Review Article

Vitamin D deficiency in India

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Abstract

Vitamin D is a fat-soluble vitamin playing a vital role in human physiology. Vitamin D deficiency is prevalent worldwide. This deficiency has many consequences which are still being explored, apart from the well-known skeletal complications. With this review, we aim to summarize the existing literature on Vitamin D status in India and understand the enormity of the problem. The prevalence of Vitamin D deficiency ranged from 40% to 99%, with most of the studies reporting a prevalence of 80%–90%. It was prevalent in all the age groups and high-risk groups alike. With the consequences of Vitamin D deficiency, namely, autoimmune diseases, cardiovascular diseases, cancer, and tuberculosis being explored, we can imagine the burden it would cause in our country. We need to create awareness among the public and healthcare providers about the importance of Vitamin D and the consequences of deficiency. Our Indian diet generally fails to satisfy the daily requirement of Vitamin D for a normal adult. This stresses on the need for fortifying various food with Vitamin D, through the national programs. This silent epidemic should be addressed appropriately with concrete public health action.

Keywords: Fortification, India, prevalence, Vitamin D deficiency

Introduction

Vitamin D is a fat-soluble vitamin, known for its antirachitic activity.[1] Calciferols are a group of lipid-soluble compounds with a 4-ringed cholesterol backbone and refer to both, Vitamin D3, i.e., cholecalciferol and Vitamin D2, i.e., ergocalciferol.[2] Vitamin D, in general, refers to Vitamin D3. Vitamin D can be synthesized endogenously. About 90% of the required Vitamin D is synthesized in the skin under sun exposure.[3]

It is needed for the maintenance of normal blood levels of calcium and phosphate that are required for normal mineralization of bone, muscle contraction, nerve conduction, and general cellular function in all cells of the body. It is also found to be important for immune function, for inflammation, cell proliferation, and differentiation.[3,4]

The active form of Vitamin D stimulates the absorption of calcium in the duodenum and increases calcium influx in distal tubules of kidney through nuclear Vitamin D receptor (VDR); latter is specifically regulated by parathormone level.[5]

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Sources of Vitamin D3

The major source of Vitamin D is the endogenous synthesis in skin on exposure to sunlight, namely, ultraviolet B (UV-B) radiation of wavelength 290–320 nm. Main dietary sources are fish, fortified food, and supplements. Vegetables and grains are poor sources.

Synthesis of vitamin in skin on exposure to UV-B is also affected by latitude, solar zenith angle, atmospheric pollution, ozone layer, and melanin pigmentation.[6]

Metabolism

In the skin, ultraviolet light catalyzes conversion of 7-dehydrocholesterol to Vitamin D3, which is released into the bloodstream, in bound form (along with Vitamin D-binding protein).[3,4,7]

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From the blood, it reaches liver to form 25-hydroxyvitamin D(25(OH)D). This is followed by formation of 1, 25-dihydroxyvitamin D, the most active form of Vitamin D in the kidney by hydroxylation and in some other tissues in which the mechanism is unclear.

Formation of 1, 25 dihydroxyvitamin D, is the key step in regulating Vitamin D metabolism, which is increased by low serum phosphate concentrations and low serum calcium, mediated by parathyroid hormone. Cellular receptors for active form of Vitamin D are found in intestine, bone, and in many other tissues also.

25(OH)D is the most useful measure and reflects the Vitamin D status in the body because the level depends on the available and circulating Vitamin D.[8] The level of 1, 25 dihydroxyvitamin D is also a direct measure for assessing Vitamin D status; however, it is not used because of its regulation by calcium, phosphate, and parathyroid hormone concentrations. The half-life of 1, 25 dihydroxyvitamin D, calciferol, and 25(OH)D are 4 h, 24 h, and 3 weeks, respectively.

Clinical manifestation of rickets occurs only when there is severe Vitamin D deficiency. The sunlight exposure can be the most important determinant of 25(OH)D concentrations. Seasonal variation should be considered as there is difference in summer and winter season.

