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Vitamin D status in Indian subjects: a retrospective analysis

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ABSTRACT

Background: The objective of the study was to conduct a systematic evaluation of vitamin D status in pan India population, to provide a comprehensive depiction of the vitamin D status among Indians.
Methods: This retrospective, cross-sectional, multicentric study considered data of subjects (≥18 years) who underwent 25(OH)D test at vitamin D screening camps, conducted at 229 sites across 81 cities in India. Primary study variables were proportion of subjects with vitamin D (25(OH)D) - severe deficiency (<5 ng/ml)/ deficiency (≥5-<20 ng/m)/ insufficiency (≥20-<30 ng/ml)/ sufficiency (≥30-<150 ng/ml) and toxicity (≥150 ng/ml).
Results: Data from 4624 subjects (mean SD) age: 45.4 (14.5 years) was considered for this analysis. A total of 3552 (76.9%) subjects had vitamin D level of <30 ng/ml, including 41 (0.9%) subjects with severe deficiency, 2310 (50.0%) subjects with deficiency and 1201 (26.0%) subjects with insufficiency. Prevalence of vitamin D level of <30 ng/ml was found marginally higher in males (77.3%) than females (76.5%). Analysis of zonal data revealed that prevalence of vitamin D level <30 ng/ml was highest in east India (83.4%) followed by south (81.6%), west (76.3%) and north (73.3%). The incidence of vitamin D level <30 ng/ml was highest in the age-group of ≥18-≤30 years (82.5%), followed by >30-≤ 40 (80.4%), >40-≤50 (76%) and >50-≤65 (74.1%) years groups.
Conclusions: Our study indicates a high prevalence of vitamin D deficiency/insufficiency in the Indian population irrespective of sex, age, and location. These clinically identified cases represent only a part of a bigger concern, necessitating the need for optimal public health action.

Keywords: Vitamin D deficiency, 25-hydroxy vitamin D, Prevalence

INTRODUCTION

Vitamin D is a fat-soluble vitamin that plays a vital role in human physiology.[1] Vitamin D has essential roles in the metabolism of calcium and phosphorus, that are required for normal mineralization of bone, muscle contraction, nerve conduction, and general cellular function in all the body cells.[1,2] It is also found to be important for immune function, inflammation, cell proliferation, and differentiation.[3,4] The uniqueness of vitamin D lies in the fact that not only it can be ingested in the diet as cholecalciferol (vitamin D3) or ergocalciferol (vitamin D2), but can also be synthesized in the skin through adequate sunlight exposure.[5]

The dominant source of vitamin D in humans is the endogenous production of vitamin D3 in the skin following exposure to ultraviolet-B (UVB) (290-320) nm radiation from sunlight.[6] But, despite the dual mechanisms of attainment (diet and sunlight), vitamin D deficiency is very common globally, with a significant geographical variation.[5] Asians, particularly people in south Asia and the middle east region, are reported to have a poor vitamin D status despite adequate sunshine in their regions.[5,7]

Circulating 25-hydroxy vitamin D 25(OH)D is considered the best determinant of vitamin D status in an individual. The vitamin D levels are categorized as deficient when 25(OH)D is <20 ng/ml, insufficient when ≥20-29 ng/ml

and sufficient when ≥30 ng/ml.[8] Vitamin D deficiency has recently been recognized as a widespread global disorder and common in metropolitan cities of the world and India.[9,10] Particularly prevalent among elderly people, it is estimated that 1 billion people globally have vitamin D deficiency or insufficiency.[11]

Although India is located between 8.4° and 37.6° north latitude and the majority of the Indian population is exposed to sufficient sunlight throughout the year, the prevalence of vitamin D deficiency in the Indian population ranges from 34.5% to 99%; with community-based and hospital-based Indian studies reporting a prevalence ranging from 34.5% to 94% and 37% to 99%, respectively.[9,12-33]

Vitamin D deficiency results in a variety of skeletal and extra-skeletal manifestations.[1] Recently vitamin D deficiency has also shown to be associated with colorectal cancer, diabetes mellitus, infection, multiple sclerosis, cardiovascular disease, breast cancer, autoimmunity and allergy, depression, and postural instability.[5] Although these associations have been identified mostly in observational studies which may be subject to many interpretations, the lack of randomized controlled study data in these areas does not negate these causative relationships.[5] Additionally, an increasing number of studies have suggested that vitamin D may influence other important health outcomes in infants, children, and pregnant and lactating women.[2]

