limited settings.[60] Rapid testing may improve screening efficiency, reduce delays in treatment initiation, and enhance healthcare accessibility in underserved regions. As these technologies become increasingly affordable and accurate, they are expected to play a growing role in pediatric preventive healthcare and large-scale nutritional surveillance programs.[60]

Precision Medicine Approaches

The emergence of precision medicine has highlighted the importance of genetic variability in determining vitamin D metabolism and responsiveness to supplementation. Polymorphisms affecting vitamin D receptors, vitamin D-binding proteins, hydroxylating enzymes, and transport proteins can significantly influence serum vitamin D concentrations and therapeutic outcomes.[60] Advances in genomic technologies have facilitated identification of genetic determinants associated with susceptibility to deficiency and variability in treatment response. Future personalized management strategies may incorporate genetic profiling to optimize dosing regimens, predict responsiveness, and minimize adverse effects. Such approaches hold considerable promise for improving management among high-risk pediatricpopulations.[60]

Digital Health Applications

Digital health technologies are increasingly being incorporated into the prevention and management of vitamin D deficiency. Mobile health applications, telemedicine platforms, electronic reminder systems, wearable activity trackers, and remote monitoring tools offer innovative approaches for enhancing patient engagement and treatment adherence.[60] These technologies facilitate supplementation tracking, appointment scheduling, symptom monitoring, and dissemination of educational content related to nutrition and healthy lifestyle practices. Telemedicine services have been particularly valuable in extending specialist support to rural and underserved communities, improving access to care and continuity of follow-up. As digital healthcare infrastructure continues to expand, such applications are expected to become integral components of comprehensive pediatric vitamin D deficiency management programs.[60]

Future Directions

Future research should aim to establish universally accepted pediatric vitamin D thresholds and determine optimal supplementation doses for children of different ages, ethnicities, and risk groups. Large longitudinal studies and randomized controlled trials are needed to clarify the long-term extra-skeletal benefits of vitamin D, including its effects on immune function, respiratory health, neurodevelopment, and metabolic disorders. Advances in genomics may enable personalized supplementation strategies based on individual genetic variations affecting vitamin D metabolism. Public health efforts should focus on expanding food fortification programs and improving awareness to reduce the global burden of deficiency. Additionally, further investigation into the interactions between vitamin D, gut microbiota, and immune development may provide new therapeutic insights. Developing affordable and accessible screening methods for low-resource settings will also be essential for early detection and effective management of vitamin D deficiency in children.

DISCUSSION

Vitamin D deficiency continues to represent a major public health challenge in pediatric populations worldwide despite substantial advances in nutritional awareness, food fortification policies, and supplementation programs. The persistence of deficiency across both developing and developed nations highlights the complex interplay of environmental, nutritional, socioeconomic, cultural, and biological factors that influence vitamin D status.[61] Contemporary lifestyle changes, including reduced outdoor activity, increased screen exposure, urbanization, air pollution, and widespread sun-avoidance practices, have significantly limited cutaneous vitamin D synthesis among children.[62] Furthermore, exclusive breastfeeding without adequate supplementation, inadequate dietary intake, maternal deficiency during pregnancy, obesity, malabsorption syndromes, chronic systemic illnesses, and genetic disorders collectively contribute to the ongoing burden of hypovitaminosis D.[63] These multifactorial determinants emphasize the need for comprehensive preventive strategies that address both individual risk factors and broader population-level influences.

The skeletal consequences of vitamin D deficiency remain the most clinically important manifestations in childhood. Nutritional rickets continues to be the hallmark disease associated with severe deficiency and remains prevalent in many regions of Asia, Africa, and the Middle East despite being largely preventable.[64] Defective mineralization of growing bone results in characteristic clinical and radiological abnormalities including metaphyseal widening, cupping and fraying of growth plates, delayed skeletal maturation, growth retardation, and permanent skeletal deformities when treatment is delayed.[64,65] In addition to rickets, chronic vitamin D deficiency contributes to reduced bone mineral density, impaired attainment of peak bone mass, osteomalacia in adolescents, and increased fracture susceptibility.[65] Since childhood and adolescence represent critical periods for skeletal development, inadequate vitamin D status during these stages may have lifelong implications, predisposing individuals to osteoporosis and fragility fractures in later adulthood.[66] Consequently, early recognition and prompt correction of deficiency are essential to ensure optimal skeletal health and maximize long-term bone strength.

