REVIEW ARTICLE

Vitamin D Deficiency in India

Reviewed by:

Dr. Rajeev Bansal

MBBS, MD (Internal Medicine),
Senior Director – Internal Medicine,
Diabetes Management and Practices,
Max Super Speciality Hospital, Delhi

Introduction

The Global and Indian Context of a Silent Pandemic

Vitamin D Deficiency (VDD) is a global pandemic and remains the most underdiagnosed and undertreated nutritional disorder, affecting people of all ages, genders, races, and geographies.[1] It impacts nearly 1 billion individuals worldwide, in both developed and developing nations, irrespective of sunshine availability.[2]

Although Vitamin D is synthesized in the skin upon UVB exposure, deficiency remains widespread even in sun-rich regions like India.[1] Despite India's equatorial advantage, VDD persists as a "silent epidemic" due to urbanization, reduced outdoor activity, pollution, darker skin pigmentation, and cultural practices limiting sun exposure. Epidemiological evidence links VDD to osteoporosis, rickets, cardiovascular disease, diabetes, autoimmune disorders, and certain malignancies.[3]

The Epidemiology and Alarming Scale of the Deficiency

Vitamin D deficiency is alarmingly high in India, with prevalence ranging from 70–100% across the general population.[1] It is widespread in children, adolescents, adults, the elderly, and particularly in pregnant and lactating women, with maternal status closely correlating with that of neonates and breastfed infants.[1] Hospital-based studies report rates between 37–99%, while community-based studies show 50–94%, with variability due to differing methodologies and diagnostic cut-offs.[4]

Demographic patterns further highlight the burden. Among children and adolescents, over half are deficient or insufficient,[5] with some regions reporting up to 81% prevalence.[1] Poor Vitamin D status has been linked to greater risk of acute lower respiratory infections in children.[6] Deficiency among pregnant women is exceptionally high, affecting nearly 90%.[4] Patients with chronic conditions also show high prevalence—84.2% in type 2 diabetes, 82.6% in hypertension, and 76.9% in hypothyroidism.[7]

The ubiquity of VDD across age, geography, and socio-economic status points to environmental and cultural factors as key drivers. Urbanization, reduced sun exposure, and lifestyle changes particularly worsen deficiency in children and adolescents, underlining modern living as a major determinant of this epidemic.[5]

Etiology and Pathophysiology

Multiple modern and traditional factors hinder natural Vitamin D synthesis in India. Urbanization drives indoor lifestyles, while pollution reduces cutaneous synthesis by blocking UVB rays. Dietary shifts with low calcium and Vitamin D intake, along with phytates and phosphates in fiber-rich diets, further deplete stores. Darker skin pigmentation, sunscreen use, cultural clothing practices (burqa, purdah), and unspaced pregnancies in nutritionally deficient women worsen deficiency.[4]

Vitamin D deficiency also arises from impaired activation pathways. Reduced intake or absorption occurs in malabsorption syndromes such as celiac disease, Inflammatory Bowel Disease (IBD), gastric bypass, chronic pancreatic insufficiency, or cystic fibrosis. Older adults consume less Vitamin D. Limited sun exposure—whether due to aging, institutionalization, hospitalization, or sunscreen use—lowers synthesis. Endogenous defects occur in liver cirrhosis (impaired 25-hydroxylation) and renal failure or hypoparathyroidism (defective 1α-hydroxylation). Medications like Pheno-barbital, Carbamazepine, Rifampin, and Steroids accelerate hepatic catabolism, while hereditary Vitamin D–resistant rickets causes end-organ resistance.[8]

Pollution is a critical determinant, as aerosols, ozone, and particulate matter scatter UVB radiation. A Delhi study showed children in highly polluted areas had lower Vitamin D and higher rickets prevalence compared to those in less polluted zones, with "haze scores" confirming reduced UVB penetration.[9]

Diagnostic Approaches and Controversies

Serum 25-hydroxyvitamin D (25(OH)D) measurement is the cornerstone for assessing Vitamin D status, essential for skeletal and extra-skeletal functions. However, the absence of universally accepted cut-offs complicates both diagnosis and research comparisons.

