Review Article

# Vitamin D deficiency in India

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**Vitamin D deficiency is prevalent in India across all age groups and geographical regions. Several factors are responsible for this widespread deficiency of vitamin D such as sun-avoiding behavior, atmospheric pollution, lack of vitamin D in common food items consumed in India and so on. Clinical features of vitamin D deficiency depends upon the age of the person. In the growing age, vitamin D deficiency causes rickets that manifest as growth plate abnormalities. In adults, vitamin D deficiency leads to osteomalacia that manifest as easy to break bones. Mild to moderate vitamin D deficiency in adults leads to bone loss, probably secondary to elevated parathyroid hormone. Vitamin D insufficiency has also been associated with a number of chronic inflammatory and neoplastic disorders. However, the causal role of vitamin D insufficiency in these disorders is yet to be proved. Several doses and regimens have been used for preventing and treating vitamin D deficiency. Overzealous correction of vitamin D deficiency has also lead to the increased incidence of vitamin D toxicity. In this article, we will discuss the overview of burden of vitamin D deficiency in India, its clinical presentations as well as some suggestions for treating vitamin D deficiency.**

[*J Indian Med Assoc* 2018; **116:** 41-4 & 55]

***Key words*** **: Vitamin D deficiency, Rickets, Osteomalacia, Osteoporosis, 25(OH)D, vitamin D toxicity**

## (1) What is the Burden of Vitamin D Deficiency in India?

Hypovitaminosis D has been reported from India across all ages: pregnant women, newborns, children and adolescents, young adults, and older men and women. A review of the global vitamin D status by the International Osteoporosis foundation in 2009 underscores the fact that South Asia may be one of the worst affected regions in the world[1]. Vitamin D deficiency disorders such as rickets in children and osteomalacia in adults continue to exist in the Indian population[2].

**Several factors have been proposed to explain the high prevalence of vitamin D in Indians. These include the following :**

***(1) Poor sun exposure, especially in urban Indians*** — Culturally, Indians avoid the sun for fear of skin darkening orbecause the summer sun delivers discomforting heat. This sun fleeing behavior contrasts with the sun seeking behavior of Europeans and North Americans, where, because of the otherwise cold environment, the sun's warmth is generally considered welcome

***(2) Clothing habits*** — Traditionally, Indians, even when in the sun, tend to keep their bodies well covered.

***(3) Skin pigmentation*** — Melanin in the skin competes with 7-dehydrocholesterol for UVB rays. Greater amounts of melanin in the skin reduce the efficacy of vitamin D synthesis. Pigmented skin requires a longer duration of sun exposure to synthesize equivalent amount of vitamin D as compared to a Caucasian skin. There are six types of skin based on degree of pigmentation and propensity to burn or tan. The lightest north European skin is classified as type 1 and African skin as category VI. Indians belong to skin category IV and V.

***(4) Atmospheric pollution*** — It may be playing a role in reducing the efficiency of vitamin D photosynthesis in Indian cities. The short UVB wavelengths are scattered by this process. There is a report of high incidence of vitamin D deficiency rickets in toddlers living in areas of high atmospheric pollution in Delhi, India.

***(5) Food habits and lack of fortification*** — effectively, there is negligible vitamin D available from dietary sources in India. Compounding this is the absence of vitamin D

- **Vitamin D is an essential factor for optimal bone health and may impact other medical disorders unrelated to bone and mineral metabolism.**
- **A serum A serum 25(OH)D level of 12.5 ng/mL is sufficient for prevention of rickets and osteomalacia.**
- **For general population, 25(OH)D values of 20 ng/mL may be considered adequate. There is no evidence to support that levels above 40 ng/mL provide any additional benefit.Therefore, 25(OH)D levels between 20-40 ng/mL are optimum for most of the population.**
- **The optimum serum 25(OH)D level for patients with bone disorders like osteoporosis is 30 ng/mL.**
- **Overzealous correction of vitamin D deficiency, especially with parenteral mega-doses of vitamin D preparations, should be avoided.**

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fortification andlow dietary calcium intake in India which further aggravates the problem.

