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ORIGINAL ARTICLE

Current Scenario of Prevalence of Vitamin D Deficiency in Ostensibly Healthy Indian Population: A Hospital Based Retrospective Study

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Abstract 25-hydroxy vitamin D [25(OH) vit D] deficiency is a serious public health problem, particularly in the Indian sub-continent. The objective of the present study was to study the prevalence of 25(OH) vit D in different age groups. The data of 25(OH) vit D assay of 26,346 ostensibly healthy individuals, enrolled under executive health checkup at Medanta The Medicity, Gurgaon, over a period of 3 years, were extracted from the hospital information system and reviewed extensively. 25(OH) vit D deficiency (VDD) was defined as 25(OH) vit D < 20 ng/ml, insufficiency (VDI) as 25(OH) vit D between 20 and 40 ng/ml and 25(OH) vit D sufficiency (VDS) as 25(OH) D > 40 ng/mL. 25(OH) vit D deficiency (VDD + VDI) was observed in 93 % of the subject population. Maximum number of the subjects belonged to the age group of 41–60 years. 59 % had frank 25(OH) vit D deficiency when cut off level was <20 ng/mL. Mean value of 25(OH) vit D in our subjects was 21.4 ± 14.4 ng/mL. Significant difference in 25(OH) vit D level was observed in between male and female subjects. Simultaneously 25(OH) vit D levels were significantly lower in the patient visited hospital in winter-spring season than the summer-autumn season ($p > 0.001$). Our study demonstrates a high prevalence of 25(OH) vit D deficiency in an ostensibly healthy Indian population. There is a need for redefining our reference ranges according to our population and extensively improving the status of vitamin D.

Keywords Vitamin D deficiency · 25-hydroxy vitamin D · Nutrient · Prevalence · Ostensibly healthy Indian

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Introduction

Vitamin D deficiency is becoming a life style problem these days especially amongst older, adults and individual who do not get enough sunlight. Majority of the Indian population live in areas receiving ample sunlight throughout the year. In spite of this, vitamin D deficiency is said to prevail in epidemic proportions throughout the entire sub-continent irrespective of age, gender, race etc. [1]. Vitamin D is a fat-soluble seco-steroid prohormone produced phytochemically in the skin and plays an important role in promoting calcium absorption in the gut to maintain adequate serum calcium and phosphate concentration for normal bone mineralization [2]. Vitamin D is acquired by nutritional means (10–20 %) and also by the cutaneous synthesis under the action of sunlight (80–90 %) [3]. Its deficiency plays an important role in the development of metabolic bone diseases like rickets and osteomalacia. Recent status of 25-hydroxy vitamin D [25(OH) vit D] has been linked with several other disorders such as metabolic syndrome, diabetes, cardiovascular diseases, autoimmune diseases such as crohn's disease, rheumatoid arthritis, infections such as tuberculosis and risk of developing cancer of breast, colon, prostate and ovary [2, 4].

Vitamin D deficiency is rampant in India. Indian literature uniformly points to low 25(OH) vit D levels in various population studies, despite abundant sunshine being present in the country [5]. However, western literature has reported 25 (OH) vit D deficiencies as being rare in the Indian sub-continent [6]. Though, the last two decades have shown an increase in the series of retrospective and prospective studies, which decipher the epidemiology and clinical significance of 25-hydroxy vitamin D deficiency and its association with several diseases in the Indian population [1, 7, 8]. However, methods for measuring

25(OH) vit D levels vary widely. Two commonly used assays presented up to 80 % differences in vitamin D levels, especially at lower values [9]. Therefore the comparison of vitamin D levels between studies is not reliable unless the same assay is used or the assays are appropriately cross-calibrated. Despite being studied so much however its deficiency is still missed by clinicians. The present hospital based study, was undertaken therefore to provide the current status of vitamin D deficiency in the Indian population.