Guidelines Vary Significantly:

- **Endocrine Society:** Deficiency <20 ng/mL, insufficiency 21–29 ng/mL, sufficiency ≥30 ng/mL
- **National & International Osteoporosis Foundation, American Geriatric Society:** Deficiency <30 ng/mL
- **Institute of Medicine (IOM) *vs.* Endocrine Society (ES):** <12.5 ng/mL *vs.* <20 ng/mL, respectively, with discrepancies due to interpretation of the PTH plateau, which varies by age, race, body composition, renal function, and geography.[2]
- **Indian Society of Bone Mineral Research (ISBMR):** Ideal range 30–40 ng/mL[7]

To address local needs, the Indian Expert Group Consensus defines deficiency as <20 ng/mL, insufficiency as 20–29 ng/mL, and recommends a target >40 ng/mL, noting that levels of 40–60 ng/mL provide extra-skeletal benefits.[7]

Clinical Manifestations and Extra-Skeletal Implications

Vitamin D deficiency has profound skeletal and extra-skeletal consequences.

Skeletal Effects: In children, it causes rickets by impairing calcium and phosphorus balance, leading to bone deformities, muscle weakness, and pain. In adults, it contributes to osteomalacia and osteoporosis through reduced calcium absorption and increased bone resorption, resulting in low bone mineral density, muscle weakness, and higher risk of falls and fractures. Supplementation improves muscle strength and postural stability, thereby reducing fall risk.

Extra-skeletal Effects: Deficiency is linked to multiple systemic disorders. Neuropsychiatric associations include depression, delayed recovery from illness, neurodegenerative diseases such as Parkinson's, and even increased suicide risk. Infectious diseases like tuberculosis, influenza, and respiratory infections show higher prevalence of deficiency, reflecting its role in immunity and echoing historical use of sunlight therapy for tuberculosis. Autoimmune diseases (e.g., type 1 diabetes, rheumatoid arthritis) also correlate with low Vitamin D, highlighting its immunomodulatory role in cell proliferation, hormone secretion, and immune regulation.

Cancer risk is influenced by Vitamin D status, with low levels associated with lung, breast, prostate, ovarian, pancreatic, colorectal, and esophageal cancers. Mechanisms include inhibition of angiogenesis, promotion of apoptosis, and reduction of inflammation. Cardiovascular consequences include increased risks of hypertension, myocardial infarction, and heart disease. Vitamin D deficiency is also linked to both type 1 and type 2 diabetes, with evidence suggesting supplementation may lower risk. Obesity shows an inverse relationship with Vitamin D, compounding metabolic and inflammatory pathways that worsen outcomes.

While many associations are drawn from observational studies and smaller clinical trials, causality and the full impact of supplementation require validation through large-scale randomized controlled trials. Nonetheless, the wide-ranging role of Vitamin D across bone, immune, metabolic, cardiovascular, and neuropsychiatric health establishes prevention and correction of deficiency as a global public health priority.[4,10]

Therapeutic and Preventive Strategies

Management of Vitamin D deficiency (Fig. 1), outlining recommended steps for diagnosis, treatment initiation, choice of supplementation, and follow-up to optimize patient outcomes.