**Vitamin D status in young adults :** Numerous reports, from across India haveshown a high prevalence of hypovitaminosis D, ranging from 70% to 98% in adult Indians. In a series of studies from North India-from Delhi, Lucknow, Srinagar and other cities-vitamin D deficiency has been shown to be very common[3-7]. Winter levels of circulating 25(OH)D have been shown to be as low as 4-5 ng/mL in Delhi and Lucknow. Data from across India, including the South-Tirupati, Vellore and surrounding areas, and West- Mumbai- is similar, although the levels seem to be slightly better in the South than in the North, probably reflecting the difference in latitude[8-10].

**Vitamin D status in older adults and elderly :** Older adults and elderly are particularly at risk for developing vitamin D deficiency as the efficiency of synthesis of vitamin D in skin declines with advanced age. A study from Delhi found that 91.3 % urban adults (aged 50-65 years) had vitamin D deficiency with mean 25(OH)D levels of 9.7 ng/mL[11-15]. Similar proportion of subjects (91.2 %) in the age group of 65 years and above had mean serum 25(OH)D levels of 9.9 ng/mL. Other studies have shown similar findings[16-17]. In a study from India, outdoor workers with prolonged sun-exposure were vitamin D-sufficient, with higher serum 25(OH)D (29.0 ng/mL) than the indoor workers (10.9 ng/mL) during summer[18].

**Vitamin D status in children :** Approximately 40-50% of total skeletal mass is accumulated during childhood and adolescence. Severe vitamin D deficiency, usually associated with 25(OH)D levels < 5.0 ng/mL, results in rickets and osteomalacia. However, these clinically overt cases of vitamin D deficiency would represent only the tip of the iceberg. The mean serum concentrations of 25(OH)D reported in children and adolescents from Delhi were 11.8 ± 7.2 ng/mL and 13.8 ± 6.9 mg/mL respectively, which are much lower than the recommended level of 20 ng/ml. Overall more than 85% of school children, both from government and private schools, had suboptimal levels of 25(OH)D.Studies from other parts of India (eg, Pune) show similar results[19- 22].

**Vitamin D status in pregnancy, neonates and infants :** Data on vitamin D status in pregnant and lactating women from Delhi, Lucknow and Mumbai reveal a very high prevalence of hypovitaminosis D (84-93%). One study suggested that vitamin D supplementation with vitamin D during pregnancy could result in better anthropometric indices the newborns up to nine months of follow up. Studies from India have shown significant correlation of serum 25(OH)D concentration between mother-infant pairs. Low vitamin D levels in mothers result in low vitamin D levels in cord blood and newborns. Exclusively breastfed infants continue to have low 25(OH)D levels[23-27]. One study suggested that the risk of infants suffering from moderate to severe vitamin D deficiency was three to four times greater if their mothers had levels below 10 ng/mL. It has also been shown that infants of mothers with hypovitaminosis D are at higher risk of hypocalcemic seizures. A recent study reevaluated the effect of weekly vitamin D supplementation up to six months, on mortality, morbidity and growth of low birth weight full term infants. It observed that vitamin D supplementation resulted in significant increase in SD scores for weight, length and arm circumference and decreased proportion of children with stunted growth[28-30].

Data from Rural populations:In a study from rural India (Agota village, about 80 kilometers from Delhi), vitamin D deficiency was found in 68.5 % of adults and the mean serum 25(OH)D levels were 14.5 ng/mL.In another study, rural postmenopausal women near Tirupatiwere found to have mean serum 25(OH)D levels of 14.6 ng/mL- 82 percent of them were deficient.Data from rural areas in the vicinity of Lucknow,(Uttar Pradesh) as well from Tamil Nadu confirms the widespread nature vitamin D deficiency in rural India[31-34].

Thus, there is high prevalence of vitamin D deficiency across all age groups, social strata and geographical regions in the Indian population.

