Review Article:

Vitamin D deficiency in India: fortify or let the sun shine in?

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ABSTRACT

Vitamin D plays a pivotal role in calcium and mineral metabolism. It is astonishing to find vitamin D deficiency in India despite plentiful sunlight. This could probably because of urbanization, life style and dress code changes, and revision of vitamin D adequacy range. Recent studies in south India using *in vitro* ampoule model with 7-dehydrocholesterol have shown adequate formation of active form of vitamin D in mid-day sun. In India 70% of populations reside in rural areas. Only 35% of Indian populations have access to regulated milk supply. We as humans can get vitamin D from abundant sunshine, by exposing 18% of body surface area (without sunscreen) to mid-day sun for 30-45 min to cause 1 minimal erythemal dose (MED) which is equivalent to taking about 600 to 1000 IU of vitamin D. This is about the recommended daily dose by expert group on human nutrient requirements and the dose used in studies with fortified milk supplementation studies. Vitamin D synthesized in the skin lasts two-times longer in the body. In populations where there is limited exposure to sunlight, like dress-code limiting sun-exposure, usage of sunscreen with (SPF) greater than 8 etc., vitamin D supplementation may also be required. Since there is widespread calcium deficiency in Indian population, calcium supplementation should be an integral part of vitamin D supplementation therapy.

Key words: *Vitamin D deficiency, India, Supplementation*

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INTRODUCTION

Vitamin D plays a pivotal role in calcium and mineral metabolism. Vitamin D is also recognized to influence wide range of fundamental biological functions such as cell differentiation, and immunomodulation that could potentially explain epidemiological and observational data linking it to variety of clinical disorders such as diabetes, hypertension, autoimmune disorders and malignancy.[1]

The 25-hydroxyvitamin D (25OHD) is the major circulating metabolite and 1,25,-dihydroxy-vitamin D3 (calcitriol) is the biologically active form. Serum 25OHD is the most reliable indicator of the vitamin D status of an individual. Serum 25OHD levels less than 20 ng/mL is considered as “deficiency” and levels greater than 30 ng/mL is considered as “normal”. The calcium absorptive performance of the gut is a function of 25OHD status of an individual and appears to achieve its peak ability at this level.[2,3] Optimal calcium absorption leading to normal blood calcium levels would minimize secondary hyperparathyroidism thus contributing to increasing bone mineral content during periods of rapid growth (childhood and adolescence). This in turn contributes to increased “peak bone mass” and may effectively prevent osteoporosis at a later age.[4,5] Adequate vitamin D and calcium levels are paramount in reducing the rate of post-menopausal osteoporosis and consequent fracture risk.

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For most people, the main source of vitamin D is skin exposure to sunlight. Exposure to ultraviolet-B (UV-B) photons (290–315 nm), causes the photolysis of 7-dehydro-cholesterol to pre-vitamin D_3, which thermally (37 °C) isomerizes to vitamin D_3 by a membrane enhanced mechanism. It has been a general belief that vitamin D deficiency is an uncommon problem in India because of abundant sunshine.[6] There is, however, now increasing evidence that this is not true and it has been observed that Vitamin D deficiency is widespread across the country and in all age groups.[7] This could probably because of urbanization, life style and dress code changes in the country or the revision of normative ranges of vitamin D sufficiency. Many factors influence the production of vitamin D_3 in the skin. In general, the cutaneous production of vitamin D declines with age.[8] An alteration in the zenith angle (angular distance between sun and object directly underneath) of the sun caused by a change in latitude, season of the year, or time of day dramatically influences the skin's production of vitamin D_3.[9] In a study[7] designed to demonstrate and calculate the efficacy of sunlight on synthesis of vitamin D at different zenith angles, calculations, using linear regression modelling, have revealed that reduction in every one degree of angle leads to increase in vitamin D by 0.285 units [previtamin D3 and vitamin D3 formed (Y) = 20.466-0.285 X zenith angle (X)].[7] Attenuating factors such as clothing, duration of exposure to sunlight (intense heat in tropics preventing people from sun exposure), type of skin (proportionately high melanin in equatorial regions), pollution (e.g., Asian brown cloud phenomenon),[7] and increasing indoor life-style have all been blamed for this now recognized widespread problem. Even in hot and arid countries of the Middle East, vitamin D status has been demonstrated to be very low in summer [97% have 25OHD levels less than 30 ng/mL and 85.2% had vitamin D deficiency (<20 ng/mL).[10] This was attributed to conservative clothing and very hot weather in summer causing people to stay indoors.[10]