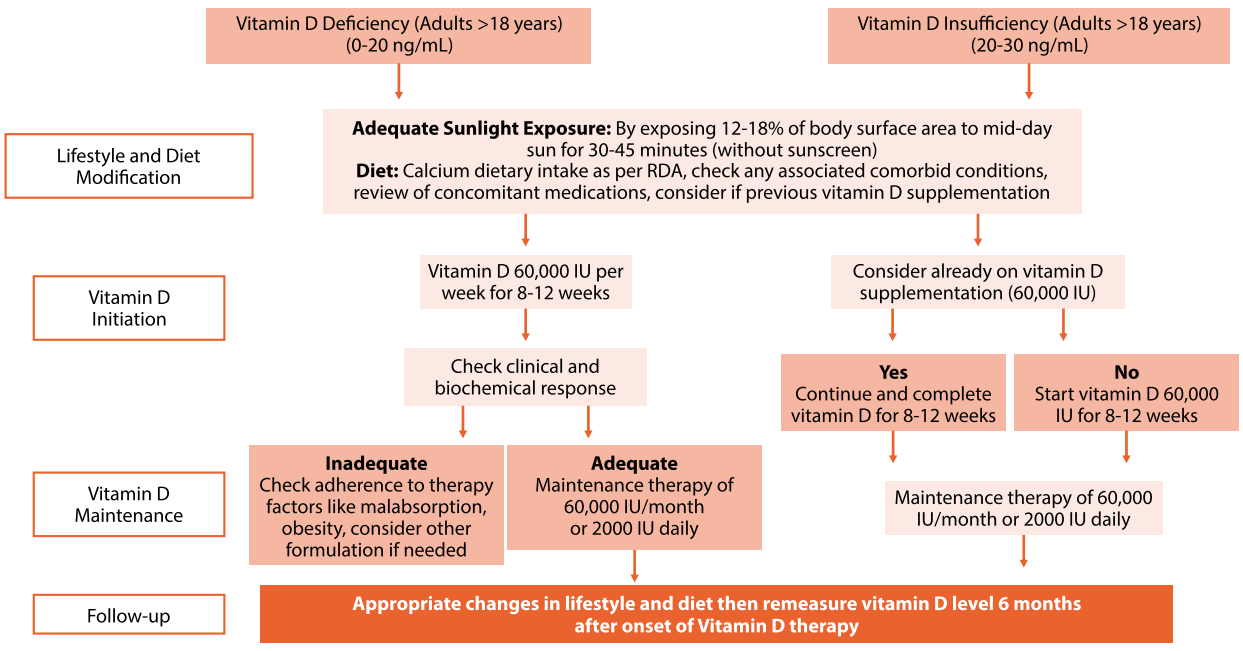
Sunlight and Vitamin D:

The most effective source of Vitamin D is near the equator (42°N–42°S). Around 30 minutes of midday sun exposure to the face and arms without sunscreen meets daily needs, with cutaneous Vitamin D lasting longer than supplements. Whole-body exposure causing minimal erythema produces the equivalent of 20,000 IU. For Asians with skin type V, exposure requirements range from 10–45 minutes depending on latitude and season. Factors like clouds and ozone can reduce synthesis, creating a "Vitamin D winter." India lies between 8.4° N and 37.6° N. A Tirupati study (13.4° N) using an *in vitro* model showed maximal conversion of 7-dehydrocholesterol to Vitamin D between 11 a.m. and 2 p.m. Indian data show an inverse correlation between 25(OH)D levels and latitude (r=–0.48; p<0.0001), with higher levels in the south than the north. In Delhi (28.38° N), outdoor workers had higher serum and bioavailable 25(OH)D than indoor workers. In Pune (18.31° N), toddlers playing outdoors >30 min/day with >40% body exposure had triple the Vitamin D status of mostly indoor peers.[11]

Food Fortification and Public Health

India faces a dual deficiency of Vitamin D and calcium. Milk and cooking oil fortification with Vitamin D has begun, but

Figure 1: Proposed Algorithm for Management of Vitamin D Deficiency



only 35% of the population has access to regulated milk supply, and rural areas—68.84% of the population—often lack organized food distribution. Rural residents, however, have greater sun exposure opportunities. In Delhi slums, toddlers exposed to sunlight had mean 25(OH)D levels of ~100 nmol/L *vs.* ~20 nmol/L in those without exposure.

Recommendations

Fortification programs should ensure nationwide reach, supported by public education on sun exposure (12–18% body area for 30–45 min daily without sunscreen) and adequate dietary calcium. Schools in sunny regions can schedule outdoor time during midday; toddlers, children, older adults, and workers should be encouraged to spend time in the sun. Urban residents with limited exposure should use supplements and fortified foods.[11]

Vitamin D Supplementation: Dosage Guidelines

Vitamin D supplementation is vital for those unable to meet requirements through sunlight or diet. Indian guidelines offer clear dosing frameworks:

- **ICMR:** 400 IU daily for individuals with low sun exposure.[12]
- **Endocrine Society of India:** 400 IU/day for infants, 600–1000 IU for children, 1000 IU for adolescents and pregnant women (after 12 weeks' gestation), and 1000–2000 IU for adults.[13]

Nanoformulations of Vitamin D3: Revolutionizing Absorption and Efficacy

Nanotechnology in Vitamin D3 Delivery

Nanotechnology has transformed the delivery of lipophilic nutrients, with nanoemulsions (droplet size <200 nm) emerging as superior alternatives to conventional coarse emulsions (droplet size >200 nm). Nanoemulsions offer enhanced bioavailability, stability, and absorption of hydrophobic compounds like Vitamin D3 (Cholecalciferol). Their small droplet size (50–200 nm) results in improved physicochemical properties, including reduced aggregation, enhanced optical clarity, and faster digestion in the Gastrointestinal Tract (GIT).

