International Journal of Innovative Research and Advanced Studies (IJIRAS)
Volume 4 Issue 3, March 2017

ISSN: 2394-4404

Vitamin D Deficiency And Its Related Health Effects: An Indian Perspective

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Abstract: ***Vitamin D is a fat soluble vitamin that can be obtained from dietary sources and through endogenous production in the skin following exposure to ultraviolet (UV)-B radiation from the sun. This vitamin D, along with any vitamin D obtained through the diet, is converted into 25(OH)D in the liver. The principal causes of low vitamin D levels are limited cutaneous synthesis due to inadequate sun exposure (sunscreen use, institutionalized or homebound status) or combined with low dietary intake of vitamin D rich foods including fortified milk. Vitamin D insufficiency affects almost 50% of the population worldwide. In India, Vitamin D deficiency was presumed to be rare. In reality, India, despite of being a tropical country is badly affected by hypovitaminosis. Studies suggest that the prevalence of vitamin D deficiency is 80% in women and 50% in men. Apart from precipitating calcium deficiency disorders, latest research has shown Vitamin D deficiency to be responsible for various disease conditions like type-2 diabetes, heart disease, influenza, depression. Indian food has minimum amount of vitamin D and thus modification of diet and fortification of food stuff can provide a possible solution to this public health problem.***

I. INTRODUCTION

Vitamin D is a fat soluble vitamin that has mainly two types - D2 (ergocalciferol) and D3 (cholecalciferol).

While vitamin D can be obtained from dietary sources (D2 isoform) the biggest contribution to an individual's circulating levels of vitamin D, in most countries, is through endogenous production in the skin following exposure to ultraviolet(UV)-B radiation from the sun. Exposure to UV-B (wavelength ~290–315 nm) converts 7-dehyrdrocholestrol in the skin into pre-vitamin D (D3 isoform) which spontaneously isomerizes into vitamin D. This vitamin D, along with any vitamin D obtained through the diet, is converted into 25(OH)D in the liver.

25-Hydroxyvitamin D is the most abundant circulating metabolite of vitamin D. Almost all vitamin D produced in the skin or obtained from food or supplements is converted in the liver to 25 OHD1. Moreover, the serum half-life of 25-OHD is almost 2–3 weeks. Thus, serum 25-OHD level is a sensitive index of vitamin D status. The development of radio assays for 25-OHD 40 years ago has made it possible to measure serum 25-OHD concentration and to define an individual's vitamin D status. Early studies indicated that serum 25-OHD under 5–8 ng/ml is invariably associated with rickets in children and with osteomalacia in adults, and levels under 12–15 ng/ ml are usually associated with secondary hyperparathyroidism or subtle osteomalacia. WHO has defined vitamin D insufficiency as level of serum 25-OHD less than 20 ng/ml. However, many studies have defined vitamin D deficiency as serum 25OHD level below 20 ng/ml and vitamin D insufficiency as levels 20-30 ng/ml.

II. CAUSES OF VITAMIN D DEFICIENCY

The principal causes of low vitamin D levels are limited cutaneous synthesis due to inadequate sun exposure (sunscreen use, institutionalized or homebound status) or combined with low dietary intake of vitamin D rich foods including fortified milk. Other risk factors include aging,

pigmented skin, smoking, obesity, air pollution, abnormal intestinal function, malabsorption, or reduced synthesis or increased degradation of vitamin D due to chronic liver or renal disease. Vitamin D inadequacy could also be affected by the ethnic and culture factors. Asian women often have a lactase deficiency and lower fortified milk consumption, and often avoid the sun exposure and skin pigmentation by using sun-screening cosmetics and parasols, which increase their risk of vitamin D insufficiency. Urbanization is also an important risk factor for an inadequate vitamin D status, which often leads to insufficient outdoor activities and is associated with highly polluted air in some cities.