Vitamin D Status in Relation to 25-Hydroxyvitamin D Levels

Adequate levels of serum 25(OH) D is essential to maintain the skeletal and extraskeletal physiologic effects. The threshold levels of serum 25(OH) D required to optimize its effects may not be the same in the various target organs. According to the classification given by the US Endocrine Society, <20 ng/mL of serum 25(OH) D with consequent and consistent elevation of parathyroid hormone and a decrease in intestinal calcium absorption is considered to be Vitamin D deficiency.[9] The diagnostic cutoffs of levels of serum Vitamin D are indicated in Table 1.[9]

Desirable and safe range of serum 25(OH) D level would be 30–100 ng/mL as at serum 25(OH) D levels of 30 ng/mL intestinal calcium absorption reaches its peak, and PTH levels continue to fall until this level of 25(OH) D is attained.[6,10]

Table 1: Diagnostic cut-offs of levels of serum Vitamin D

Vitamin D status	The serum level of Vitamin D in ng/ml
Deficiency	<20
Insufficiency	21-29
Sufficiency	>30
Toxicity	>150

Magnitude of Vitamin D Deficiency in India

The prevalence of Vitamin D deficiency is reported worldwide, both in sunshine deficient and sunshine sufficient countries. Still, it is the most underdiagnosed and undertreated nutritional deficiency in the world.[11,12] However, various studies showed poor Vitamin D status irrespective of age, sex, and geography. As there is no standard guideline which is followed all over the world for classifying the Vitamin D status, these studies had different cutoff values for the deficiency. The vast majority of these studies used serum 25(OH) D level of <20 ng/ml as Vitamin D deficiency. Studies which used other cutoffs have been so indicated in footnotes.

The community-based Indian studies of the past decade done on apparently healthy controls reported a prevalence ranging from 50% to 94%, except for one study which reported a prevalence of 34.5% which can be due to the low cutoff. These studies which included various age groups reflect the magnitude of the problem. High prevalence was seen throughout the country[13-30] [Table 2].

Hospital-based studies showed a prevalence of Vitamin D deficiency ranging from 37% to 99%.[31-46] Studies on Vitamin D deficiency in specific disease conditions have been excluded from the study [Table 3].

A school-based study on premenarchal girls (n = 214) in Pune was conducted by Kadam *et al.* in 2011. It showed a prevalence of 34.2% of Vitamin D.[47] Another school-based study done by Kapil *et al.* in 2017 on 1222 school children aged 6–18 years in Kangra and Kullu districts of Himachal Pradesh, showed the prevalence of 81% and 80% respectively.[14] Both the studies reported the prevalence of Vitamin D deficiency based on the U. S. Endocrine Society cutoff.[9]

Causes of Vitamin D Deficiency

It is evident from the above tables that Vitamin D deficiency is quite rampant in India. Apart from low intake in diet, people with liver, kidney and skin disorders also have Vitamin D deficiency. There are many reasons for it being so common in our country.

- Increased indoor lifestyle, thereby preventing adequate exposure to sunlight. This is mainly in the urban population due to modernization.
- Pollution can hamper the synthesis of Vitamin D in the skin by UV rays[48]
- Changing food habits contribute to low dietary calcium and Vitamin D intake
- Phytates and phosphates which are present in fiber rich diet, can deplete Vitamin D stores and increase calcium requirement[49]
- Increased skin pigmentation and application of sunscreens
- Cultural practices such as the burqa and purdah system[34]
- Unspaced and unplanned pregnancies in women with dietary

Table 2: Community-based studies on prevalence of Vitamin D deficiency in India

Author, year of publication	Site of the study	Sample size	Study participants	Prevalence (%)
Suryanarayana *et al.*, 2018[13]	Hyderabad, Urban	298	≥60 years	
			Total	56.3
			Men	57.2
			Women	54.2
Kapil *et al.*, 2017[14]	Shimla, Himachal Pradesh	626	Children (6-18 years)	93
Chowdhury *et al.*, 2017[15]	Delhi	960	6-30 months	34.5*
Srimani *et al.*, 2017[16]	West Bengal	222	Rural postmenopausal women (45-70 years)	51
Misra *et al.*, 2017[17]	Ballabgarh	381	Rural women (20-60 years)	90.8
Rattan *et al.*, 2016[18]	Cuttack, Odisha	3056	30-65 years	84.9†
Gunjaliya *et al.*, 2015[19]	Ahmedabad, Gujarat	444	No specific age group/gender preference	93.3‡
Bachhel *et al.*, 2015[20]	Punjab	150	17-68 years	90§
Marwaha *et al.*, 2014[21]	Jammu Kashmir	312	Postmenopausal women	53.4
Agrawal and Sharma, 2013[22]	Varanasi	200	Adults ≥50 years	58
Harinarayan *et al.*, 2011[23]	Tirupati	55	Reproductive female age	76.3
Marwaha *et al.*, 2011[24]	Delhi	1346	Urban adults ≥50	91.2
Sahu *et al.*, 2009[25]	Barabanki	139	Rural pregnant	74
		121	Rural female adolescent	88.6
Paul *et al.*, 2008[26]	Tirupati	150	Semi-urban postmenopausal women	50
Puri *et al.*, 2008[27]	Delhi	404	Urban female adolescents	90.8
Goswami *et al.*, 2008[28]	Agota village, Delhi	57	Rural adults	68.5
Vupputuri *et al.*, 2006[29]	Delhi	105	Urban adults	94
Harinarayan, 2005[30]	Tirupati	164	Rural postmenopausal women	82