These attributes increase the bioaccessibility of lipophilic bioactives, such as curcumin, carotenoids, and Vitamin D3, making nanoemulsions a promising delivery system in the nutrition and pharmaceutical industries.

Research demonstrates that Cholecalciferol nanoemulsions (<200 nm) exhibit significantly higher bioavailability and homogeneity compared to conventional emulsions (>200 nm). Moreover, studies in animal models of Non-Alcoholic Fatty Liver Disease (NAFLD) highlight the superior hepatoprotective effects of Vitamin D3 nanoemulsions, attributed to their enhanced anti-inflammatory and antioxidant properties.[14]

Advantages of Nanoemulsions over Conventional Vitamin D3 Formulations

Nanoemulsions of Vitamin D3 offers several advantages over traditional preparations, making them a preferred choice for addressing Vitamin D deficiency, particularly in patients with complex needs:

1. *Improved Patient Compliance*

The ease of administration and enhanced efficacy of nano-emulsions lead to better adherence to supplementation regimens.

2. *Enhanced Efficacy in Malabsorption Syndromes*

Nanoemulsions are particularly beneficial for patients with conditions such as IBD, celiac disease, short bowel syndrome, hepatobiliary disorders, pancreatic insufficiency, or post-bariatric surgery, where deficiencies in fat-soluble vitamins and essential fatty acids are common.

3. *Superior Hepatoprotective Effects*

Histopathological and biochemical evidence from animal studies indicates that nanoemulsions provide greater liver protection compared to conventional formulations, particularly in NAFLD models.[14]

Nano-Carrier Entrapped Vitamin D3-Oral Solution (powered by Aqueol® Nanotechnology): A Break-through in Delivery

The Nano-Carrier Entrapped Vitamin D3-Oral Solution utilizes the patented Aqueol® Nanotechnology (Fig. 2), a precision-engineered platform that produces stable, uniform nanoparticles with an average size of <150 nm. This technology offers several key features:

Stability and Uniformity

The ultra-fine nanoparticles are evenly dispersed, water-miscible, and resistant to enzymatic degradation and pH variations in the GIT.

Enhanced Absorption

A stable hydrophilic surface facilitates smooth passage through the unstirred water layer of the intestine, enabling direct delivery of Vitamin D3 to absorption sites without reliance on lipid digestion.

Improved Bioavailability

Unlike conventional formulations (granules, soft-gelatin capsules, or micellar syrups), this nanoformulation does not require dietary fat for optimal absorption.[14]

Clinical Features of Nano-Carrier Entrapped Vitamin D3-Oral Solution

Clinical trials conducted in Indian patients across various indications have demonstrated the following benefits:

1. *Superior Bioavailability*

Outperforms granules, soft-gelatin capsules, and micellar syrups in delivering higher serum Vitamin D3 levels.

