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Vitamin D Deficiency in Indian Population- Myth or Reality

Rateesh Sareen*[1], Akanksha Dutt[2], G N Gupta[3]

[1]Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital cum Research Center, Jaipur, India

[2]Department of Anesthesia, Bhagwan Mahaveer Cancer Hospital & Research Center, Jaipur, India

[3]Department of Pathology, Santokba Durlabhji Memorial Hospital cum Research Center, Jaipur, India

***Corresponding author:** Rateesh Sareen, Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital cum Research Center, Jaipur, India. Tel: +91-9414216471; Email: drrateeshsareen@yahoo.co.in

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Abstract

There has been spurt in the diagnosis of Vitamin D deficiency cases in the country. As there are lacks of data for reference ranges for Indian population for Vitamin D levels, many times clinicians face the dilemma of treating patients who have ample sunlight exposure and have low Vitamin D levels. There is also lack of guidelines for fortification of food in the country as well as testing methodologies. All these factors may contribute to over enthusiastic treatment of patients causing hyper vitamin sis D. There is immediate need for multidisciplinary approach for diagnosis, treatment curative and preventive strategies so that a balance is maintained among those who genuinely require Vitamin D supplementation and those who do not need.

Vitamin D the fat-soluble Vitamin is crucial for calcium homeostasis and its metabolites is an integral part of Calcium – Vitamin D- Parathyroid hormone endocrine axis. [1] Vitamin D is the only Vitamin that can be synthesized in skin upon exposure to sunlight [2,3]. It is estimated that nearly 1 billion people worldwide have vitamin D deficiency [2]. As per the International osteoporosis foundation regarding the prevalence of Vitamin D deficiency the figures stand at 96% in neonates, 95% in healthy school girls, 78% in healthy hospital staff and 84% in pregnant women. [4] In a study from South India by Harinarayan, et al 76% of women of reproductive age group and 70% of post menopausal women were found to be Vitamin D deficient [5]. Similar studies from luck now have shown that 84.3% urban and 83.6% rural women suffer from Vitamin D deficiency [6] whereas from Kashmir nearly 58.5% of adults were found to be Vitamin D deficient [7].

There are mainly three sources of Vitamin D-sunshine exposure, dietary intake and pharmaceutical supplementation. Very few foods in nature contain vitamin D. The flesh of fatty fish (such as salmon, tuna, and mackerel) and fish liver oils are among the best sources. Small amounts of vitamin D are found in beef liver, cheese, and egg yolks. Vitamin D in these foods is primarily in the form of vitamin D3 and its metabolite 25(OH) D^3. Some mushrooms provide vitamin D2 in variable amounts [2]. Vitamin D (D representing D2 OR D3 or both) after ingestion is absorbed from intestine and transported by chylomicrons into lymphatic system and subsequently in venous blood. Vitamin D synthesized in skin or the one absorbed from diet is biologically inert. It undergoes hydroxylation in liver by Vitamin D25 hydroxylase to 25(OH)D. [2,3,8] It is then further hydroxylated in kidneys by 25(OH) D-1α OHase (CYP27B1) to form Vit D 1, $25(OH)_2D$ (active Vit D).

$1,25(OH)_2D$ cats on nuclear receptors of cells and stimulates intestinal calcium absorption [9]. The active Vitamin D stimulates osteoblasts to induce immature monocytes to become mature osteoclasts which dissolve the matrix and mobilize calcium and other minerals from skeleton, further stimulates calcium reabsorption from glomerular filtrate [2,10]. $1,25(OH)_2D$ functions include cellular proliferation, stimulation of insulin production, inhibition of rennin production and stimulation of catechecolamine production [11-13]. It enhances the expression of $25(OH)_2D$ Vitamin D-24 OHase (CYP24R) to metabolize $25(OH)_2D$ and $1,25(OH)_2D$ into water soluble inactive forms.

Vitamin D levels less than 20ng/ml are considered to be deficient state as per the recommendations of Institute of Medicine (IOM) [14-18]. As very few foods contain naturally occurring Vitamin D, the major source of Vitamin D for children and adults remains sun exposure. The use of sunscreen with sun protection factor of 30 reduces Vitamin D synthesis in the skin by more than 95% [19]. Dark skin tone have natural sun protection and require 3 to 5 times longer exposure to make same amount of Vitamin D as a person of white skin tone [20,21]. Vitamin D deficiency in India has been defined as levels less than 20ng/ml and insufficiency for levels between 21-29ng/ml [22].

The geographical of India is located between 8.4°and 37.6°north latitude with most of the population receiving ample sunshine throughout the year. As per the World Health Organization (WHO) definition of Vitamin D deficient country considering the latitudinal location India should have been a Vitamin D deficiency resistant country but unfortunately it is not. In spite of the abundant sunshine available naturally to the habitants there is a growing Vitamin D deficient population. We are all aware of the fact that sunlight is responsible for endogenous production of Vitamin D in the skin from 7-dihydrocholesterol present in subcutaneous fat. Adequate Vitamin D and Calcium are needed to maintain peak bone mass and their deficiency causes low bone mass, muscle weakness and thereby increased risk of fractures. If not corrected on time they lead to the development of secondary hyperparathyroidism leading to increased bone turnover and osteoporotic fractures [23,24]. Levels above 30 ng/ml may have additional health benefits in reducing common cancers. However, the current recommendations do not advocate supplementation for these non-calcemic benefits. Vitamin D is also linked to the pathogenesis of Crohn's disease, multiple sclerosis, rheumatoid arthritis, Diabetes Mellitus type II and increased risk for cancer in breast, colon, ovary and prostate [2].