## (2) What are the Optimum Circulatory 25(OH)D Levels for Bone Health?

There is lack of unanimity in international guidelines on this issue. A serum 25(OH)D level of 12.5 ng/mL is sufficient for prevention of rickets and osteomalacia. For general population, 25(OH)D values of 20 ng/mL may be considered adequate. There is no evidence to support that levels above 40 ng/mL provide any additional benefit.Therefore, 25(OH)D levels between 20-40 ng/mL are optimum for most of the population. The optimum serum 25(OH)D level for patients with bone disorders like osteoporosis is 30 ng/mL.It must be noted that many Indians may require supplementation to achieve this level[35-36].

## (3) What is the Clinical Presentation of Vitamin D Deficiency ?

Most people with low vitamin D levels do not have any symptoms, and the adverse impact of the deficiency is on bone health in the long term. Severe vitamin D deficiency, particularly when coupled with low calcium intake gives rise to numerous clinical symptoms, traditionally described, and enumerated in Tables 1 and 2.

## (4) What are the Indications for Vitamin D Testing ?

There is a consensus among expert groups that univer-

sal screening for vitamin D status is not recommended. Persons who should be tested for Vitamin D status include:

- Those with symptoms and/or signs suggestive of vitamin D deficiency, for example suspicion of osteomalacia, osteoporosis or musculoskeletal symptoms
- Those at high risk of vitamin D deficiency such as inflammatory bowel disease, bariatric surgery, those on drugs like antiepileptics, antitubercular medication, glucocorticoids, antiretroviral drugs and ketoconazole, those with chronic kidney or liver disease.
- In a resource constrained environment recommended doses may be used without estimating levels even in these situations after ruling out hypercalcemia.

## (5) How do we Treat Vitamin D Deficiency?

Cholecalciferol is the only preparation available in India. Available preparations and strengths include drops containing 400 IU/mL and 800 IU/mL, capsules containing 1000 and 2000 IU /capsule, syrup/sachets/softgel capsules containing 60,000 IU and injections containing 300,000 and 600, 000 IU. In addition, calcium preparations also contain variable amounts of vitamin D (100-1000 IU/tablet)

The active form of vitamin D (calcitriol) should not be used in routine treatment of vitamin D deficiency. Its use should be limited to hypocalcemic emergencies and resistant forms of rickets (hypophosphatemic and vitamin D dependent rickets), or in patients with kidney disease.

**Treatment option 1: Weekly doses followed by maintenance**. In 60,000 IU of vitamin D3, once a week for 8 Weeks, followed by maintenance therapy of 1500–2000 IU/Day or 60000 IU once a month.

This option is for patients with metabolic bone disease (rickets/Osteomalacia) along with calcium supplementation. This regimen can also be used sometimes in asymptomatic individuals if levels are very low (25OHD<10 ng/ml).

**Treatment Option 2: 60,000 IU to 120,000 IU per Month.** This option is for apparently healthy subjects with vitamin D deficiency can be given monthly doses of 60,000 in summer and 120,000 in winter.

**Treatment Option 3: Daily Supplementation of 1000-2000 IU.** This option is typically used in those who need of simultaneous calcium with vitamin D (elderly, low intake of calcium) and have mild deficiency/borderline 25 (OH)D levels. Can also be used for prevention /maintenance therapy with or without calcium.

**Treatment Option 4: Parenteral mega doses 0f 300,000 to 600,000 IU**. Intramuscular vitamin D can be used if there are issues with absorption of oral vitamin D-not more frequently than once in 6 months. It can also be used occasionally in cases where compliance is a challenge. Parenteral vitamin D should not be the first-line recommendation primarily due to significant inter-individual variability in absorption and risk of misuse/overdose leading to severe hypercalcemia.