*<10 ng/ml, †<29 ng/ml, ‡<30 ng/ml, §<25 nmol/L. All studies have used a cutoff of <20 ng/mL except the following

Table 3: Hospital-based studies on the prevalence of Vitamin D deficiency in India

Author, year of publication	Site of the study	Sample size	Study participants	Vitamin D deficiency (%)
Sofi *et al.*, 2017[31]	Delhi	224	Reproductive age, nonpregnant, nonlactating women	88
Bawaskar *et al.*, 2017[32]	Mahad, Maharashtra	640	OPD patients, no age preference	65.4
Pal *et al.*, 2016[33]	Agra	1132	Patients attending orthopedic OPD and emergency department, 21-69 years	61.2
Ajmani *et al.*, 2016[34]	Delhi	200	Burka-clad Pregnant women, 18-40 years	37.5
Shukla *et al.*, 2016[35]	Gurgaon	26346	Executive health check-up data, retrospectively	93
Sharma *et al.*, 2016[36]	New Delhi	418	Primigravida with single live pregnancy	93.5*
Kumar *et al.*, 2015[37]	Bengaluru	106	Mothers in labor	70.7
			Cord blood of newborn	83
Basu *et al.*, 2015[38]	Kolkata	310	1-16 years	52.9
Garg *et al.*, 2014[39]	Delhi	1829	Adolescents	96.9
Angurana *et al.*, 2014[40]	Chandigarh	338	3 months-12 years	40.2
Baidya *et al.*, 2012[41]	Kolkata	40	Doctors	92.5
Dasgupta *et al.*, 2012[42]	Guwahati	50	Pregnant females 20-40 years	42
Beloyartseva *et al.*, 2012[43]	Different regions in India (19 cities)	2119	Healthcare professionals (middle age adults)	71
Marwaha *et al.*, 2011[44]	Delhi	521	Pregnant women	96.3
		342	Lactating mothers	99.7
		342	EBF infants	98.8
Multani *et al.*, 2010[45]	Mumbai	214	Urban adults	87.5
Farrant *et al.*, 2009[46]	Mysore	559	Pregnant women	66.5

*<32 ng/ml. All studies have used a cutoff of <20 ng/mL except the following. EBF: Exclusive breastfeeding; OPD: Outpatient department

deficit can lead to worsening of Vitamin D status in both mother and child.

Consequences of Vitamin D Deficiency

Vitamin D deficiency results in a variety of skeletal and extraskeletal manifestations. Very few Indian studies have been published on the consequences of Vitamin D deficiency. Hence, overseas studies on this issue are cited.

Skeletal manifestations

The commonly known consequences of Vitamin D deficiency are rickets in children and osteomalacia and osteoporosis in adults. In children, it causes defective mineralization of bone

due to imbalance between calcium and phosphorous in the bone, resulting in rickets and external skeletal deformity. It also causes muscle weakness and bone pain. In adults, inadequate dietary intake of Vitamin D leads to poor absorption of calcium from diet and increased calcium resorption from the bone and kidney and reduces bone mineral density resulting in osteoporosis and osteomalacia, muscle weakness and increased risk of falls. It is theorized that Vitamin D may increase muscle strength, thereby preventing falls. Many studies have shown an association between low Vitamin D concentrations and an increased risk of fractures and falls in older adults.[50-53]

Depression

Vitamin D deficient patients took significantly longer duration for recovery than nondeficient persons. It signifies the importance of treating hypovitaminosis D for the effective management of depression.[54]

Parkinson's disease

Vitamin D insufficiency was seen in patients with Parkinson's disease (PD). Evidence suggests VDR as a genetic risk factor for PD, thereby underlining the potential importance of Vitamin D in PD. As Vitamin D status is a modifiable factor, Vitamin D acts as a potential preventive/therapeutic strategy for this disorder. However, there is a need for further studies on VDR as well as its interaction with Vitamin D levels in PD.[55-57]

Suicide

Lower 25(OH) D levels are associated with an increased risk for suicide.[58]

Infectious disease

Infectious disease such as tuberculosis, upper respiratory tract infections of viral origin, i.e., influenza is seen in individuals with Vitamin D deficiency.[59-61]

