Review Article

Vitamin D Status in India – Its Implications and Remedial Measures

CV Harinarayan*, Shashank R Joshi**

Abstract

Vitamin D deficiency is epidemic in India despite of plenty of sunshine. The interpretation of vitamin D levels should be done with the solar zenith angle, minimal erythemal dose, skintype, UV Index and geographical location. All Indian studies uniformly point to low 25(OH)D levels in the populations studies despite abundant sunshine. All studies have uniformly documented low dietary calcium intake compared to Recommended Daily/Dietary Allowances (RDA) by Indian Council of Medical Research (ICMR). The vitamin D status of children is very low in both urban and rural population studied. Pregnant women and their new born had low vitamin D status. The effect of short course of loading doses of vitamin D doesn't have a lasting effect and a maintenance dose is needed. Low 25(OH)D levels has its implications of lower peak bone mass and lower BMD compared to west. There may be a public health need to fortify Indian foods with vitamin D. ©

Introduction

For nearly more than a century vitamin D is of interest to an internist, pediatrician, physician, radiologist, orthopediacian, pathologist, endocrinologist, nutritionist, ecologist, environmentalist, geneticist etc., for its various etiological and varied spectrum of clinical, biochemical, and pathological presentations. It is indeed surprising that endogenous synthesis of vitamin D that does not require men, material or money has intrigued the scientific community by its spectrum of presentation.

Vitamin D has been traditionally known as anti-ricketic factor or sunshine vitamin. Vitamin D is unique because it is a vitamin synthesized by the body and it functions as a hormone. Besides its pivotal role in calcium homeostasis and bone mineral metabolism, vitamin D endocrine system in now recognized to subserve a wide range of fundamental biological functions in cell differentiation, inhibition of cell growth as well as immunomodulation.[1-8] It is a steroid that regulates complex system of genomic functions and has a role in prevention of neo plastic transformation. Recent evidences from genetic, nutritional and epidemiological studies link vitamin D endocrine system with diseases like hypertension, myopatic disorders, and proneness to infection, autoimmune disorders and cancer.[3,9-13] Vitamin D modulates the transcription of cell cycle proteins, which decrease cell proliferation and increase cell differentiation of a number of specialized cells of the body (osteoclastic precursors, enterocytes, keratinocytes).[13-15] This property may explain the actions of vitamin D in bone resorption and intestinal calcium transport. The immunomodulatory properties may explain the reported associations between vitamin D deficiency on one hand and metabolic diseases such as type 2 diabetes, autoimmune diseases, infections such as tuberculosis and some malignancies on the other.

*Professor and Head, Department of Endocrinology and Metabolism, Sri Venkateswara Institute of Medical Sciences, Tirupati – 517 507, Andhra Pradesh, India. **Consultant Endocrinologist, Lilavati Hospital, Bhatia Hospital and Joshi Clinic, Mumbai.

Synthesis And Terminology

Vitamin D orchestrates (coordinates) the "Ca-vitamin D-Parathyroid hormone endocrine axis". To understand the vitamin D endocrine system one needs to be familiar with the different forms of vitamin D, namely cholecalciferol, calcidiol (25-OHD), and calcitriol (1,25-OHD). Cholecalciferol is the naturally occurring form of vitamin D. Cholecalciferol is made in large quantities in skin when sunlight is exposed to it (UV – B rays 290 to 310 nm). Cholecalciferol is transported to the liver where it is metabolized into calcidiol or 25(OH) D. Calcidiol (25-hydroxyvitamin D) is a prehormone which is directly made from cholecalciferol. Calcidiol's main importance is that it is the storage form of vitamin D. Serum 25-hydroxyvitamin D [25(OH)D] is the most reliable indicator of vitamin D adequacy of an individual.[16] Vitamin D status depicts the vitamin D stores of an individual. The production of 25(OH)D is not regulated and the serum concentration thus reflects both cutaneous synthesis and absorption from diet. This is what is tested routinely for vitamin D deficiency. Calcidiol has also got to have steroid like properties. But, after hepatic conversion of cholecalciferol into calcidiol, calcidiol follows either of the two pathways. One responsible for bone and other for cellular effects. Calcitriol (1,25-dihydroxy-vitamin D) is made from calcidiol in both the

kidneys and in other tissues and is the most potent steroid hormone derived from cholecalciferol.