Materials and Methods

The present retrospective cross-sectional study was conducted in the Department of Biochemistry and Laboratory Services at Medanta—The Medicity, Gurgaon, India. Those cases in which 25 (OH) vit D assay had been performed on individuals visiting under executive health check-up from 1st July 2011 till 30th June 2014 were included. Data of vitamin D level, age and sex were collected from hospital information system (HIS). Serum levels of 25-hydroxy vitamin D [25(OH) vit D] (analytical measurement range is 4.0–160 ng/mL) were estimated on venous blood sample by using electrochemiluminescence method on Architect ci4100 analyser (Abbott, Max-Planck-Ring 2, Germany), having a detection limit of 4.0 ng/mL and an intra-assay and interassay coefficients of variation of 5–7 and 13–15 %, respectively. Internal and external quality control was run routinely and results were within the recommended range of assay. As per latest recommendation of International Endocrine Society on serum vitamin D level [10], subjects were divided into three groups, (1) 25(OH) vit D level < 20 ng/ml were diagnosed as vitamin D deficient (VDD), (2) 25(OH) vit D level = 20–40 ng/mL were considered as vitamin D insufficient (VDI) and 3) 25(OH) vit D > 40 ng/mL were considered as vitamin D sufficient (VDS). Those subjects having 25(OH) vit D level > 150 ng/mL were excluded from the study. Subsequently, subjects were divided into four groups as per their age, <20, 21–40, 41–60 years and age >60 years. Similarly patient data were analysed as per visit of patients in hospital during summer and autumn (1st April–30th September) and winter and spring (1st October–31st March) season.

Statistical Analysis

Results of the study were expressed in percentage. Student's t test was used to compare 25(OH) vit D values in male and female subjects. One-way analysis of variance (ANOVA) was used to compare 25(OH) vit D levels in male vs female and between different age groups. A p value < 0.05 was considered as statistically significant. Data was analyzed by using the Statistical Package for the Social Sciences software, version 12.0 for Windows.

Results

In the present study records of 26,346 ostensibly healthy subjects enrolled for executive health check-up at Medanta–The Medicity Hospital, Gurgaon, India were retrieved from hospital information system. Amongst these, 67 % were male and 33 % female with a sex ratio of 2.07:1. The mean 25(OH) vit D level in the population was found to be 21.47 ± 14.4 ng/mL (median 17.7) whereas upon segregation, in males the mean level was 20.78 ± 13.24 ng/mL (median 17.4) and 22.70 ± 16.49 ng/mL (median 18.4) in females ($p < 0.0001$) as shown in Table 1. On further evaluating these 26,346 subjects on the basis of their 25(OH) vit D status as shown in Table 2, 59 % were found to have 25(OH) vit D deficiency (<20 ng/mL) which included 69 % male and 31 % female. Similarly 25(OH) vit D insufficiency (21–40 ng/mL) was observed in about 34 % individuals including 66.5 % male and 33.5 % female. Only 7 % of the total population had sufficient 25(OH) vit D levels (>40 ng/mL) which included 56 % male and 44 % female. The mean 25(OH) vit D level in the male VDD group was 13.49 ± 3.57 ng/mL which was significantly higher as compared to the female group with 12.83 ± 3.83 ng/mL as mean value ($p < 0.0001$).

However in the VDI group, 25(OH) vit D level in male was 27.05 ± 5.18 ng/mL which was lower than the female mean level of 27.7 ± 5.33 ng/mL ($p < 0.0001$). In the VDS group, there was no statically significant difference between male and female vitamin D level.

Table 3 shows the mean 25(OH) vit D levels in male and female subjects belonging to different age groups. Only 0.2 % males were found in the <20 years age group with a mean 25(OH) vit D level of 15.55 ± 11.47 ng/mL. Similarly there were only 0.4 % females in the <20 years age group with mean value of 25(OH) vit D as 12.68 ± 3.98 ng/mL. In the 21–40 years age group there were 14.1 % males and 15.3 % females with mean 25(OH) vit D levels as 18.07 ± 13.62 ng/mL and 19.13 ± 7.20 ng/mL respectively ($p < 0.01$). Majority of the patients were

Table 1 Mean value of Vitamin D in male and female subjects

SEX	N (%)	Mean ± SD (ng/mL)	SEM	Median
Male	17,754 (67.0 %)	20.78 ± 13.24	0.093	17.4
Female	8592 (33.0 %)	22.70 ± 16.49*	0.177	18.4
Total	26,346 (100 %)	21.47 ± 14.4	0.089	17.7

*p value < 0.0001 versus male

Table 2 Sex-wise distribution of the subjects of all age group in accordance to their vitamin D status

N (%)	VDD (<20 ng/mL)		VDI (20–40 ng/mL)		VDS (>40 ng/mL)	
	15,452 (59.0 %)		8970 (34.0 %)		1924 (7.0 %)	
SEX	Male	Female	Male	Female	Male	Female
N (%)	10,705 (69.0 %)	4747 (31.0 %)	5972 (66.5 %)	2998 (33.5 %)	1077 (56.0 %)	847 (44.0 %)
Mean ± SD (ng/mL)	13.49 ± 3.57	12.83 ± 3.83*	27.05 ± 5.18	27.7 ± 5.33*	58.57 ± 21.47	60.45 ± 23.3#
SEM	0.035	0.056	0.067	0.098	0.657	0.798
Median	13.5	12.8	26.0	26.7	50.6	51.6