Autoimmune diseases

Vitamin D is a potent modulator of immune system, and it is involved in regulating cell proliferation and differentiation.[62-64] It was shown in a case–control study that Vitamin D deficiency was considerably higher in Type 1 diabetic (91%) children when compared to nondiabetic (85%) children. Supplementation of Vitamin D resulted in 30% reduction in the risk of developing Type 1 diabetes mellitus. Lower levels of Vitamin D were found to be associated with rheumatoid arthritis.[50]

Cancer

Vitamin D has a protective role in certain tissues by promoting apoptosis and inhibiting angiogenesis. Low level of Vitamin D in stores, such as lung, breast, colorectal, prostate, ovary, pancreas and esophagus, are associated with cancers. Vitamin D decreases cell proliferation and increases cell differentiation. It stops the growth of new blood vessels and has significant anti-inflammatory effects.[65-67]

Heart disease

In the Framingham Heart Study, patients with low Vitamin D concentrations (<15 ng/Ml) had a 60% higher risk of heart disease (through the renin-angiotensin hormone system) than those with higher concentrations. Severe Vitamin D deficiency is seen in patients with acute myocardial infarction and it is associated with many of its risk factors.[68,69]

Type 2 diabetes mellitus

Vitamin D deficiency has been associated with increased risk of type 2 diabetes mellitus, insulin resistance, and decreased insulin production, and hence, it has been associated with syndrome X. A trial of nondiabetic patients aged 65 years and older found that those who received 700 IU of Vitamin D (plus calcium) had a smaller rise in fasting plasma glucose over 3 years versus those who received placebo. Evidence reveals that Vitamin D reduces the risk of progression and development of type 2 diabetes mellitus.[70-72]

Obesity

Levels of 25(OH) D are inversely associated with body mass index, waist circumference, and body fat but are positively associated with age, lean body mass, and Vitamin D intake.[73-75]

The Way Forward

Although we are aware of the causes of Vitamin D deficiency, we are not able to prevent it to a large extent. India being a tropical country has adequate sunshine. Most of the Indian population live in areas with adequate sunlight throughout the year and are expected to have adequate Vitamin D. Contrary to this, the prevalence of Vitamin D deficiency is high in India.

This is due to the skin complexion, poor exposure to sunlight, sunscreen creams, Indian dietary habits and lower intake of Vitamin D fortified foods.[48] Indians are mostly vegetarians and Vitamin D rich foods are of animal origin. All the above-mentioned factors can be a cause in urban population. However, the rural population, who by the virtue of their occupation have sufficient sunlight exposure, too have low Vitamin D levels. This can be due to the high phytate and low calcium diet they consume. Phytate rich diet is known to reduce the intestinal absorption of calcium. Hence, low dietary calcium increases the catabolism of 25(OH) D and increases the inactive metabolites with the resultant reduction in 25(OH)D concentrations.[49,76]

This calls for appropriate and concrete public health action. The following measures can be taken to reduce the burden of the disease.

- Food fortification with Vitamin D is the best option to address this issue. All grades of milk can be fortified. Oil and milk products such as curd, yogurt, infant formulas, and butter can be fortified with Vitamin D. Widely consumed food items such as atta, maida, and rice flour can also be

fortified. Vitamin D fortified food items should be made available to the public at minimal cost and be included in the public distribution system. Effective legislation is required to ensure this. Sustained political and administrative will and support are a must for the development of a fortification program. In India, Vanaspati (dalda) is fortified with 200 IU of Vitamin D per 100 g. Milk products of certain brand are also fortified with Vitamin D

- Educational programs are a must to create awareness about Vitamin D deficiency as it is the most underdiagnosed and undertreated nutritional disease. Both physicians and the public should be made aware of its implications. To develop, launch and sustain such a program, adequate investment in the form of time, money, and effort is required
- Vitamin D supplements of good quality should be made available at PHC level for the population at risk, i.e., pregnant women, lactating women, children, and elderly
- Revision of RDA for Vitamin D by ICMR is needed as it is less compared to other guidelines
- School going children can be benefitted from the following: educating them about the need for Vitamin D sufficiency and healthy lifestyle; providing Vitamin D fortified foods at mid-day meals in schools; daily physical exercise which would ensure exposure to sunlight.
- Testing facilities for Vitamin D levels should be made affordable and accessible to those at high risk of clinical Vitamin D deficiency (pregnant women, children, elderly especially women), as mass screening is not feasible
- Government should support research groups to study and monitor the impact of supplementation programs and fortification strategies.

Conclusion

In India, Vitamin D deficiency is widespread. However, the clinically diagnosed cases represent only the tip of the iceberg. With the knowledge of the multiple consequences, it can lead to; we can imagine the burden, this silent epidemic would cause the development of the country. Vitamin D deficiency needs to be addressed with due attention and strong action.

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Conflicts of interest

There are no conflicts of interest.

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