Vitamin D synthesis is affected by latitude, atmospheric pollution, clothing, melanin pigmentation and sunlight exposure. Any one of these factors can be etiological for vitamin D deficiency apart from decreased vitamin D intake as breast feeding, maternal vitamin D deficiency and unusual diets; defects in vitamin D metabolism as low calcium intake, intestinal malabsorption and genetic variation.

Assays And Normal Range

In the past measurement of serum vitamin D was limited by methodological differences (issues)[17-19]. With the evolution of ^{125}I radioimmunoassay (RIA) for estimation serum 25-hydroxyvitamin D [25(OH)D] the methodological differences have vanished (disappeared) permitting an inter-laboratory comparison of the values. [The currently available assays have antibodies cospecific to both 25(OH) D2 and 25(OH)D3 and hence the terminology 25(OH) D assays are used. The laboratory normally estimates 25(OH)D levels and not 25(OH)D2 or 25(OH)D3].[18-24] These advancements are limited by improper definition of vitamin D deficiency and hypovitaminosis D.[25-30] In the clinical chemistry departments, the normal range for most of the analytes measured is derived from the values found in 95 percent of the population. It is unreliable to establish such a reference data for 25(OH)D. Since vitamin D levels are subject to variations in diet, dress code, latitude and altitude of residence, skin color, climate etc., the normative data varies between laboratories.[31-35] These genuine geographic variations in calcium homeostasis restrict the locally estimated reference range to be used across the countries. A locally developed "population based reference values" could result in a person becoming vitamin D deficient enroute from one country to another. A "functional health based reference value" which physiologically defines hypovitaminosis D as the concentration of 25(OH)D at which PTH begins to increase is largely replacing the hitherto used "population based reference values". It is no longer appropriate to analyze serum 25(OH)D levels with respect to ranges supplied by a manufacturer.[25-30]

Vitamin D status is an estimate of vitamin D stores. The best determinant of vitamin D status is the concentration of 25(OH)D in serum because it is the major circulating metabolite that is directly dependent on substrate supply from both skin and oral sources. It is essential to set criteria for vitamin D deficiency and insufficiency (hypovitaminosis D) so that means to exceed this level can be established (by monitored food fortification program). Setting thresholds for varying degree of vitamin D insufficiency addresses the issue of vitamin D deficiency.

The terminology vitamin D denotes 25(OH)D2 and 25(OH)D3. The term Vitamin D status denotes 25(OH) D stores in the body. The term "vitamin D deficiency" is reserved for severe vitamin D deficient state associated with osteomalacia, and the term "vitamin D insufficiency" or "inadequacy" or "hypovitaminosis D" for mild and moderate deficiency which is associated with SHPT.[25,30,36-38] While osseous signs often diagnose severe vitamin D deficiency [25(OH)D], biochemical abnormalities reflect the cause and effect of vitamin D deficiency. Mild or sub clinical vitamin D deficiency escapes diagnosis because of its nonspecific symptomatology and invariably requires evaluation of "calcium-vitamin D-parathyroid hormone axis (Ca-Vit D-PTH axis). While serum calcium may not truly reflect the degree (severity) of vitamin D deficiency, PTH is only a surrogate marker.[25,27] While vitamin D deficiency [25(OH)D levels <20ng/ml] is associated with osseous changes (rickets/osteomalacia), vitamin D insufficiency [25(OH)D levels between 20 to 30 ng/ml] is associated with secondary hyperparathyroidism (SHPT) and negative skeletal consequences. 25(OH)D levels greater than 30 ng/ml is considered as normal. Because, the calcium absorption from the gut is maximal at this level of 25(OH)D levels.[27] It well documented that calcium absorptive performance of the gut is a function of 25(OH)D status of an individual.[25,27] When there is 25(OH)D deficiency the effective calcium absorption from the gut is reduced. The SHPT, which results, leads on to bone resorption. The accompanying SHPT in all these situations is a "physiological adaptive phenomenon". The increased PTH levels and subsequent accelerated bone remodeling leads to decrease in bone mass and increased risk of fracture .[39-42]