Owing to its wide-ranging impact on health, the epidemic of vitamin D deficiency in India is likely to significantly contribute to the enormous burden on the healthcare system.[8] However, in a large country like India covering several latitudes, ethnicities, cultures, traditions, and attitudes, the current data on vitamin D status is inadequate and classified in different ways, making interpretation difficult.[7] At present, there is no Pan-India data depicting the extent of vitamin D deficiency among Indians, and also across different age groups. The objective of the present retrospective, cross-sectional, multicentric study was to evaluate the vitamin D levels in the pan Indian populace at large, in order to provide a comprehensive picture of the vitamin D status among Indians.

METHODS

Study design and population

In this retrospective, cross-sectional, multicentric study, data were collected from the medical records of subjects who underwent 25(OH)D testing at vitamin D screening camps conducted at 229 sites across 81 cities in India, between February and June 2019.

Data of subjects ≥18 years of age, having valid records, was considered for this retrospective analysis. Subject records having incomplete information were excluded. The data was collated from central laboratory information management systems of SRL Limited, Mumbai, India. The laboratory data included subjects' demographic details (sex, age, and city of residence) and results of 25(OH)D test.

The study was conducted in conformity with the principles of the declaration of Helsinki, international council for harmonization-good clinical practices (ICH-GCP) guidelines, Indian council of medical research, Indian GCP guidelines, and as per the approved protocol. The process of data analysis was only initiated after approval from the independent ethics committee. Since this was a retrospective data collection study, informed consent was not required. Patient confidentiality was maintained during the data entry and analysis process.

Assessments

Vitamin D status in Indian population was categorized as.[34,35] Severe vitamin D deficiency: (25(OH)D) <5 ng/ml, vitamin D deficiency: (25(OH)D) ≥5 –<20 ng/ml, vitamin D insufficiency: (25(OH)D) ≥20-<30 ng/ml, vitamin D sufficiency: 25(OH)D ≥30-<150 ng/ml and vitamin D toxicity: 25(OH)D ≥150 ng/ml.

Study variables

The primary study variables were the proportion of subjects with vitamin D deficiency/ insufficiency/ sufficiency and toxicity. The secondary study variables included proportion of subjects categorized with severe vitamin D deficiency, proportion of subjects categorized with vitamin D severe deficiency/ deficiency/ insufficiency/ sufficiency and toxicity on the basis of sex, age groups (≥18-≤30, >30-≤40, >40-≤50, >50-≤65, and >65 years), zone (north/ south/ east/ west), along with further bifurcation of sex and age group prevalence on the zonal (north/ south/ east/ west) basis.

Statistical analysis

Qualitative (categorical) and quantitative (continuous) variables are presented using descriptive statistics. Qualitative variables were evaluated by the chi-square to assess the relationships between variables in the study population, and the corresponding p value is presented. Data were analyzed using SPSS® statistics software, version 23.0 (Armonk, NY, USA: IBM Corp.).

Ethical approval

Data analysis was initiated after approval from independent ethics committee.

RESULTS

Out of 4785 Indian subjects, data of 4624 (male:female-1647:2977) with the mean (SD) age of 45.4 (14.5) years, meeting eligibility criteria, was considered for this

retrospective data analysis. The demographic characteristics of the subjects are summarized in Table 1.

Out of 4624, 3552 (76.9%) subjects had vitamin D level of <30 ng/ml, which included 41 (0.9%) subjects with severe deficiency (<5 ng/ml), 2310 (50.0%) subjects with deficiency (≥5-<20 ng/ml) and 1201 (26.0%) subjects with insufficiency (≥20-<30 ng/mL). The analysis of zonal data revealed that the prevalence of vitamin D level <30 ng/ml was highest in east India. Out of 458 subjects in the east zone, 382 (83.4%) subjects had vitamin D level of <30 ng/ml, which included 04 (0.9%) subjects with severe deficiency (<5 ng/ml), 239 (52.2%) subjects with deficiency (≥5-<20 ng/ml) and 139 (30.3%) subjects with insufficiency (≥20-<30 ng/ml).