VDD vitamin D deficient, *VDI* vitamin D insufficient, *VDS* vitamin D sufficient

* p value < 0.0001 vs male, # p value < 0.0665 versus male

Table 3 Age and sex-wise distribution of the subjects

Characteristic	Male			Female		
Age group (years)	N = 17,754 (%)	Mean ± SD (ng/mL)	Median (SEM)	N = 8592 (%)	Mean ± SD (ng/mL)	Median (SEM)
<20	42 (0.2 %)	15.55 ± 11.47	14.1 (2.13)	31 (0.40 %)	12.68 ± 3.98	12.8 (0.83)
21–40	2503 (14.1 %)	18.07 ± 13.62	15.2 (0.289)	1313 (15.3 %)	19.13 ± 7.20#	14.8 (0.504)
41–60	9084 (51.2 %)	20.57 ± 15.5	17.0 (0.171)	4897 (57.0 %)	22.66 ± 16.55*	18.3 (0.247)
>60	6125 (34.5 %)	22.93 ± 14.29	19.6 (0.191)	2351 (27.3 %)	25.33 ± 17.20*	21.4 (0.371)

* p value < 0.0001, # p value < 0.01

Table 4 Age-wise distribution of the subjects as per Vitamin D status

Characteristic	VDD (<20 ng/mL)			VDI (20–40 ng/mL)			VDS (>40 ng/mL)		
Age group (years)	N = 15,452 (%)	Mean ± SD (ng/mL)	Median (SEM)	N = 8970 (%)	Mean ± SD (ng/mL)	Median (SEM)	N = 1924 (%)	Mean ± SD (ng/mL)	Media (SEM)
<20	70 (0.4)	13.13 ± 3.55	13.3 (0.498)	0	0	0	3	0	0
21–40	2717 (17.6)	12.86 ± 3.7	12.8 (0.709)	958 (10.6)	24.2 ± 2.8	23.8 (0.103)	142 (7.4)	30.31 ± 17.2	24.8 (0.829)
41–60	8384 (54.3)	13.29 ± 3.7	13.3 (0.403)	4624 (51.6)	27.1 ± 5.2	26.0 (0.77)	972 (50.4)	59.8 ± 22.6	51.65 (0.725)
>60	4281 (27.7)	13.6 ± 3.6	13.7 (0.586)	3387 (37.8)	27.7 ± 5.4	26.6 (0.962)	808 (42.0)	57.9 ± 21.3	49.75 (1.780)

VDD vitamin D deficient, *VDI* vitamin D insufficient, *VDS* vitamin D sufficient

found in the 41–60 years age group which included 51.2 % males and 57 % females showing a mean value of 20.57 ± 15.5 and 22.66 ± 16.55 ng/mL respectively ($p < 0.0001$). The geriatric age group comprised of 34.5 % males and 27.3 % females with mean 25(OH) vit D levels as 22.93 ± 14.29 and 25.3 ± 17.20 ng/mL respectively ($p < 0.0001$).

Table 4 shows the distribution of the subjects in the different age groups according to their vitamin D status. Only 0.4 % of the subjects were found in the age group of <20 years, however all were found to be VDD with mean 25(OH) vit D level being 13.13 ± 3.55 ng/mL. No subject in this age group was found in the VDI or VDS group. In the 21–40 years age group 17.6 % individuals had VDD with mean level of 12.86 ± 3.7 ng/mL, 10.6 % had VDI with mean level of 24.2 ± 2.8 ng/mL, whereas only 7.4 % individuals were VDS with mean vitamin D level as 30.31 ± 17.2 ng/mL. 54.3, 51.6 and 50.4 % individuals were observed in the VDD, VDI and VDS groups of 41–60 years age group, with mean 25(OH) vit D levels being 13.29 ± 3.7, 27.1 ± 5.2 and 59.8 ± 22.6 ng/mL respectively. In the geriatric age group of >60 years 27.7 % individuals had VDD with mean 25(OH) vit D level as 13.6 ± 3.6 ng/mL, 37.8 % were VDI with mean value as 27.7 ± 5.4 ng/mL and 42 % had VDS with average value of 57.9 ± 21.3 ng/mL.