The natural history of vitamin D deficiency is well understood that encompasses hypovitaminosis D as the initiating event, followed by secondary hyperparathyroidism (a prolonged phase of high bone turnover with possible irreversible bone loss, especially cortical bone) and culminating in defective mineralization of bone as osteomalacia in adults and rickets in children. The SHPT, which ensues, mobilizes mineral and matrix from skeleton, leads to an enhanced bone loss and to a high risk of fracture and, low peak bone mass in children.[38-42] Low dietary calcium intake further amplifies the parathyroid response to vitamin D insufficiency.[43] Vitamin D deficiency is the first step in the evolution towards osteomalacia. Dietary calcium intake influences the duration of progression. Normal vitamin D levels are important for the fully normal control of calcium absorption efficiency form the gut.

Interpretation Of 25(OH) D Levels

In a non-disease, state vitamin D levels are influenced by season, skin pigmentation, atmospheric pollution, geographical location (altitude and altitude), time of the day, cloud cover, indoor living, dress code etc. Whenever we interpret 25(OH)D levels it should be done in the background factors mentioned above. The most important of them is the solar zenith angle (SZA), minimal erythemal dose (MED) and skin type, UV index and geographical location of the study is conducted.

Solar Zenith angle is the angular distance between an

object in the sky, such as the sun, and an object directly overhead (Fig. 1). The zenith angle varies from the time of the day, season and geographic location. Solar zenith angle in three different locations Delhi, Lucknow and Tirupati are given in Fig. 2.

UV Index is the calculated prediction of the amount of skin damaging UV radiation that will reach a specific location ($1m^2$) during solar noon hour. It is derived from the combination of five elements namely; Latitude, year of the day, total ozone overhead, elevation above sea level and amount of cloud covers. The UV index is obtained from the following websites:

1. http://sedac.ciesin.columbia.edu/ozone/rtm/mval.html
2. http://www.temis.nl/uvradiation/nrt/uvindex.php

Minimal Erythemal Dose (MED) is the amount of sun exposure which causes barely perceptible skin burn (erythema) appears within 24 hours in previously unexposed skin. Skin type of various races are categorized based on skin color(pigmentation), eye color and hair color, reaction to sun whether it freckles, burns, peels, blisters or tans. There are six skin types. Indians come under the skin type V category.

The geographical location of the study can be sought from the Global Positioning System which indicates the latitude and longitude of the place of study.

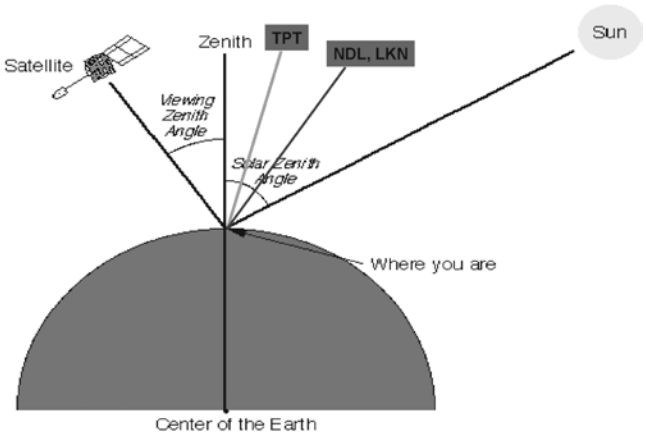

Fig. 1 :

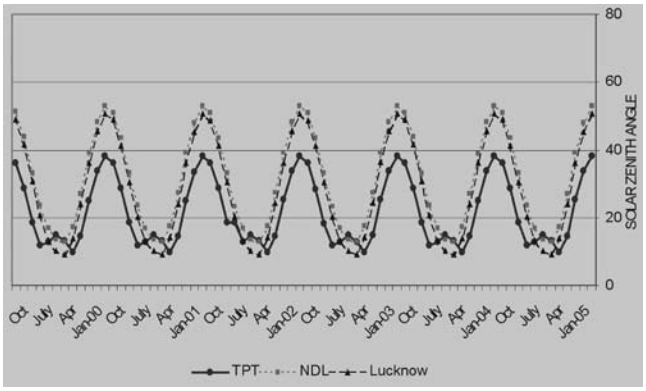

Fig. 2 : Zenith angle for locations Tirupati, Delhi and Lucknow year 2000 to 2005.