Growing evidence indicates that the clinical significance of vitamin D extends far beyond bone metabolism. Vitamin D receptors are expressed in numerous tissues throughout the body, supporting its involvement in diverse physiological processes including immune regulation, cellular differentiation, endocrine function, and cardiovascular homeostasis.[67] Deficiency has been associated with increased susceptibility to respiratory tract infections, impaired antimicrobial responses, allergic diseases, autoimmune disorders, obesity, insulin resistance, and adverse cardiometabolic outcomes.[67,68] Several observational studies have further suggested associations between low vitamin D concentrations and neurodevelopmental outcomes, cognitive performance, and behavioral disorders in children. Although causality remains incompletely established for many of these associations, the accumulating evidence supports the concept that maintaining adequate vitamin D status contributes to overall pediatric health beyond prevention of rickets alone.[68] Future large-scale randomized controlled trials are required to clarify the extent to which vitamin D supplementation influences these extra-skeletal outcomes and to identify populations most likely to benefit from intervention.

Despite considerable research, important controversies persist regarding the optimal definition, diagnosis, and management of vitamin D deficiency. Different professional organizations continue to recommend varying thresholds for deficiency, insufficiency, and sufficiency based on serum 25-hydroxyvitamin D concentrations, leading to inconsistencies in clinical practice and epidemiological reporting.[69] Variability in laboratory assays, differences in population characteristics, seasonal fluctuations, and ethnic diversity further complicate interpretation of vitamin D status. Similarly, disagreement remains regarding optimal supplementation dosages for prevention and treatment across different age groups and risk categories.[69] Establishing universally accepted diagnostic criteria and evidence-based treatment guidelines remains a priority for improving clinical decision-making and ensuring consistent patient care globally.

Public health interventions continue to represent the cornerstone of vitamin D deficiency prevention. Maternal supplementation during pregnancy and lactation is critical because neonatal vitamin D stores depend largely on maternal status.[63] Universal infant supplementation programs have demonstrated significant effectiveness in reducing the incidence of nutritional rickets and severe deficiency.[70] Food fortification strategies involving milk, infant formulas, cereals, edible oils, and staple foods have emerged as highly cost-effective population-based approaches capable of improving vitamin D intake across diverse socioeconomic groups.[70] Promotion of safe sunlight exposure, balanced nutrition, outdoor physical activity, and community education programs further complements these preventive measures. Importantly, targeted screening and supplementation of high-risk groups—including premature infants, exclusively breastfed infants without supplementation, obese children, children with chronic illnesses, and those with malabsorption disorders—may enhance the efficiency of preventive strategies while minimizing healthcare costs.[70] As emerging technologies such as point-of-care testing, digital health monitoring systems, and precision medicine approaches become increasingly accessible, future management strategies may allow more individualized assessment and treatment of vitamin D deficiency. Collectively, these integrated preventive and therapeutic approaches offer the greatest potential for reducing the global burden of vitamin D deficiency and improving long-term health outcomes among children and adolescents.

CONCLUSION

Vitamin D deficiency is a common and preventable pediatric disorder with substantial implications for skeletal growth and overall health. The primary causes include inadequate sunlight exposure, poor dietary intake, maternal deficiency, obesity, malabsorption disorders, chronic illnesses, and genetic abnormalities. Skeletal manifestations range from reduced bone mineralization and delayed growth to severe nutritional rickets and fractures. Early detection through serum 25-hydroxyvitamin D measurement and prompt intervention with supplementation and calcium replacement are essential for optimal outcomes. Recent advances in supplementation strategies, food fortification, genetic research, and digital health technologies offer promising opportunities for improved prevention and management. Comprehensive public health policies and evidence-based clinical practices remain crucial for addressing this persistent global health challenge.

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