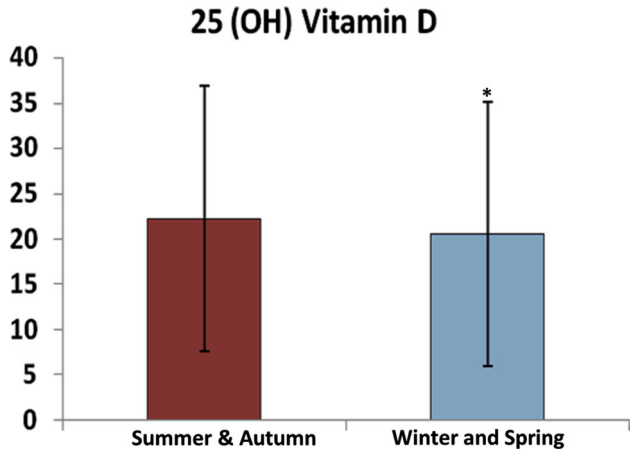

Fig. 1 Seasonal prevalence of 25-hydroxy vitamin D status in ostensibly healthy individuals. Summer and Autumn (1st April–30th September); n = 29,596, Winter and Spring (1st October to 31st May); n = 22,835, *p value < 0.001 (summer and autumn vs. winter and spring)

Simultaneously, these data were analysed into summer and winter visit of patients. Vitamin D level was significantly lower in the patient visited during winter-spring season than in the summer-autumn season ($p < 0.001$). The mean (SD) 25(OH) vit D concentration in the summer-autumn season was higher i.e. 22.2 ± 14.69 ng/mL than that in winter-spring (20.52 ± 14.56 ng/mL). Serum 25(OH) vit D concentrations of subjects in both groups are shown in Fig. 1.

Discussion

Vitamin D deficiency is now a pandemic, yet it is the most under diagnosed and under-treated nutritional deficiency in the world. Vitamin D can be obtained in sufficient amounts by most vertebrates on adequate exposure of the skin to sunlight. It is critical that most vertebrates obtain a sufficient amount of vitamin D either from their diet or from adequate exposure of the skin to sunlight [1]. Since most Indians are vegetarian and vitamin D rich dietary sources are limited and unaffordable to the socio-economically underprivileged populations, therefore sun exposure is the only major source for vitamin D. Fortified vitamin D rich supplements are available, but most Indians are not aware of the need for additional vitamin D. Additionally, the cost of vitamin D rich/fortified supplements is also a major challenge in India. Vitamin D fortification of food may improve hypovitaminosis of vitamin D in the Indian population. Simultaneously in a country like India, cultural and social taboos often dictate lifestyle patterns such as clothing-that may limit sun exposure and vegetarianism-which limits vitamin D rich diet option [1]. The present retrospective study included 26,346 subjects in which 67 % were male and 33 % female. Total prevalence of 25 (OH) vit D deficiency (VDD + VDI) was 93 % in which 34 % subjects were 25(OH) vit D insufficient and 59 % had frank deficiency. Highest prevalence of vitamin D deficiency was observed in male i.e. 60 % whereas, 55 % female was vitamin D deficient. Similarly vitamin D insufficiency (VDI) was observed to be 34 % in male and 35 % in female whereas VDS was seen in only 6 and 10 % male and female subjects respectively. The mean 25(OH) vit D level in our subject population was 21.47 ± 14.4 ng/mL, which was lower than the normal range. This observation may be explained by the fact that most of the subjects were residents of metropolitan cities with high population areas and were living in over-crowed tenements, which were closely packed and 5–6 stories high, consequently limiting the exposure to sunlight in the privacy of one's home. Lack of space also limited the options for outdoor activities and recreation. Atmospheric pollution in big cities also affects the exposure of UV rays to the skin and interferes in vitamin D synthesis [1]. On age wise analysis of population, vitamin D level increased with every two decades in the male and female subjects. Vitamin D deficiency and insufficiency was maximum in population belong to 41–60 years age group, as probably the large number of these subjects underwent executive health check-up. Also cutaneous production of Vitamin D declines with age. Most often the elderly have to be confined indoors for prolonged periods of time which further enhances the problem [11]. At present, diagnosis of vitamin D level is one of the most ordered tests by the Indian clinician due to increase awareness in its widespread prevalence of deficiency in different populations of India. Since maximum individuals of our study belonged to the middle and upper socio-economic strata and were aware for the need of routine health check-up.