The quantum of UV – B rays (290 to 310 nm) received by an individual determines the amount of vitamin D synthesized by the skin. Apart from the zenith angle and the skin type other factors in atmosphere affect the UV – B rays. Most UV-B rays are transmitted from 10 am to 2 pm. Cloud retain 10% of the rays, snow absorbs 20% and reflects the rest, the rays increase by 10% per kilometer above sea level, shades reduces the rays by about 50%, only 10% of the outdoor rays will be experienced indoors, sand reflects 25% of the rays and up to 40% of the rays is present at about half a meter depth of water.

Vitamin D Status In India

It has been a general belief that rickets and vitamin D deficiency are uncommon problems in India because of abundant sunshine.[44] There is, however, now increasing evidence that this is not true. It all centers round a new emerging global threat called vitamin D deficiency which is not merely rickets or osteomalacia but a huge hidden problem now being unraveled and is reaching epidemic proportions both in the developed and developing world alike. The problem has increased to alarming proportions after new definition of 25OHD levels and its impact on bone health.

The FAO/WHO Expert Consultation[45] stated that in most locations in the world around the equator (between latitudes 42^0 N and 42^0 S) the most physiologically relevant and efficient way of acquiring vitamin D is to synthesize it endogenously from skin from 7-dehydrocholesterol present in the subcutaneous fat by 30 minutes of skin exposure (without sunscreen) of the arms and face to sun (Ultraviolet spectrum of wavelength 290-310 nm).

Nutritional factors play a vital role in the bone homeostasis. Nutrition and bone health is tale of two nutrients: calcium and vitamin D. Adequate calcium intake along with vitamin D helps to maintain bone mineral mass attained at the end of growth period (peak bone mass). During infancy, childhood and adolescence, increasing dietary calcium intake favors bone mineral accrual.[38] Adequate nutrition and sufficient activity provide mechanical impetus for bone development which may be critical in attaining bone growth potential. Vitamin D and calcium status correlate with increased bone mineral density and have the potential to increase the peak bone mass.[41,46,47] Increasing bone mineral content during periods of rapid growth (childhood and adolescence) increases "peak bone mass" and may effectively prevent osteoporosis at later age.

Studies From Different Parts Of India

The first laboratory documentation of vitamin D status was in a group of patients with primary hyperparathyroidism and control population.[48] Later other reports ensued. Table 1 summarizes the vitamin D status of various groups studied from India. The table is arranged to comprehend the vitamin D status starting from birth through adolescence reaching the peak bone mass up to post menopausal

period. Few studies which have documented the vitamin D status of the population based on the sunlight exposure and season of sampling. Also different studies have used different yardstick of normal range of 25(OH)D levels. The table depicts the values (mean ± SD/SEM) of various studies so that the reader can use the current normogram to make decisions. For conversion from nmol to ng – multiply by 0.4. The subsequent sections will take the readers through the vitamin D status of population available from birth through postmenopausal status in India.

Vitamin D status in pregnant women and their new born

Studies from northern India have shown vitamin D deficiency (< 20 ng/ml) in pregnant women and their new born.[49-52] One of the studies[52] has shown pregnant women in winter had higher 25(OH)D levels than in summer. Studies from south India, Tirupati also show a similar trend.

Toddlers have shown to have low vitamin D status.[53,54] In one study[54] it was clearly shown that a small group of toddlers had higher vitamin D status compared to their counter parts with low dietary calcium and poor exposure to sunlight living in the location and environment. Higher vitamin D status in this group was attributed to education on nutrition and sunlight exposure in this community.

Vitamin D status in children and adolescence

It is important to know the vitamin D status of this age group as the bone accrual is taking place and the peak bone mass is achieved during this period. There are numerous studies in this category from north and south India.[55-60] These studies clearly bring forth the fact that approximately 75 to 85% of the groups studied have varying degrees of vitamin D deficiency or insufficiency (hypovitaminosis D). Another important fact drawn out in these studies is the fact that nutritional status and sunlight exposure has a positive impact on the vitamin D status on the population. One of the studies has shown a positive impact on dietary calcium supplementation to a group of children.