The vitamin D levels were comparable in the other 3 zones. The incidence of vitamin D level <30 ng/ml was 81.6% in south India, followed by 76.3% and 73.3% in the west and north India, respectively. Results of the chi-square (χ^2) test showed a significant association between zones and vitamin D status (χ^2 12, (N=4624)= 63.083, p<0001) in Indian subjects. The prevalence of vitamin D level <20 ng/ml was 51.8% in north India, followed by 51.6% and 49.3% in south and west India, respectively. Vitamin D status in the Indian population along with zonal distribution is illustrated in Figure 1.

Vitamin D status in the Indian population overall and as per age-group is summarized in Table 2. In the Indian population, the prevalence of vitamin D level <30 ng/ml was higher in the age-group of ≥18-≤30 years. Out of 863 subjects in ≥18-≤30 years age-group, 712 (82.5%) subjects had vitamin D level of <30 ng/ml, which included 11 (1.3%) subjects with severe deficiency (<5 ng/ml), 523 (60.6%) subjects with deficiency (≥5-<20 ng/ml) and 178 (20.6%) subjects with insufficiency (≥20-<30 ng/ml).

Table 1: Summary of demographic characteristics and vitamin D status.

Variables	Total		North		South		East		West	
Subjects	**4624**		**1513**		**731**		**458**		**1922**	
Sex n (%)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Male	1647	35.6	535	35.4	279	38.2	161	35.2	672	35.0
Female	2977	64.4	978	64.6	452	61.8	297	64.8	1250	65.0
Age (years)										
Mean±SD	45.4±14.5		44.5±14.1		45.3±15.1		47.5±14.1		45.5±14.6	
Minimum-maximum	18-92		18-90		18-85		18-90		18-92	
Range	74		72		67		72		74	

Table 2: Vitamin D status in Indian population - age group distribution.

Age groups (years)	Total		≥18-≤ 30		>30-≤ 40		>40-≤ 50		>50-≤ 65		>65	
Subjects	**4624**		**863**		**1056**		**1058**		**1224**		**423**	
Vitamin D status n (%)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Severe deficiency	41	0.9	11	1.3	10	0.9	11	1.0	07	0.6	2	0.5
Deficiency	2310	50.0	523	60.6	587	55.6	526	49.7	526	43.0	148	35.0
Insufficiency	1201	26.0	178	20.6	252	23.9	268	25.3	373	30.5	130	30.7
Sufficiency	1071	23.2	151	17.5	207	19.6	253	23.9	317	25.9	143	33.8
Toxicity	01	0.02	0	0	0	0	0	0	01	0.1	0	0

The prevalence of vitamin D levels <30 ng/ml was 80.4% in >30-≤ 40 years age-group, followed by 76% and 74.1% in >40-≤50 and >50-≤65 years age-groups, respectively; and minimum in >65 years age group at 66.2%. Likewise, the prevalence of vitamin D level <20 ng/ml was 56.5% in >30-≤ 40 years age-group, followed by 50.7% and 43.6% in >40-≤50 and >50-≤65 years age-groups, respectively; and minimum in >65 years age group at 35.5%. Further, data indicated a significant association between age and vitamin D status (χ^2 16, (N = 4624) =131.316, p<0001) in Indian subjects.

The zonal data also revealed the same trends. In the Indian population, the prevalence of vitamin D <30 ng/ml was also found to be higher in ≥18-≤30 years age-group and was maximum in east India (90.2%), followed by south (85.3%) and west India (83.5%). However, in north India, the prevalence of vitamin D <30 ng/ml was higher in >30-≤40 years age-group at 79.5%. Similarly, the prevalence of vitamin D level of <20 ng/ml was found to be highest in the age-group of ≥18-≤30 years across all the four zones; and was highest in east India (73.8%), followed by west (63.0%), north (59.7%) and south India (59.0%). The results are summarized in Table 3.