Vitamin D levels were found to be significantly different in the male and female subjects of VDD and VDI groups of our study ($p < 0.05$). Social and religious norms of public modesty related to our culture warrant most parts of the body to be covered especially in females. Furthermore the desire to obtain a fairer skin complexion in females may extinguish any desire for any sun exposure. The use of sunscreen and umbrella does not help either. In the blazing heat of India the quest to obtain sufficient vitamin D levels takes a backseat and improvement in vitamin D status cannot be attained only by sunlight exposure. The darker Indian skin does not produce significant amount of vitamin D when compared to individual with fairer skin, hence dark skinned individuals require greater duration of exposure than their light- skinned counterparts to synthesize comparable amounts of vitamin D [12–14]. Skin pigment is probably a major factor in the low 25 (OH) D levels in the Indian

sub-continent despite abundant sunshine. Our study showed females however to have marginally higher levels of vitamin D in comparison to males. Though, no confirmatory genetic or hormonal study has been reported till date yet gender may be an important factor for vitamin D deficiency. Various studies have shown that since females have a higher prevalence of osteoporosis than male and experience a sudden drop of oestrogen production at menopause [15], therefore most women are encouraged to take calcium and iron supplements at an earlier age which may be one of the reasons for increased vitamin D level in females as compared to males. Use of sunscreen could be one of the factors that affect vitamin D level. Few authors have reported that sunscreens block the cutaneous absorption of UV-B radiation and prevent sunburn. So sunscreen use may lower the vitamin D levels but in a practical matter, very few people put on enough sunscreen to block all UVB light, or they use sunscreen irregularly. So the effect of sunscreen on vitamin D levels may not be considered significant. However, Matsuka et al. [13] showed that the long-term use of sunscreens may be associated with low body stores of vitamin D in some persons. Thus, it was the limitation of our study that we could not collect any information regarding calcium and iron supplementation taken by our subjects as well as duration and amount of sunscreens used by females and males. Further analysis of prevalence of vitamin D status in different age groups showed maximum subjects of all age group i.e. adolescence, younger, middle and elderly as vitamin D deficient (97, 71, 60 and 50 % respectively). Vitamin D deficiency in children and adults can cause growth retardation and skeletal mineralization defect which is a major health concern in India [16]. Since most of the Indians do not get adequate sun exposure to produce sufficient amounts of vitamin D endogenously, this may lead to a major cause of deficiency. Earlier countrywide studies have reported vitamin D deficiency as being very prevalent in India [1] even healthy young soldiers and sports woman with sufficient intake of calcium, adequate sun exposure and regular exercise regimen were found to be vitamin D deficient [7, 17]. Studies have shown that the 25(OH) D levels are directly proportional to the duration of exposure to sunlight [7, 18]. The amount of UV light at a geographical location depends on the length the sun's rays which have to travel through the atmosphere, where it is more or less absorbed. Countries at latitudes nearer to the equator receive more sunlight yearly compared to those nearer the poles, which also changes with seasons. The northern and southern hemispheres are tilted towards the sun from April to September and October to March, respectively. Therefore, both latitude and seasons influence the degree of possible solar radiation a population may receive. The literature reports strong evidence that hypovitaminosis D is greater in winter months for all age groups in Asia, Europe, Latin America, Middle East, North America, and Oceania [11]. However, in very hot countries and where the majority of women wear veils, vitamin D levels were not significantly higher and were even lower in the summer months, as these women avoided the heat and sun by staying indoors. Our study also found the same outcome with 25 (OH) D levels being significantly higher in summer/autumn season with respect to winter/spring season however value was still lower than the normal reference range. This result also follows the report of Goswami et al. [7] showed that despite of abundant sunlight, healthy persons in Delhi remained vitamin D deficient. This may be because of skin pigmentation, inadequate direct sun exposure as well as low-calcium, high-phytate diets, pregnancy, and winter-related reduced sunlight exposure which may affect vitamin D levels.

Limitation of the Present Study

In spite of major outcomes of current prevalence of vitamin D status, this study had some limitations. We could not collect information regarding dietary vitamin D intake, UVB exposure, sunscreen use or measures of adiposity and calcium levels. Regarding multi-vitamin use, we do not have any data on vitamin D content or adherence, which may confound the effects of multivitamin use in different subgroups. Therefore, current retrospective data does not throw insight on longitudinal changes in vitamin D.

Conclusion

The present study clearly demonstrated the high prevalence of vitamin D deficiency in an otherwise healthy Indian population. Sun exposure is an untenable solution for most individuals in conjunction with low calcium intake makes matters worse. Scheme for conducting awareness program on vitamin D deficiency should be started from government as well as private organization at the local level to impart the importance of vitamin D and its clinical significance. The need of the hour is to develop reference values with respect to the Indian population. Further prospective studies are warranted to establish continent wise reference range and restrict USA criteria for defining various categories of Vitamin D deficiency.

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Compliance with Ethical Standards

Conflict of interest Authors declares no conflict of interest.

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