Vitamin D status in middle age group (20 to 45 years)

It is important to have vitamin D status in this group of population as the peak bone mass is achieved (up to 30 years of age). Apart from the peak bone mass achieved, parity of women and their nutritional status (bone health) determines the pattern of post menopausal bone loss and age related osteoporosis. All the reports uniformly available so far show universal vitamin D deficiency/ hypovitaminosis states in these populations. Rural population have better vitamin D status compared to urban population.[58-61] Most of the rural workers in these studies are agriculture laborers who have longer exposure to sunlight. It is pertinent to point out that soldier and subjects of Indian Para military forces who undergo rigorous outdoor exercise in sunlight with high dietary calcium intake had higher vitamin D status.[49,62]

Vitamin D status in post menopausal women

There are two studies[24,63-65] to show the low vitamin D status. It has important implications in interpretations of bone mineral density and therapy of post menopausal osteoporosis.

Vitamin D status and atmospheric pollution

There is a report of toddler in mori gate (Delhi) where the atmospheric pollution is high had lower vitamin D status compared to toddler in Gurgaon(Delhi).[53]

Vitamin D status and calcium intake

Uniformly all studies have clearly documented dietary calcium intake less than RDA of ICMR. Besides this, it has been shown that the calculated values for all nutrients are significantly higher than the analytical values.[65] Hence, a patient with a calculated low intake of calcium with a background diet containing foods high in phytates, may be more calcium deficient than calculated from dietary intake data. The inadequate dietary calcium intake is significant when viewed in the background of high phytate/calcium ratio associated with low 25 (OH)D levels.

The calcium absorptive performance of the gut is a function of a person's 25(OH)D status.[23,27,33] When the 25(OH) D concentrations are low, the effective calcium absorption from the gut is reduced.[23,27] This is further amplified by the low dietary calcium intake. It was shown that low dietary calcium converts the 25(OH)D to polar metabolites in the liver and leads to secondary 25(OH)D deficiency.[33] The SHPT consequent to inadequate dietary calcium intake and low 25(OH)D concentrations mobilizes mineral and matrix from the skeleton. This increases the risk of fractures, especially in postmenopausal women and elderly patients. These are further amplified by age related changes with calcium supplementation.[55,66] High phytate/calcium ratio amplifies the inadequate dietary calcium intake. Also, low calcium intake increases 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.[59,60]

The RDA for calcium in India recommended by the Indian Council of Medical Research (ICMR) is lower than the recently revised recommendations by the USA and Canada[57-72] (Table 2). Recently the RDA has been revised and redefined as the Dietary Reference Intake (DRI), which is a collaborative effort between USA and Canada. There is neither a recommendation for dietary intake of vitamin D nor a monitored food fortification program for the intake of calcium or vitamin D by ICMR.

Vitamin D status in Urban and rural locations

Studies[52,55,58-61] have clearly shown the vitamin D status of urban population is lower than the rural population. This is attributable to dress code and occupation, longer duration of exposure to sunlight.

Vitamin D status in higher altitude and latitude

It is known that cloud retain 10% of the rays, snow absorbs 20% and reflects the rest, the UV-B rays increases