The prevalence of vitamin D level of <30 ng/ml was marginally higher in males than in females. Out of 1647 males, 1273 (77.3%) had vitamin D level of <30 ng/ml, which included 7 (0.4%) males with severe deficiency (<5 ng/ml), 818 (49.7%) with deficiency (≥5-<20 ng/ml) and

448 (27.2%) with insufficiency (≥20-<30 ng/m). Similarly, out of 2977 females, 2279 (76.5%) subjects had vitamin D level of <30 ng/ml, which included 34 (1.1%) females with severe deficiency (<5 ng/ml), 1492 (50.1%) females with deficiency (≥5-<20 ng/ml) and 753 (25.3%) females with insufficiency (≥20-<30 ng/ml). The result of the chi-square test also revealed that there was no association between sex of subject and vitamin D status (χ^2 (4, N=4624) = 8.458, p>0.05.

The zonal data revealed that the prevalence of vitamin D level of <30 ng/ml was relatively higher in male than in female subjects in the north zone (male: 76.3%; female: 71.4%), reasonably higher in female subjects in the south zone (male: 79.2%; female: 83.0%) and the east zone (male: 79.5%; female: 85.5%); but comparable between male and female subjects in the west zone (male: 76.8%; female: 75.9%).

Table 3: Vitamin D status in Indian population - overall and zonal distribution as per age group.

Age groups (years)	Zonal total		≥18-≤30		>30-≤40		>40-≤50		>50-≤65		>65	
North zone												
Subjects (n)	**1513**		**290**		**376**		**360**		**369**		**118**	
Vitamin D status n (%)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Severe deficiency	12	0.8	04	1.4	02	0.5	03	0.8	02	0.5	01	0.8
Deficiency	772	51.0	169	58.3	220	58.5	186	51.7	159	43.1	38	32.2
Insufficiency	325	21.5	54	18.6	77	20.5	72	20.0	91	24.7	31	26.3
Sufficiency	404	26.7	63	21.7	77	20.5	99	27.5	117	31.7	48	40.7
Toxicity	0	0	0	0	0	0	0	0	0	0	0	0
South zone												
Subjects (n)	**731**		**156**		**156**		**135**		**208**		**76**	
Severe deficiency	0	0	0	0	0	0	0	0	0	0	0	0
Deficiency	377	51.6	92	59.0	80	51.3	71	52.6	102	49.0	32	42.1
Insufficiency	219	30.0	41	26.3	43	27.6	40	29.6	67	32.2	28	36.8
Sufficiency	134	18.3	23	14.7	33	21.2	24	17.8	38	18.3	16	21.1
Toxicity	01	0.1	0	0	0	0	0	0	01	0.5	0	0
East zone												
Subjects (n)	**458**		**61**		**97**		**112**		**144**		**44**	
Severe deficiency	04	0.9	0	0	03	3.1	01	0.9	0	0	0	0
Deficiency	239	52.2	45	73.8	57	58.8	56	50.0	69	47.9	12	27.3
Insufficiency	139	30.3	10	16.4	26	26.8	36	32.1	50	34.7	17	38.6
Sufficiency	76	16.6	6	9.8	11	11.3	19	17.0	25	17.4	15	34.1
Toxicity	0	0	0	0	0	0	0	0	0	0	0	0
West zone												
Subjects (n)	**1922**		**356**		**427**		**451**		**503**		**185**	
Severe deficiency	25	1.3	07	2.0	05	1.2	07	1.6	05	1.0	01	0.5
Deficiency	922	48.0	217	61.0	230	53.9	213	47.2	196	39.0	66	35.7
Insufficiency	518	27.0	73	20.5	106	24.8	120	26.6	165	32.8	54	29.2
Sufficiency	457	23.8	59	16.6	86	20.1	111	24.6	137	27.2	64	34.6
Toxicity	0	0	0	0	0	0	0	0	0	0	0	0

Table 4: Vitamin D status in Indian population - overall and zonal distribution as per sex.

Variables	Total				North				South				East				West			
Subjects	4624				1513				731				458				1922			
Sex (n)	Male		Female		Male		Female		Male		Female		Male		Female		Male		Female	
	1647		2977		535		978		279		452		161		297		672		1250	
Vitamin D status	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Severe deficiency	07	0.4	34	1.1	01	0.2	11	1.1	0	0	0	0	0	0	04	1.3	06	0.9	19	1.5
Deficiency	818	49.7	1492	50.1	301	56.3	471	48.2	128	45.9	249	55.1	68	42.2	171	57.6	321	47.8	601	48.1
Insufficiency	448	27.2	753	25.3	106	19.8	219	22.4	93	33.3	126	27.9	60	37.3	79	26.6	189	28.1	329	26.3
Sufficiency	374	22.7	697	23.4	127	23.7	277	28.3	58	20.8	76	16.8	33	20.5	43	14.5	156	23.2	301	24.1
Toxicity	0	0	01	0.03	0	0	0	0	0	0	01	0.2	0	0	0	0	0	0	0	0