Apart from vitamin D, a mineral that is equally important in bone health and vitamin D metabolism is Calcium. A study showed that the daily dietary calcium intake of both the urban and rural populations in India was low compared with the recommended dietary allowances issued by the Indian Council of Medical Research. The factor that aggravates calcium absorption is consumption of phytates that seems to be higher in this population. Also, low calcium intake increases Para Thyroid Hormone (PTH) which increases conversion of 25(OH)D to 1,25-dihydroxyvitamin D which, in turn, stimulates the intestinal calcium absorption. In addition, 1,25-dihydroxyvitamin D induces its own destruction by increasing 24-hydroxylase. This is the likely explanation for the low 25(OH)D concentrations in persons on a high-phytate or a low calcium diet. The discussion of Calcium further is beyond the scope of this review.

In a nutshell, Older age, female sex, higher latitude, winter season, darker skin pigmentation, less sunlight exposure, dietary habits (foods poor in vitamin D and Calcium, richer in phytates), and absence of vitamin D fortification are the main factors that are significantly associated with lower 25(OH)D levels.

III. BURDEN OF VITAMIN D DEFICIENCY IN THE WORLD

Vitamin D insufficiency affects almost 50% of the population worldwide. An estimated 1 billion people across all ethnicities and age groups, have a vitamin D deficiency (VDD). This pandemic of hypovitaminosis D can be attributed to lifestyle (for example, reduced outdoor activities) and environmental (for example, air pollution) factors that reduce exposure to sunlight, which is required for ultraviolet-B (UVB)-induced vitamin D production in the skin. High prevalence of vitamin D insufficiency is a particularly important public health issue because hypovitaminosis D is an independent risk factor for total mortality in the general population.

IV. BURDEN OF VITAMIN D DEFICIENCY IN INDIA

Data on the vitamin D status of the population in a tropical country such as India have seldom been documented. Vitamin D deficiency was presumed to be rare.

In reality, India, despite of being a tropical country is badly affected by hypovitaminosis. It is intriguing as to why vitamin D deficiency is such a common problem among Indians in spite of abundant sunshine.[9] None of the age group is immune from this pandemic. Studies suggest that the prevalence of vitamin D deficiency is 80% in women[10]and 50% in men.

There are few data from India about the prevalence of hypovitaminosis D in pregnancy and in the newborn. The increasing prevalence of disorders linked to vitamin D deficiency is reflected in the several hundred children with rickets treated each year. However, these children represent a small proportion of the individuals with a suboptimal vitamin D status in the population.

A study done by Khadilkar in Pune showed that the vitamin D level in adolescents in Pune is similar to that of adolescents in Manchester (UK). This was probably because it was seen that Pune girls had very low calcium intake and a high fiber diet which may have led to a depletion of body stores of vitamin D. Other reasons may be genetic factors. For example, South Asians have increased 25(OH)D-24-hydroxylase, which degrades 25(OH)D to inactive metabolites. Another study done in Pune on pre and post-menopausal women reveals that the prevalence of Vitamin D deficiency was 54.5% pre and 41.8% post-menopausal women.

A study by Marwaha RK etal done in Delhi on 1346 healthy subjects showed that 91.2% had vitamin D deficiency (25 OHD level<20ng/ml) and another 6.8% had vitamin D insufficiency (25 OHD level=20-30ng/ml).

It is expected that since rural people are more exposed to sunlight so they should be less deficient in vitamin D and should have better bone health. Contrarily, a study done by Sahu et al on rural girls and pregnant women had contradictory findings. The age-adjusted community prevalence of vitamin D deficiency (25OHD < 50 nmol/l) in adolescent girls was 88.6% and in pregnant women was 74%. Although for rural subjects more body surface area is exposed to sunlight for longer durations by virtue of their occupation, the poor quality of diet impedes the bone homeostasis significantly.

V. VARIOUS HEALTH EFFECTS RELATED TO VITAMIN D DEFICIENCY

The importance of vitamin D for bone health and the prevention of rickets is well-established, a study by Harinarayan et al has shown association between bone mineral density and Vitamin D level; however, observational data suggest that low levels are also associated with increased incidence of chronic diseases.

Latest research has shown Vitamin D deficiency to be responsible for various disease conditions like type-2 diabetes, heart disease, influenza, depression. Vitamin D receptors have a broad tissue distribution that includes vascular smooth muscle, endothelium, and cardiomyocytes thus the research has been focusing on the effect of vitamin D on various functions of the body.

Low levels of vitamin D have also been implicated for increase in all-cause mortality. It is also possible that the associations between vitamin D and mortality seen in

observational studies are due to confounding with, for example, obesity or reduced physical activity causing both reduced vitamin D and negative health outcomes.