Table 1 : Indian Studies of Vitamin D

Location	n	Study population	Age (Yrs)	25 OH D	unit	Diet cal	Ref No
Delhi	29	Pregnant Women in summer	23 ± 3	21.9 + 10.73	nmol/l	345 ± 78	49
	29	New born in summer	new born	16.72 + 4.99	nmol/l	-	
Delhi	26(5)	Toddlers (Mori gate)	16± 4 mo	12.4 ± 7	ng/ml	-	53
	1	Infants(Gurgaon)	16± 4 mo	28 ± 7	ng/ml	-	
Delhi Slums	47	Sunder Nagar Jan 2001	9– 30 mo	96 ± 25.7	nmol/l	-	54
	49	Rajiv colony Feb 2001	9– 30 mo	23.8 ± 27	nmol/l	-	
	48	Rajiv Colony Aug 2001	9– 30 mo	17.8 ± 22.4	nmol/l	-	
	52	Gurgoan Aug 2001	9– 30 mo	19 ± 20	nmol/l	-	
Lucknow	140	Pregnant Women (Urban)	24 ± 4.1	14 ± 9.5	ng/ml	842 ± 459	50
	67	Pregnant Women (Rural)	24.7 ± 5.1	14 ± 9	ng/ml	549 ± 404	
	29	Cord Blod (OSM)	-	12± 8	ng/ml	-	
	178	Cord Blod (no OSM)	-	14.3± 9.5	ng/ml	-	
Lucknow	139	Pregnant women –Summer	26.7 ± 4.1	55.5 ± 19.8	nmol/l	214 ± 150	52
	139	Pregnant women –winter		27.3 ± 12.3	nmol/l		
	28	Girls – winter	14.4 ± 2.7	31.3 ± 13.5	nmol/l	198 ± 159	
	34	Boys – winter	14 ± 3	67.5 ± 29	nmol/l	384 ± 600	
Lucknow	53	Controls		61± 36	nmol/l	404 ± 149	55
	40	Rickets/OSM		49 ± 38	nmol/l	285 ± 113	
Mumbai	42	Mothers Suppl Ca 250 – 500 apart	20 to 35	23 ± 11	ng/ml	800 - 1500	51
	42	Cord Blood	-	19.5 ± 9.6	ng/ml		
	35	Infants	3 months	18.2 ± 9.8	ng/ml		
Delhi	193	LSES School girls	12.4 ± 3.2	34.6 ± 17.43	nmol/l	454 – 187	56
	211	USES School girls	12.3 ± 3	29.4 ± 12.7	nmol/l	686 – 185	
	42	LSES School Boys	10 – 12	12.4 ± 5.5	ng/ml	314 ± 194	57
	85		13 – 15	11.3 ± 5.8	ng/ml	-do-	
	40		16 – 18	11.3± 5.3	ng/ml	-do-	
	33	USES School Boys	10 – 12	19.3± 8.8	ng/ml	713 ± 241	
	70		13 – 15	13.1± 7	ng/ml	-do-	
	55		16 – 18	13.5 ± 7	ng/ml	-do-	
	78	LSES School Girls	10 – 12	11 ± 6.5	ng/ml	314 ± 194	57
	123		13 – 15	10 ± 6.2	ng/ml	-do-	
	62		16 – 18	11± 5.7	ng/ml	-do-	
	47	USES School Girls	10 – 12	12.5± 8.9	ng/ml	713 ± 241	
	62		13 – 15	10.2± 5.7	ng/ml	-do-	
	63		16 – 18	12.9 ± 10.5	ng/ml	-do-	
Kashmir	64	Men	28.8 4.9	37.7 30	nmol/l	230 63	73
Valley	28	Women	26.8 4.8	13.8 11	nmol/l	178 45	
Delhi	12	Controls	25 – 35	8.3 ± 2.5	ìg/ml	~ 350	48
Delhi	40	Indian Paramiltary forces Men	20 – 30	18.4 ± 5.3	ng/ml	~1100	62
	50	Indian Paramiltary forces Women	20 – 30	25.3 ± 7.4	ng/ml		
Delhi	31	Soldiers males in winter	21.2 ± 2	41.17±11.73	nmol/l	1104 ± 666	49
	19	Phys. & nurse in summer	23 ± 5	7.89 ± 3.49	nmol/l	879 ± 165	
	19	Phys. & nurse in winter	24 ± 4	17.97 ± 7.98	nmol/l	880 ± 165	
	15	Depigmented persons in winter	43 + 16	18.2 ± 11.23	nmol/l	980 ± 300	
Delhi	32	Rural Males	42.8 ± 16.6	44.2 ± 24.4	nmol/l	905 ± 409	61
		Rural females	43.4 ± 12.6	26.9 ± 15.9	nmol/l	595 ± 224	
Lucknow	92	Healthy volunteers	34.2 ± 6.7	12.3 ± 11	ng/ml	439 ± 123	64
Tirupati	134	Urban men*	47 ± 1.5	18.54 ± 0.8	ng/ml	323 ± 8	60
	109	Rural Men*	45 ± 1.4	23.7 ± 0.8	ng/ml	271 ± 3	
	807	Urban Women*	46 ± 0.4	15.5 ± 0.3	ng/ml	306 ± 2	
	96	Rural Women*	41 ± 1.4	19 ± 0.9	ng/ml	262 ± 3	
	30	Urban children Male*	11± 1	15.57 ± 1.2	ng/ml	293 ± 6	60
	34	Rural children Male*	12 ± 0.7	17 ± 1.3	ng/ml	277 ± 6	
	39	Urban children Female*	13.5 ± 0.6	18.5 ± 1.66	ng/ml	317 ± 9	
	36	Rural children Female*	12.6 ± 0.5	19 ± 1.6	ng/ml	270 ± 7	
	164	Post menopausal	54± 8	14.6 ± 7	ng/ml	322 ± 6	30
Vellore	150	Post menopausal women	60.1± 5	20.85 ± 8.63	ng/ml	399 ±190	63