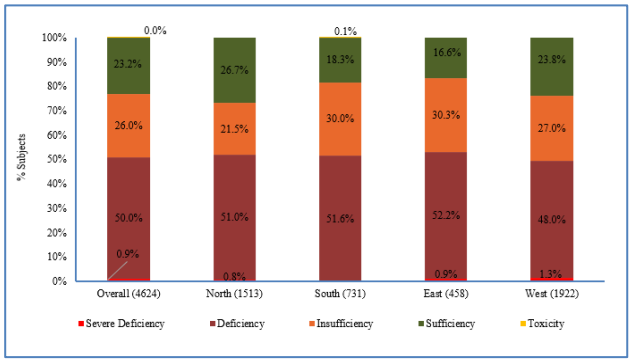

Figure 1: Vitamin D status in Indian population along with zonal distribution.

Likewise, the prevalence of vitamin D levels <20 ng/ml was relatively higher in male than in female subjects in north India (male: 56.5%; female: 49.3%), and comparatively higher in females in the south (male: 45.9%; female: 55.1%) and east India (male: 42.2%; female: 58.9%). The prevalence of vitamin D level of <20 ng/ml was comparable between male and female subjects in west India (male: 48.7%; female: 49.6%).

The further assessment of zone wise vitamin D status in male and female subjects revealed that there was a significant association between zones and vitamin D status in males (χ^2 (9, N=1647)=35.740, p=0.000) and in females (χ^2 (12, N=2977)=63.083, p<0.001), Indian subjects. The results are presented in Table 4.

DISCUSSION

The global prevalence of vitamin D deficiency/ insufficiency is increasing irrespective of age, gender, race, and geography, and India is no exception. The intent of the present retrospective, cross-sectional, multicentric study was to conduct a systematic evaluation of vitamin D status in pan India population, in order to provide a comprehensive picture of the vitamin D status among Indians.

Data of 4624 Indian subjects (male: female-1647:2977) with the mean (SD) age of 45.4 (14.5) years, was considered for this retrospective analysis. Data revealed that in the Indian population, the prevalence of vitamin D levels <30 ng/ml and <20 ng/ml was 76.9% and 50.9%, respectively. The rate of vitamin D deficiency (<20 ng/ml) reported in our study is comparatively less than that reported in other studies, conducted amongst apparently healthy Indians.[8,30] Country wide studies have reported vitamin D deficiency (<20 ng/ml) as high as 70%–100% in ostensibly healthy individuals.[8] A pan India study among healthcare professionals revealed that 94% of the subjects had vitamin D levels <30 ng/ml and 79% of the subjects were vitamin D deficient (<20 ng/ml).[30]

The result of this retrospective analysis indicated a significant (p<0.0001) association between zones and vitamin D status in Indian subjects; suggesting that the lifestyle of people in the four different zones of India has an impact on their vitamin D status. In our study prevalence of vitamin D level <30 ng/ml and <20 ng/ml amongst people from north India was 73.3% and 51.8%, respectively. However, other studies from north India have reported vitamin D deficiency (<20 ng/ml) rate ranging from (78.3-94.3) % including studies from Lucknow, Kashmir, Punjab, and Delhi in healthy individuals.[17,20,23,24,28,36,37]

The prevalence of vitamin D level <30 ng/ml and <20 ng/ml from south India in our study was 81.6% and 51.6%, respectively. This is similar to 50% and 56.3% incidences of vitamin D levels <20 ng/ml reported among the urban elderly from Tirupati and Hyderabad, respectively.[12,22] However, authors from southern India have also reported a higher prevalence rate of (66.5-82)% for vitamin D levels <20 ng/ml.[19,25,33]