The most common causes for Vitamin D deficiency in India include -Dietary changes and switch over to diets that are low in dietary Calcium and Vitamin D ,Increase consumption of dietary fibers that contain phosphate and phytates which eventually deplete Vitamin D stores [25], genetic factors like increased 25(OH) D-24 Hydroxylase enzyme activity which degrades 25(OH)D to inactive form [26], increased air pollution that hamper Ultraviolet rays to adequately synthesize Vitamin D in skin [27], reduced sun exposure in urban areas and unplanned pregnancies responsible for Vitamin D deficiency in mothers and neonates.

Obesity is associated with Vitamin D deficiency such as Vitamin D levels follow inverse association with Body Mass Index (BMI) greater than 30 kg/m^2.other causes of Vitamin D deficiency include fat malabsorbtion, patients of nephritic syndrome that loose 25(OH)D bound to the Vitamin D binding protein in urine. [2] Anticonvulsants and anti-retroviral drugs enhance catabolism of 25(OH)D and1,25$(OH)_2$D leading to Vitamin D deficiency [28].

Vitanin D deficiency causes decrease absorption of intestinal calcium and phosphorous from diet leading to increased PTH levels [29,30]. The secondary hyperthyroidism maintains serum calcium in normal range by mobilizing calcium from the skeleton and wasting of phosphorous from kidney. PTH mediated osteoclastic activity causes bone weakness resulting in osteopenia and osteoporosis. The excessive loss of phosphate in urine causes mineralization defect in skeleton [31]. In children it manifests as Rickets and in adults with closed epiphysieal plates it leads to osteomalachia.

The major source of Vitamin D is skin exposure to sunlight, it is interesting to note that sun exposure induced Vitamin D has a longer half-life than ingested form [32]. The skin production of Vitamin D is adversely affected by skin pigmentation and topical application of sunscreen [19,20]. An alteration in zenith angle of sun caused by change in latitude, season or time of day influences skin production of Vitamin D3 [2,3,8]. The naturally occurring food which are rich sources of Vitamin D include- cod liver oil, salmon fish, tuna, suitakre mushroom and egg yolk.

25(OH)D is the major circulating form of Vitamin D with half life of 2-3 weeks and is the best indicator to monitor Vitamin D status [33-36]. 1,25$(OH)_2$D on the other hand circulates at 1000 times lower concentration than 25(OH)D with a half life of 4 hours only and is therefore not useful for monitoring Vitamin D status of patients. Multiple methodologies for 25(OH)D measurement exist including RIA, HPLC and Tandem Mass spectroscopy [2,35]. All the current methods are adequate. Food fortification is a debatable issue in India although world over it has shown good results [37]. The lack of data on dietary Calcium intake and sun exposure limits the application of generalized fortification in India [38].

The recommended dietary intake of Vitamin D for children aged 0-1 year is 400 IU/d (1 IU=25ng), adults 19-50 year is at least 600 IU/d, for 50-70-year 600IU/d, for 70+ year adults 800IU/d and for pregnant & lactating women 600 IU/d [39].

Major source of Vitamin D is unprotected sun exposure however concerns about melanoma and other types of skin cancers necessitate avoidance of excessive exposure to midday sun. there is plethora of evidence to suggest Vitamin D supplementation especially suggest Vitamin D supplementation especially for people living above 330 latitudes [40]. The evidence suggests that children and adults should maintain a blood level of 25(OH)D above 20 ng/ml to prevent rickets and osteomalachia.

Apart from all the above-mentioned causes of Vitamin D deficiency we also need to ponder over the fact that the reference ranges that define Vitamin D deficiency in Indian population are either provided by the kit manufacturer or from international standards. Indian population is diverse and unfortunately Indian data published have largely overlooked the issue of defining reference range as per Indian population. The application of reference range for Vitamin D levels derived from western population might not be suitable to Indian population because of the latitudinal geographic location, abundant sunshine and dietary eating habits. It is recommended that assessment of Vitamin D should be performed by Tandem Mass Spectrometry (TMS) but most of the testing facilities perform testing by ELISA, Chemiluminescence, and radioimmunoassay [13]. All these above-mentioned factors suggest that one must not overenthusiastically over treat Vitamin D deficiency in Indian population particularly without monitoring Vitamin D levels and ultimately culminating in hypervitaminosis D.

Moreover, currently there are no regulations for food fortification and Indian guidelines for evaluation, treatment and prevention of Vitamin D deficiency in adult population.

One of the reasonable safe approach can be to inculcate the useful ness of sun exposure in children, toddlers and teenagers by imparting in curriculum mandatory outdoor lunch hours during day time, a 'Vitamin D boost hour'. At the same time, it warrants clinicians for interpreting the results of Vitamin D assays with caution without over treating the patients. A multidimensional approach is needed in the country at various levels by: redefining the cut offs for Vitamin D levels in Indian population, dietary Vitamin D & Calcium supplementation, life style changes, education of masses, public health policy for fortification to bring down the prevalence of Vitamin D deficiency in India as always, 'Prevention is better than cure'.

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