*Mean ± SEM;

For conversion from nmol to ng – multiply by 0.4.

Latitude: Kasmir 34.6 ^{0} N; Delhi 28.35 ^{0} N; Lucknow 26. 55 ^{0} N; Mumbai18.56 ^{0} N; Tirupati 13.4 ^{0} N;Vellore 12.55 ^{0} N.

by 10% per kilometer above sea level though the solar zenith angle is obtuse at these locations. The studies from Kashmir valley have shown lower vitamin D status of the group studied.[73]

Vitamin D and Bone Mineral Density

Low vitamin D has been related to low vitamin D status of our population.[57,63,64] Genetic factors also influence the BMD status.[75] It has been shown in cultured fibroblasts that the 25(OH)D-24-hydroxylase activity is markedly increased in Asian Indians and are at increased risk of developing vitamin D deficiency.[76]

Summary Of Indian Studies

- All studies uniformly point to low 25(OH)D levels in the populations studies despite abundant sunshine in our country.
- All studies have uniformly documented low dietary calcium intake compared to Recommended Daily/ Dietary Allowances (RDA) by Indian Council of Medical Research (ICMR).
- The vitamin D status of children is very low in both urban and rural population studied.
- In some of the studies it has been clearly shown that the 25(OH)D levels were directly proportional to the duration of exposure to sunlight.[64,52] This is evident from the vitamin D status of rural population who were agricultural workers and had their chest and tarso exposed to sunlight compared to the urban population who were white collared workers.[59-61] Hence exposure to sunlight has positive effect on the vitamin D status of individuals.
- Pregnant women and their new born had low vitamin D status.
- Residents of northern tip of India in Kashmir valley had low 25(OH)D levels.
- Indian paramilitary forces who had dietary calcium well above the RDA and daily exercises in sunlight in the morning hours had better 25(OH)D levels compared to the civilian counterparts.[62]
- Dietary calcium supplementation had positive effect on 25(OH)D levels.
- The effect of single course of loading doses of vitamin D (60,000 IU) doesn't have a lasting effect and a maintenance dose is needed long term. There is a need to evolve an Indian therapy protocol which is cost-effective. Vitamin D analogues have a narrow therapeutic window (should be avoided), while agents like calcirol sachets or bolus vitamin D injection have a wider therapeutic window (are more economical). Situations of hypervitaminosis D should be avoided.
- Low 25(OH)D levels has its implications of lower peak bone mass and lower BMD compared to west.[63,64]

Table 2 : Recommended dietary allowances (RDA) of calcium in India and USA [67-72]

Category Units	India mg/day	USA mg/day
Infants		
Infants 0–6 months	500	500
Infants 6– 12 months	500	750
Children Boys & Girls		
1 – 9 yrs	400	800
10 – 15 yrs	500	1200 -1300
16 – 18 yrs	500	1200 -1300
Men	400	800 -1000
Women	400	800 - 1000
Pregnant & Lactating mothers	1000	1200 - 1300