It has long been recognized that one of the key non-skeletal effects of vitamin D is to modulate the immune response to pathogens. As part of the innate immune response, 1, 25(OH) 2D induces the production of antimicrobial peptides including cathelicidin and β-defensin 2. Cathelicidins and defensins have a broad spectrum of antimicrobial activity and kill bacteria by disruption of microbial membranes. In addition, they also act as chemo attractants for other inflammatory cells and contribute to wound repair. In addition to its immediate impact on the production of antimicrobial peptides vitamin D has been implicated in modifying the signaling pathways that bind respiratory viruses. For example, 1,25-dihydroxyvitamin D decreases the expression of ICAM-1, the major cellular receptor for human rhinovirus in human umbilical vein endothelial cell cultures and peripheral blood mononuclear cells. Given the importance of rhinovirus in the exacerbation of both asthma and COPD this has important implications for lung health.

Vitamin D deficiency has been associated with higher blood pressure levels, which was already shown in most, but not all, prospective studies, as well as meta-analyses of observational studies. Possible mechanisms for this association of vitamin D and blood pressure include the inverse association of vitamin D levels with the renin-angiotensin-aldosterone system (RAAS) activity, the effect of improving endothelial function and the prevention of secondary hyperparathyroidism. In this context, it should be noted that high parathyroid hormone (PTH) levels are a hallmark of vitamin D deficiency and are known to be associated with myocardial hypertrophy and higher blood pressure levels. In addition, increasing evidence suggests that the mutual interplay between vitamin D, parathyroid hormone and aldosterone mediates cardiovascular damage independent of the RAAS.

Obesity is closely associated with vitamin D deficiency. It had been hypothesized that this may be due to vitamin D deposition in adipose tissue, resulting in lower circulating 25(OH)D levels in the blood. Others hypothesized a causal relationship of vitamin D deficiency leading to obesity.

In observational and prospective studies, low vitamin D levels have largely been associated with disturbances in glucose metabolism, as well as higher risk of developing diabetes in the future. It should also be kept in mind that vitamin D deficiency in diabetic patients may partly be a consequence of reduced physical activity and consecutive obesity, as well as limited sun exposure. Therefore, residual confounding in observational studies due to the close link of obesity with both vitamin D deficiency and glucose intolerance cannot be ruled out with certainty. On the other hand, it must also be considered that reverse causality may exist, since there are data suggesting that an inflammatory insult might decrease 25(OH)D levels.

Adequate vitamin D intake is essential for maternal and fetal health during pregnancy, and prevention of adverse outcomes. Recent work emphasizes the importance of non-classical roles of vitamin D in pregnancy and the placenta. Vitamin D deficiency during pregnancy is associated with the non-classical actions of this hormone, being linked with preeclampsia, insulin resistance, gestational diabetes mellitus, bacterial vaginosis, and an increased risk for caesarean section delivery.

VI. MEASURES TO REDUCE THE PREVALENCE OF VITAMIN D DEFICIENCY

In spite of widespread vitamin D deficiency, it is surprising that the Indian Council of Medical Research, even in its current updated guidelines does not give any specific recommendations for Vitamin D intake, as it is believed that we Indians get sufficient Vitamin D from sunlight.

But it can be seen from the few studies that have been done in India, that sunlight does not suffice the vitamin D requirement even in rural India.

Fresh guidelines about dietary recommendations of vitamin D are required. Foods naturally containing rich vitamin D are limited. Oily fish (salmon, mackerel, and sardines) and cod liver oil are good sources of vitamin D3. Other food source includes egg yolk, fortified milk and orange juice, some cereals, mushrooms and cheese. It has been estimated that for every 100 IU of vitamin D ingested, the blood level of 25(OH) D increases by around 1 ng/mL (2.5 nmol/L).

An average Indian diet has minimum amount of these food items. Thus, another way is by fortification of various food items, mainly milk. However, it is a costly exercise and thus has limited applicability.

Hence, the author would like to conclude that the path towards tackling this emerging public health condition is difficult and full of challenges.

CONFLICT OF INTEREST

The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript. Hence, there is no conflict of interest.

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