Sunshine vitamin

The Food and Agricultural Organization (FAO)/ World Health Organization (WHO) Expert Consultation states that the most physiologically relevant and efficient way of acquiring vitamin D, in most locations in the world around the equator (between latitudes 42° N and 42° S) is to synthesize it endogenously from skin from 7-dehydro-cholesterol present in the subcutaneous fat by minimum of 30 minutes of skin exposure (without sunscreen) of the arms and face to mid day sun.[11]

It has been concluded from the experimental data that exposure of the body in a bathing suit (almost 100% of body surface area) to sunlight that causes slight pinkness of the skin [1 minimal erythemal dose (MED)] is equivalent to ingesting approximately 20,000 IU of vitamin D orally. Therefore, exposure of 6% of the body to 1 MED is equivalent to taking about 600 and 1,000 IU of vitamin D.[12] Applying the rule of nines used in burns, exposure of both forearms, and face is 12% of body surface area. For Caucasian skin (type 2 or 3), exposing face, arms and legs for a period equal to 25% of the time that it would take to cause 1 MED, for two-to three-times a week can satisfy the body's vitamin D requirement while minimizing sun damage ("Holick's rule").[12] Compared to Caucasians, Asians have darker skin (type 4 or 5) and, therefore, with the same amount of MED, they would require greater duration of exposure than their light-skinned counterparts to synthesis comparable amount of vitamin D_3.[13] Vitamin D synthesized in the skin lasts two times longer in the body compared to supplemental/ ingested dose.

The time required to obtain recommended UV dose for adequate vitamin D synthesis is "1 standard vitamin D dose" (SDD). Throughout the year 1 SDD for skin type V (Asians) at 11.5° N is 10 - 15 minutes, and at 29° N is 10-45 minutes at solar noon, with longer duration in winter. SDD for skin types is collected on MED. Clouds, aerosols and thick ozone can reduce vitamin D synthesis and force "vitamin D winter" even at equator. India is located 8.4 and 37.6° N.

In a study[14] conducted on sun exposure in elderly women in Jakarta, Indonesia (latitude of 6°S),[14] repeated measurement of sun exposure intensity from 7 A.M. to 4 P.M. by using ultraviolet (UV) meter to calculate exposure in terms of MED/hour, the highest intensity of UVB was observed to have occurred at 11 A.M. to 1 P.M. ($\sim$2 MED/hour). But for convenience, they decided to ask subjects (n = 74 elderly women with type – 4 skin) to expose to sunlight at 9 A.M. which contained by average about 0.6 MED/hour. After exposing to sunlight at this specific time and duration for 6 weeks, mean 25 OHD levels of participants increased from 59 nmol/L compared to the baseline to 84 nmol/L clearly proving the efficacy of sunlight in increasing the level of vitamin D. Similarly, a study from south India (Tirupati latitude 13.40 °N and longitude 77.2° E) using *in vitro* ampoule model with precursors of vitamin D (7-dehydrocholesterol) when exposed to sunlight converted to active vitamin D best between 11 A.M. to 2 P.M. clearly demonstrating the efficacy of sunlight in vitamin D synthesis.[7] The median percent conversion of 7-dehydro-cholesterol to previtamin D3 and its photo-products and percent of previtamin D3 and vitamin D3 formed was 11.5% and 10.2% respectively at a solar zenith angle of 36.8° and at 12:30 P.M.[7]