Implications Of Low Vitamin D Status And Low Dietary Calcium Intake In India

- The prevalence of "sub-clinical 25(OH)D deficiency (hypovitaminosis D)" may be over looked due to vague clinical presentation.
- It has important connotations in therapeutic aspect of the disease process. Vitamin D supplementation has to be considered in patients with osteoporosis (keeping in mind the hypovitaminosis D in majority of the population).
- The 25(OH)D levels and the dietary calcium pattern of the urban and rural population differs in the same region and different regions of our country. The dress code varies from latitude; season (winter/summer); religion (Purdhas in Muslims); the nature of work (white collar workers/ manual laborers) etc.
- There is an urgent need to revise the RDA of calcium and propose new guidelines for 25(OH)D for Indian population. Multicentre studies with a large sample size are required to generate normal standards and evolve those guidelines.
- Food fortification programs have to be thought of in various parts of the country depending on their vitamin D status and dietary calcium intake.
- The Bone Mineral Density (BMD) measured in these populations could be incorrect. Early osteomalacia could co-exist with osteoporosis in the elderly population and can give fallacious BMD values misleading the diagnosis.[64,74]
- It may not be valid to extrapolate the normogram of BMD of the west to the Indian population (a nation with diverse culture, food habits, work culture and exposure to sunlight, especially when there are racial differences in BMD, vitamin D status, metabolism etc.).
- The clinical presentation of various diseases is modified. Early osteomalacia can coexist with osteoporosis; clinical presentation of primary hyperparathyroidism is altered (the clinical presentation is that of bone disease and the adenomas are large).[78,79] Patients with primary hyperparathyroidism require vitamin D and calcium supplementation to prevent "Hungry bone syndrome" in the post operative period.
- Vitamin D insufficiency is associated with secondary

hyperparathyroidism (SHPT), which is further amplified by inadequate calcium intake. Thus, in the background of low vitamin D levels and inadequate dietary calcium intakes, when an individual is exposed to the additional insult of an environmental toxin like fluoride, the clinical expression of the disease is altered. Various studies have shown that the effect of an environmental toxin like fluoride on bone mineral metabolism is severe and more complex in children with poor dietary calcium intake when compared to the children with adequate dietary calcium intake.[79,80]

Limitations

The major limitation of the available data is to translate it to the whole country with more than a billion populations. We have limited data of populations residing at higher latitudes and altitude (soldier in Himalayas, northeastern part of India), in deserts of Rajasthan, fisherman in the sea coasts, and the rural population who are below the poverty line.

Measures

Until more data is available to document the low vitamin D status in Indian population in the length and breadth of the country, the following preventive measures could be adopted.

- Direct exposure to sunlight, at least 30 minutes/day.
- Good dietary calcium intake (equivalent to one liter of milk and milk products).
- Supplementation to lactating mothers.
- Artificial fortification of infant food products.
- Making physical training to children in the schools compulsory daily.
- If on supplements, check for optimum dosage.
- Artificial fortification of food product may have to be considered. The major limitation before making a decision on this issue is on economics. Considering the huge cost involved it would be wise to propagate and advocated direct exposure to D – liteful sunlight and fortify the food with calcium.
    a. Food fortification through the nutritious mid day meal scheme
    b. Supplementation to pregnant and lactating mother
- Preventive use of sun screens with SPF greater than 6
- Outdoor activities of the elderly and aged.

Role In Other Systems

Vitamin D is an old hormone which has been produced by lifeforms since last 750 million years with most plants and animals that are exposed to sunlight have a capacity to make vitamin D. In humans we know know that Vitamin D is critically important for development, growth and maintenance of health at all times during the life cycle from birth till old age. There is now a vast body of evidence to suggest that vitamin D deficiency as a major factor in the pathology of at least 17 varieties of cancer as well as heart disease, stroke, hypertension, autoimmune diseases, diabetes, depression, chronic pain, osteoarthritis, osteoporosis, myopathies, birth defects, periodontal disease, and many more diseases.[81]

Conclusion

In the developing countries, a scientist or medical personnel who think more seriously in terms of continuing importance of deficiency diseases per se are often derogated or relegated to quackery fringe. The result is inattention to the real deficiency diseases masquerading as other disorders that may be simply ignored altogether. We are doing disservice to these group of patients failing to diagnose vitamin D deficiency merely because of lack of proper definition if hypovitaminosis D.

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