Table 1 — *Clinical presentation of vitamin D deficiency in adulthood*

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|---|
| **Symptoms :** |
| • Isolated or generalized aches and pains in bones and muscles |
| • Muscle weakness |
| • Difficulty in squatting standing, walking |
| • More frequent falls |
| **Signs :** |
| • Waddling gait/Proximal muscle weakness |
| • Anteriortibial tenderness |
| • Rib cage tenderness |
| • presentation with fractures |

Table 2 — *Clinical features of rickets*

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|---|
| **Symptoms and Signs Due To Deformities** |
| **Skull :** |
| o Frontoparietal bossing |
| o Wide open anterior fontanelle (AF), delayed closure of AF |
| o Craniotabes- Ping pong ball sensation of skull bones- best felt on occiput and parietal bones away from the sutural lines. |
| **Chest :** |
| o Rachitic rosary- beading of costo-chondral junction, best examined by palpation along the long axis of the rib |
| o Harrison's groove- along the lower thoracic cage corresponding to costal attachments of diaphragm. |
| **Limbs :** |
| o Wrist widening |
| o Genuvalgum( knockknees), genuvarum ( bowlegs) |
| o Windswept deformity- combination of varus deformity of one leg and valgus deformity of the other |
| o Ankle widening, double malleolus – secondary to grooving of tibia by the tendon of tibialisanterior |
| o Pelvic deformities, coxavara |
| **Spine :** |
| o Kyphoscoliosis- seen in longer and more severe deficiency |
| **Symptoms Due To Hypocalcaemia** (more common in young infants) |
| o Apnoea |
| o Seizures |
| o Tetany |
| o Irritability |
| o Stridor, wheezing |
| o Dilated cardiomyopathy |
| **Other Features :** |
| o Hypotonia- proximal weakness, delay in gross motor milestones, protuberant abdomen, visceroptosis |
| o Delayed dentition, enamel hypoplasia, dental caries |
| o Bone pains |
| o Repeated infections due to impaired phagocytosis, repeated chest infections due to ciliary dysfunction, respiratory muscle weakness, compliant chest |

**Duration of therapy :** Once the treatment phase is over, long term- maybe lifelong- maintenance is probably required, in the doses outlined in options 2 and 3. The levels of 25(OH)D tend to fall to baseline values over a period of few weeks to months if supplementation is discontinued.

## (6) What Causes Vitamin D Toxicity ?

Improper use of pharmaceutical preparations of vi-

tamin D is the most common cause of vitamin D toxicity[37-39]. The Food and Nutrition Board recommends the tolerable upper intake level (UL) as 1000 IU daily for infants 0-6 months of age, 1500 IU daily for infants 6-12 months of age, 2500 IU daily for children 1-3 years of age, 3000 IU daily for children 4-8 years of age, and 4000 IU daily subsequently throughout life. The IOM has concluded that vitamin D below 10,000 IU/day is not usually associated with toxicity. Most of the reports of vitamin D toxicity have documented vitamin D intake of >40,000 IU/day. Hypercalcemia and vitamin D toxicity were noted in children when they received total dose of 240,000-4,500,000 IU of vitamin D.

Presentation of vitamin D toxicity usually depends on the serum calcium level. Patients with mild or moderate hypercalcemia are usually asymptomatic. The usual symptoms are anorexia, nausea, weight loss, constipation, rarely acute pancreatitis, polyuria/polydipsia, dehydration, confusion or coma. Vitamin D toxicity should be strongly suspected clinically in patients who are being treated with pharmacological dosages of vitamin D. It can be life threatening if not treated promptly. The characteristic laboratory findings of vitamin D intoxication are high serum and urinary calcium level, normal or high serum phosphate level, low parathormone and high vitamin D levels. The final diagnosis of vitamin D intoxication is made by determining the serum 25(OH)D level.Risk factors for vitamin D toxicity include extremes of ages, concurrent use of thiazide, impaired renal function and coexisting disorders such as sarcoidosis and tuberculosis.

People with asymptomatic vitamin D deficiency can be managed with maintenance dose with negligible risk of vitamin D toxicity.Parenteral preparations of vitamin D should be used only in cases with documented evidence of malabsorption.

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