Observational data

Studies from Pune (latitude 18.31° N and longitude 73.55° E) have shown that toddlers exposed to sunlight (playing outside) for more than 30 min a day exposing more than 40% of their body surface area have a normal vitamin D status (males: 91.6 nmol/L and females: 67.7 nmol/L) which was three times more compared with the toddlers who were indoors for most part of the day (males: 32 nmol/L and females: 21.1 nmol/L).[15] Similarly, another study[16] on toddlers in Delhi slums (latitude 28.35° N and longitude 71.12° E) demonstrated that those toddlers who were exposed to sunlight had better Vitamin D levels (~ 100 nmol/L) compared to those who were not (~20 nmol/L). Interestingly authors of this study[16] also identified (albeit retrospectively) that those families whose toddlers were exposed to sun were given educational material by the local healthcare workers explaining the benefits of sunshine. The 25OHD levels in South Indian subjects are relatively higher compared with the subjects from North India.[17] From the same data, a strong inverse correlation between the 25 OHD levels and latitude ($r = -0.48$; $p < 0.0001$) has been established clearly proving the effectiveness of equatorial closeness (smaller zenith angle) to natural Vitamin D synthesis.[7]

Dietary calcium

Even though Vitamin D surveys from rural south India (Tirupati) have similarly demonstrated higher Vitamin D levels in agricultural workers who are exposed to long hours of sunlight as part of their work (~24 ng/mL Vs 19 ng/mL) compared to urban dwellers,[17] measured vitamin D levels were significantly lower than expected for the duration of sunlight exposure. Rather interestingly, same group studied dietary habits in the area[18] and have demonstrated calcium deficiency in diet and evidence of high phytate consumption. Similar calcium deficient diet has been demonstrated by other groups in the country.[19] The average dietary calcium intake children adults in India has been observed to be is 430 $\pm$ 180 mg/day and 560 $\pm$ 310 mg/day respectively.[20]

It is known that low dietary calcium converts the 25OHD to polar metabolites in the liver and leads to secondary 25 OHD deficiency.[21] Also, low calcium intake increases parathyroid hormone (PTH) which increases conversion of 25OHD to 1,25-dihydroxyvitamin D. In addition, 1,25-dihydroxyvitamin D induces its own destruction by increasing 24-hydroxylase. This probably explains the low 25OHD concentrations in persons on a high-phytate or a low-calcium diet underlining the importance of dietary calcium for not only maintaining good bone health but in interpretation of 25OHD levels and subsequent therapy. Hence calcium supplementation should be an integral part of vitamin D supplementation therapy in India.

Daily recommended dietary allowances for Indians

The recent expert group of the Indian Council of Medical Research (ICMR) 2009, gathered to revise and update our knowledge on the human nutrient requirements and recommend the daily recommended dietary allowance (RDA) for Indians, based on their dietary style and composition. The committee released the 2010 RDA draft document (http://www.ninindia.org/Dietary guidelines for Indians-Final draft.pdf). The RDA (mg/day) of calcium for children 1-9 years of age is 600; children 10-18 years age is 800 (both genders); adults (men and women) is 600; and for pregnant and lactating women is 1200.

The committee felt that the recommendations (by international agencies) for populations living in advanced countries where exposure to sunlight is limited, hence the need to obtain vitamin D from fortification of diet and supplementation. The committee felt that outdoor physical activity is a means of not only achieving adequate vitamin D but also controlling overweight and obesity in Indian population. The committee retained the recommendation of 400 IU (10 µg) per day.

Fortification

Pooled analysis of the data in a systematic-review[22] of several randomized controlled studies across the world involving vitamin D fortification in healthy young adults showed positive results in improving vitamin D levels. There are similar data from India demonstrating the efficacy of milk fortification (vitamin D 600 IU and 1000 IU) in improving serum levels of vitamin D.[23,24] The major limitation of interpretation of fortification studies in Indian children is the lack of data on dietary calcium intake and sun exposure in these children before and at the end of the study which limits its extrapolation in daily life. The improvement in serum vitamin D levels had been shown to be dependent on both the baseline vitamin D status (lower levels leading to greater change) and the dose of vitamin D used in fortification (higher doses leading to a greater change). In a systematic review[25] of available evidence from published data it was calculated that 1 µg of vitamin D (40 IU) will increase serum 25OHD levels by 0.79 ng/mL (1.95 nmol/L) amounting to 360 IU of vitamin D to raise serum Vitamin D levels to more than 25 nmol/L. Studies on fortification so far have demonstrated no significant adverse events including hypercalcaemia and hypercalciuria in all age groups proving both safety and efficacy. Study of fortification of food items with cereal-legume snack (calcium fortified ladoos) along with vitamin D supplementation monthly in underprivileged children has shown improvement bone mineral content at the end of one year of study.[26] This study underscores the importance of calcium supplementation along with vitamin D.