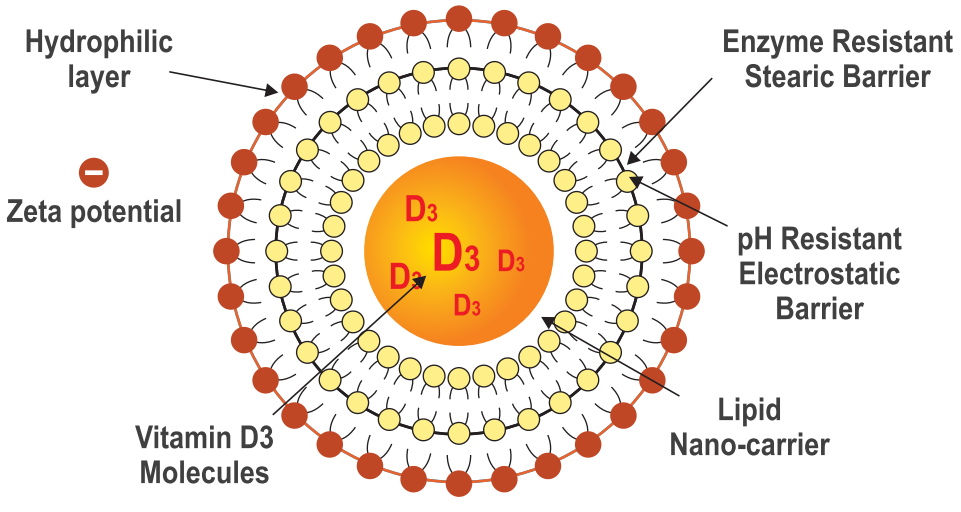
2. *Fat-Independent Absorption*

Achieves optimal Vitamin D3 levels (>40 ng/mL) without requiring dietary fat, making it ideal for patients with malabsorption disorders.

3. *Rapid and Consistent Results*

Achieves a fourfold increase in Vitamin D3 levels within 8 weeks, with predictable outcomes across age, gender, and BMI.

Figure 2: Nano-Carrier Entrapped Vitamin D3-Oral Solution Powered by Aqueol® Nanotechnology



4. *Safety Profile*

No risk of hypervitaminosis or toxicity observed in clinical trials, ensuring safe use across diverse patient populations.

The Nano-Carrier Entrapped Vitamin D3-Oral Solution, powered by Aqueol® Nanotechnology, represents a significant advancement in Vitamin D supplementation. Its superior bioavailability, fat-independent absorption, and enhanced hepatoprotective effects make it a transformative solution for addressing Vitamin D deficiency, particularly in patients with malabsorption syndromes or chronic liver conditions. This innovative formulation sets a new standard for efficacy, safety, and patient compliance in the management of Vitamin D3 supplementation.[14]

Clinical Evidence

In a prospective, open-label, post-marketing study in adults with Vitamin D deficiency/insufficiency (<30 ng/mL), weekly oral doses of 60,000 IU nanoparticle-based vitamin D for 8 weeks significantly increased mean serum 25(OH)D from 15.9 ng/mL at baseline to 41.03 ng/mL at 4 weeks and 31.38 ng/mL at 8 weeks (p<0.0001). Among those treated for ≥4 weeks (n=38), 84.2% achieved >30 ng/mL. In a post-marketing study, weekly doses of 60,000 IU nanoformulated Vitamin D for 8 weeks significantly increased serum 25(OH)D levels from a baseline of 15.9 ng/mL to above 30 ng/mL in over 84% of patients. A multicenter controlled study further confirmed the superior efficacy of nanoformulations, with serum 25(OH)D levels rising more than threefold by week 8, significantly higher than with tablets or capsules. Importantly, nanoformulations also reduced iPTH levels by over 60%, a marker of Vitamin D sufficiency, more effectively than conventional formulations.[7]

Clinical trials involving over 300 Indian patients across various indications have demonstrated the effectiveness of Nano-Carrier Entrapped Vitamin D3-Oral Solution. Compared to conventional formulations such as granules, soft-gelatin capsules, and micellar syrups, the nano-formulation showed significantly greater bioavailability. It provided a consistent and predictable rise in serum Vitamin D levels across different age groups, genders, and BMI categories. Importantly, no cases of hypervitaminosis or toxicity were reported in any of the clinical studies, confirming both its safety and efficacy.[14]

Conclusion

Vitamin D deficiency, widespread in India due to limited sun exposure and low calcium intake, poses a significant public health challenge. National strategies must include revising RDAs for calcium and Vitamin D, improving diagnostic access, and promoting awareness. Food fortification of staples like milk, oils, and flours, backed by legislation, is a cost-effective solution.

Education for healthcare providers and the public is vital, with schools contributing through fortified meals and lifestyle programs. Affordable supplements and testing should be accessible at Primary Health Centers for at-risk groups, supported by ongoing research to monitor outcomes.

The Nano-Carrier Entrapped Vitamin D3-Oral Solution, powered by Aqueol® Nanotechnology, represents a groundbreaking advancement in addressing this crisis. With superior bioavailability, fat-independent absorption, and enhanced hepatoprotective effects, this innovative nanoformulation is uniquely positioned to address Vitamin D deficiency, particularly in patients with malabsorption syndromes or chronic liver conditions. By setting a new benchmark for efficacy, safety, and patient compliance, this solution offers a transformative approach to improving Vitamin D status and overall public health in India.

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