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Indian J Community Med. 2015 Oct-Dec; 40(4): 215–217. doi: 10.4103/0970-0218.164378: 10.4103/0970-0218.164378 PMCID: PMC4581139 PMID: <u>26435592</u>

Vitamin D Deficiency: Is The Pandemic for Real?

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In the recent years, vitamin D has generated a keen interest among clinicians, public health specialists, and researchers. The publication output, including research studies, related to vitamin D has trebled in the last decade. The prevalence of vitamin D deficiency is reportedly increasing, and assay of serum 25-hydroxy vitamin D [25(OH)D] is one of the most frequently ordered nutrition-related blood investigations. The number of vitamin D preparations is also increasing day by day, with manufacturers coming out with new formulations and combinations since large number of people have been found to be having low blood 25(OH)D levels.

Vitamin D, traditionally labeled the "sunshine vitamin" is produced endogenously in the skin on exposure to ultraviolet B radiation. Very few food products – such as dairy products, eggs, fish, and cod liver oil – contain natural vitamin D. Foods fortified with vitamin D are the main sources of dietary vitamin D in some industrialized countries but such programs are practically nonexistent in most low- and middle-income countries. In the absence of food fortification programs, a majority of the populations in the world solely depends on the sun for their vitamin D nutriture. However, sunlight alone is not considered a reliable or adequate source as production of vitamin D in the skin minimizes in winters, and among those living at high latitudes (above 35°). Dark skin color exacerbates the problem of low endogenous vitamin D production. Religious body-covering habits, staying indoors for the majority of daytime (particularly children, women, and the elderly), and lack of open spaces and direct access to sunlight in high human density habitations have resulted in the high prevalence of vitamin D deficiency, even in countries close to the equator where sunshine is abundant. With this background, vitamin D can easily be classified as a "problem nutrient" with the potential of high risk of its deficiency in a large proportion of the human population.

Vitamin D deficiency, as defined by low levels of serum 25(OH)D, is widespread throughout the world irrespective of age, gender, country of origin, latitude of residence, or dietary practices. High rates of biochemical vitamin D deficiency or insufficiency among healthy individuals have been reported in large-scale studies from all parts of the world - the United States, (1) Canada, (2) South America, (3) Europe, (4) Australia, (5) the Middle East, (6) South Asia, (7) and Africa. (8) Severe vitamin D deficiency is common in

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China, India, South America, and the Middle East. In India, studies from different parts of the country have reported a prevalence of vitamin D deficiency varying from 30% to $100\%.(\underline{7,9,10})$ The cutoff to define vitamin D deficiency, however, varies between the studies. Studies utilizing higher cutoffs (75 nmol/L or 30 ng/mL) to diagnose vitamin D deficiency have reported a near-universal presence of vitamin D deficiency among diverse age groups, including pregnant and lactating women, newborns, adolescents, and healthy professionals.(<u>10</u>)

When a nutrient deficiency is found to be near-universal, a key question that emerges is whether the basis of diagnosis of the deficiency is valid and whether there are any adverse health consequences if the deficiency is not corrected. Traditionally, vitamin D has been known to be relevant only for bone health that included its role in calcium homeostasis. In the first half of the twentieth century, the recommended dietary intake of vitamin D was based only on the basis of preventing overt skeletal deformities, and a level of 100 IU (2.5 µg) of vitamin D/day was considered sufficient.(11) When assays of serum 25(OH)D were developed in the 1970s, recommendations were upgraded so as to maintain the level of 25(OH)D within the normal range (about 25-60 nmol/L) detected in healthy adults. The off-cited Institute of Medicine (IOM) recommendations (1997) specified a serum 25(OH)D concentration of 27.5 nmol/L (11 ng/mL) and above as an indicator of vitamin D adequacy from birth through 18 years of age, and a concentration of 30 nmol/L (12 ng/mL) and above as an indicator of vitamin D adequacy for adults.(12) Over the last two decades, observational studies have linked the status of vitamin D to a diverse range of health conditions such as diabetes, cancer, coronary artery disease, infections, immunity, autoimmune diseases, and respiratory diseases.(11) Consequently, some societies have upgraded the recommended cutoff level of 25(OH)D as well as the recommended dietary intake of vitamin D so that its potential of benefit in other health conditions could be exploited while some others have deferred from doing so because of lack of good-quality evidence on these benefits.(11,13,14,15,16,17) The higher cutoffs recommended in some of these guidelines are also based on the plateauing effect on the levels of parathyroid hormone (PTH) with increasing levels of serum 25(OH)D. The functional significance of these higher cutoffs is unknown, and these cutoffs are likely to overestimate the burden of vitamin D deficiency in large populations leading to unwarranted use of vitamin D supplements. In fact, some individuals or agencies have recommended such a high level that almost every human being on the earth will be classified as having insufficient vitamin D nutriture.(18) These high cutoff levels cannot be physiologically met by diet or sun exposure alone, and will require a substantial dose of vitamin D supplements throughout life. On the other hand, the IOM (2010) committee has still based its recommendations (deficiency <30nmol/L, insufficiency 30-50 nmol/L, and sufficiency 50-75 nmol/L) on the indicators of bone health as a review of plethora of the literature did not suggest any additional evidence of benefit beyond the recommended levels.(13) The committee recommended that "given the concern about high serum 25(OH)D levels as well as the desirability of avoiding misclassification of vitamin D deficiency, there is a critical public health and clinical practice need for consensus cut points for serum 25(OH)D."(13) It is apparent that raising the level of vitamin D beyond the cutoffs of deficiency/sufficiency (30–50 nmol/L) is inappropriate unless there is a clear benefit (without any risk) of this strategy.

From the foregoing, it is apparent that much of the reported high prevalence of vitamin D deficiency/insufficiency in healthy populations of the world is artificial, created by unjustified high cutoff values of serum 25(OH)D. Most of the individuals diagnosed as vitamin D-deficient based on these criteria lack any marker of ill health, including bone mineral deficiency. In developing countries, an assay of 25(OH)D is presently available only to a small number of high-income people who get it done on the recommendation of the physicians or on routine screening. The use of high cutoff values of the normal range by the laboratories creates unnecessary panic leading to potentially irrational intervention in the form of high-dose supplementation with medicinal vitamin D, often posing a risk of toxicity.(<u>19,20</u>) Screening of healthy populations utilizing these cutoffs leads to higher estimations of the prevalence of deficiency among the population, and may lead to unjustified public health policies. Nevertheless, in most of the low- and middle-income countries, diseases caused by vitamin D deficiency - including rickets and

osteomalacia - are very common. The priority from a public health perspective should be to ensure that the risk of clinical vitamin deficiency is minimized through educational- and food-based strategies to improve the vitamin D status of populations at large. Screening of healthy individuals for vitamin D deficiency should be discouraged. Strategies, including fortification of foods with vitamin D, should be evaluated and implemented so as to bridge the gap between current and recommended intakes of vitamin D. Health consequences of raising the vitamin D status beyond what is required to promote bone health are presently controversial, and should not form the basis of public health policies.

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