The prevalence rate of 83.4% for vitamin D level <30 ng/ml and 53.1% for vitamin D level <20 ng/ml was reported from east India in our study. This is similar to 51% prevalence of vitamin D levels <20 ng/ml reported from a study by Srimani et al from West Bengal, but comparatively lower than 84.9% and 92.5% reported in a study from Cuttack and Kolkata.[14,16,29] Our study reported prevalence of vitamin D level <30 ng/ml as 76.3% and <20 ng/ml as 49.3% amongst subjects from west India; which is comparatively lower than the incidence rate of 70% and 87.5% reported in healthy individuals, in studies by Shivane et al and Multani et al from Mumbai.[32,37]

In our study, the prevalence of vitamin D level of <30 ng/ml in male and female subjects was 77.3% and 76.5%, respectively; and vitamin D level of <20 ng/ml was 50.1% and 51.2%, respectively. The vitamin D status was comparable (p>0.05) between both sexes, implying that the sex of the subject has no influence on vitamin D status in the Indian population. Vitamin D is a very important nutrient for women's health. In this retrospective analysis, vitamin D levels of <20 ng/ml were reported in 51.2% female subjects. Result reported in our study are similar to 50% and 53.3% incidence of vitamin D levels <20 ng/ml reported by Paul and Tandon et al, but comparatively lower than 64%, 74%, 76%, 88% and 90.8% reported by Garg et al, Sahu et al, Harinarayan et al, Shivane et al, Sofi et al, and Misra et al, respectively.[15,18,19,21,22,26,38,39]

Vitamin D deficiency in adults was previously thought to be limited to older persons.[40] But the result of this retrospective analysis revealed that the prevalence of vitamin D level of <20 ng/ml was highest in the age-group of ≥18-≤30 years (61.9%), with the trend resonating across all the four zones of India; and data revealing a significant (p<.0001) association between age group and vitamin D status in Indian subjects. Bone mineral density (BMD) studies in healthy Indians also showed that a significant proportion of younger Indians too are suffering from this silent disease.[8] In a study by Shivane et al, out of 1137

patients in the age group of 25-35 years, 70% had vitamin D levels of <20 ng/ml.[38] Likewise, in a study by Garg et al, 65.5% of females in the age group of <30 years were found to be vitamin D deficient.[39] Similarly, even healthy young soldiers with adequate consumption of calcium, adequate sun exposure, and regular exercise regimen were found to be vitamin D deficient, as were young sportswomen.[8]

The assessment of vitamin D status is a continuous process. This fat-soluble vitamin plays an important role in brain homeostasis, neurodevelopment, immunological modulation, aging, and also, importantly, in gene regulation.[41] Vitamin D binds to more than 2700 genes and regulates the expression of more than 200 of them; including genes responsible for the regulation of cellular proliferation, differentiation, apoptosis, and angiogenesis.[41,42] Of immense interest is the role vitamin D can play in decreasing the risk of many chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, and cardiovascular disease.[42] Despite its health benefits, lack of awareness about the importance of maintaining optimal vitamin D levels has been one of the main reasons for the global spread of this nutritional disorder.[43] Awareness campaigns about vitamin D at the community level and among health care professionals of all specialties are required to ensure optimal vitamin D level, irrespective of age or sex, to prevent the complications that are associated with its deficiency.

To best of our knowledge, this is the first of its kind pan-India study evaluating vitamin D status in the general Indian population. The previous Indian studies assessing vitamin D status in the Indian population have primarily been community-based or hospital-based.[12-33] This retrospective analysis has made an effort to present insight into vitamin D status not only in the Indian populace at large but also on the basis of sex, age-group, and zones.

Our study has certain limitations. Retrospective design and sample size not statistically powered can limit the inference-drawing ability of this study. However, we have used data from a central lab, which originated from the uniform analytic method platform; and analyzed data using standard definitions of conditions and outcomes. Moreover, we feel the results of this retrospective analysis will be useful for providing preliminary data and guiding the development of future prospective studies.

CONCLUSION

Vitamin D deficiency/insufficiency is prevalent among the Indian population, irrespective of sex, age, and geographical location. Despite the close link of vitamin D with human health, vitamin D deficiency/insufficiency is still not widely recognized as a problem in India. Greater awareness about the multiple consequences of vitamin D deficiency/insufficiency is required among clinicians and patients to enable them to foresee the burden of this silent epidemic. Additionally, a concerted effort on the policy, medical, and social fronts will be required to combat this preventable epidemic.

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