Loading dose/Therapeutic dose and continued vigilance

A study[27] done in Indian adults showed that normal serum levels of 25OHD (30 ng/mL) achieved after loading dose (250,000 – 500,000 U) could not be sustained after 1 year without further supplementation.[27] Similar observation was made school children in Lebanon where serum levels started to decline after stopping supplementation at 8 weeks.[28] Most of the supplementation schedules for correcting vitamin D deficiency from India have used vitamin D alone[29] or vitamin D and calcium[27,30] have shown achieving normalcy with doses used at the end of two months (60,000 IU weekly for 8 weeks along with elemental calcium of 1 gm/day).[30] One study[30] from India has emphasized the need for maintenance therapy after achieving normal vitamin D levels. These data clearly raises two important concerns. Firstly, at the population scale in short term at least, simple supplemental doses without adequate loading doses may not be sufficient to achieve therapeutic levels particularly in those who would benefit from immediate increase (e.g., elderly at risk of osteoporotic fractures) and secondly, fortification/supplementation of vitamin D if not sustained in long term may not yield desired vitamin D levels and health benefits. Hence despite fortification there will be a need for appropriately treating 'at risk' groups with therapeutic doses in a supervised environment and an equal need for vigilance of the fortification programme with robust and continued quality assessment to ensure its long term success. There are no Indian guidelines for evaluation, treatment and prevention of vitamin D deficiency.

Census data from the Government of India shows that the urban population has increased from 11% in the year 1901 to 31% in the year 2011, and is likely to increase further keeping in with the trend across the world further adding to the problem with natural (*in vivo*) synthesis of Vitamin D.[31] India is the world largest producer of dairy products by volume. This accounts for more than 13% of world's milk production with per capita consumption of milk at approximately 250 mL/day. Despite this, it has been calculated that only 35% of this milk consumption happens via organized sector[32] leaving the majority without the benefit. In a recent review, fortification via wheat flour has also been proposed as an alternative to milk.[33] Though wheat flour consumption probably exceeds milk consumption, distribution of wheat flour via organized sector in India is far less than milk unlike in Jordan which has been quoted as an example of success in wheat fortification programme and hence seriously dents argument against wheat fortification as a sole public policy guideline. At present there is no regulation or fortification of other food products with vitamin D in India.

Majority who do not have access to organized food supply chain (both dairy and non dairy products) in India tend to be from rural and semi urban areas with much better opportunity to have sun exposure than those in urban areas. Hence in addition to milk fortification with vitamin D and attempts to improve distribution via organized sector (e.g., adding calcium/ vitamin D to mid day meal of the children), the authors of this review feel that increasing efforts to mobilize available resources that would help improve knowledge and education about the benefits of regular sunlight exposure for 30 min in mid day sun would be a valuable addition in improving the status of 'sunshine' vitamin in the country. We as humans can get vitamin D from abundant sunshine, by exposing 18% of body surface area to mid day sun for 30-45 minutes (without sunscreen). Pragmatically, in those geographical areas and in seasons with abundant sunshine, school teachers could be educated as part of their curriculum training to encourage students to expose themselves for as much as possible in 'lunch hour' for example by naming it 'sunshine hour'. Toddlers and children, elderly adults, should be encourage to expose to mid day sunlight. Such an approach with equal emphasis on knowledge empowerment (importance of sunlight exposure) we think will go a long way in improving the current status. In populations where there is limited exposure to sunlight, dress code – limiting sun exposure, usage of sunscreen with SPF greater than 8 etc., vitamin D supplementation may also be required.

As deficiency in dietary calcium is widely reported and given its importance in bone health in addition to vitamin D, it goes without mention that any fortification program should consider also include intake of calcium with equal priority.

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