

# Is there A Need to Reasses Reference Levels of Vitamin D for India?-A Preliminary Survey of Vitamin D Levels in the Normal Population of Punjab

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**Abstract:** Introduction: Majority of population of India including the state of Punjab lives in areas receiving ample sunshine throughout the year. Despite this fact various studies have shown wide prevalence of vitamin D deficiency in Indians. There is a need to establish reference ranges for vitamin D in Indian population as the referral values currently being used are based on western studies. The actual prevalence of vitamin D deficiency then needs to be re-evaluated in our population based on these new reference ranges. This is because a large number of Indians have lower levels of vitamin D without actual signs and symptoms of deficiency. Aims & Objectives: The present pilot study was planned to get a preliminary estimate of vitamin D levels present in healthy normal population of Punjab. Methodology: The study subjects included were 52 healthy adults who did not have any signs and symptoms of Vitamin D deficiency. Serum Vitamin D levels were estimated in all the subjects by Chemiluminiscence method. Other parameters measured were serum Calcium, Phosphorous, Albumin, Total protein, Alkaline Phosphatase (ALP) & Cholesterol. Results: Vitamin D levels in the subjects ranged from 10.5 to 49.19 nmol/l with a mean value of 16.88 nmol/l. None of the subjects had sufficient levels (75-250 nmol/l) of vitamin D whereas 45 had frank deficiency (<25nmol/l) & 7 had insufficient levels (25-74nmol/l). Therefore 86.5% of subjects had deficient levels of vitamin D. The levels of other parameters like serum Calcium, Phosphorous, ALP, Albumin, Total Protein & Cholesterol were within normal limits in all the subjects. There was no significant correlation between vitamin D levels & the other parameters like calcium, ALP, & Cholesterol. Conclusion: The present study gave us a preliminary estimate of vitamin D levels in normal healthy outdoor population. There is an urgent need to conduct further studies on a much larger scale with more parameters in the general population of India of different age groups, sexes and ethnic groups to re-evaluate the reference ranges currently being used to label Indian population as vitamin D deficient.

**Keywords:** Vitamin D, Normal population, India, Reference levels, Punjab

## 1. Introduction

There is widespread prevalence of vit D defi in the world and it is re-emerging as a major health problem globally<sup>(1)</sup>. But it is seen that VDD is not uncommon in India also<sup>(2,3,4,5)</sup> and has been reported in all age groups including toddlers, school children, pregnant women, neonates, adult males & females residing in rural or urban areas<sup>(6,7,8,9,10,11,12)</sup>. This high prevalence has been attributed to a number of factors like poor sun exposure, skin complexion, vegetarian food habits & a lack of vitamin D fortification programme in our country, older age, female sex and increasing pollution<sup>(1,2,4,5,13)</sup>. Although there is adequate sunshine in India high temperatures during daytime and sultry humid climate are deterrants to sun exposure<sup>(2)</sup>.

The reference ranges currently used for evaluating vitamin D levels in Indians are the same as given in Western literature<sup>(2,14,15,16,17)</sup>. There are almost no studies till date done in Indian population for the purpose of establishing reference ranges for our country. This is important as India being a country with ample sunshine has such high prevalence of vitamin D deficiency.

Even though many factors can lead to vitamin D deficiency there is a doubt as to whether we are following the correct reference ranges for our country. Therefore the present study was planned with the purpose of evaluating vitamin D status in normal individuals.

## 2. Materials & Methods

The present study was conducted after obtaining permission from the ethics committee of the hospital. The study was carried out in 52 adult subjects after obtaining informed consent from them. The study subjects included were relatives of patients visiting out patient of surgery department of the hospital. They were apparently healthy individuals who had ample exposure to sunlight, worked outdoors, did not use sunblock and included field workers, agriculturists, policemen, labourers etc. Only those individuals were included in the study who had no signs & symptoms of vitamin D deficiency & were not taking any vitamin D supplements. Various parameters like vitamin D, calcium, phosphorous, total proteins, albumin, Alkaline Phosphatase (ALP) & cholesterol were evaluated in serum of these subjects. Vitamin D levels were analysed on a chemiluminescent analyser. The reference ranges of vitamin D followed in this study were those specified with the chemiluminescent analyser.

Deficiency - < 25 nmol/L  
Insufficiency - 25-74 nmol/L  
Sufficiency - 75-250 nmol/L  
Toxicity - > 250 nmol/L

### 3. Results

Vitamin D levels in the 52 study subjects ranged between 10.5 & 49.19 nmol/L with a mean level of 16.88 nmol/L. None of the subjects had sufficient levels of vitamin D whereas 86.5% had frank deficiency and 13.46% had insufficient levels (Graph 1). Levels of all other parameters like Calcium, Phosphorous, ALP, Total Protein, Albumin & Cholesterol were within normal limits (Table 1). There was no significant correlation seen of levels of vitamin D with other parameters like Calcium, ALP & Cholesterol (Table 2).

### 4. Discussion

Vitamin D is very essential for the normal functioning of our body as it serves many functions. It has been directly related to bone health in men & women of all ages<sup>(18)</sup>. Maternal vitamin D sufficiency is required for proper fetal & tooth development<sup>(19,20)</sup>. Also vitamin D deficiency has been associated with increased prevalence of type II Diabetes Mellitus, cardiovascular disorders, auto-immune disorders like multiple sclerosis, tuberculosis, many types of malignancies like that of prostate, breast, ovaries, bladder, colon etc<sup>(4,21,22,23,24)</sup>. The elderly have strong need for vitamin D as cancers & osteoporotic fractures are the most likely among them and they spend less time in sunlight and their efficiency of photoproduction is less<sup>(25,26,27,28)</sup>. Numerous Indian studies have shown widespread deficiency in all ages, sexes and people of all walks of life<sup>(2,3,4,6,7,8,9,10)</sup>.

In our study we wanted to make a preliminary survey of vitamin D levels in normal healthy population and see how many people were deficient according to the currently used reference ranges. We excluded children and elderly subjects from the study and we found that out of 52 subjects none had sufficient levels of vitamin D. We did not see any correlation between the low vitamin D levels & calcium levels, between vitamin D & ALP levels and between vitamin D & cholesterol levels. This means there was no decrease in serum calcium levels with grossly decreased calcium levels. Also the precursor required for vitamin D synthesis ie cholesterol was also within normal limits in the study subjects. Similarly ALP levels were also not affected by low vitamin D levels. All this raises a doubt as to whether we are following the correct reference ranges for our country where the population has access to ample sunlight. References to other studies in literature further confirmed our doubts as discussed in the following paragraphs.

Kanekar A et al<sup>(3)</sup> observed widespread vitamin D deficiency without any signs & symptoms of disease. They found no correlation between vitamin D levels & symptoms of disease & between severity of vitamin D deficiency & number of symptoms displayed. This study observed a subclinical preosteomalacic state for individuals with vitamin D deficiency producing non-specific musculoskeletal symptoms like backache, joint pains, generalised body aches. The authors were not able to explain absence of clinical osteomalacia in individuals with very low vitamin D levels & thought that even at low vitamin D levels there may be enough 1,25(OH)2D3 to maintain homeostasis.

It is common knowledge that Vitamin D deficiency causes secondary hyperparathyroidism<sup>(2)</sup>. But in a study by Marwaha RK et al<sup>(29)</sup> the anticipated PTH(Parathyroid Hormone) response to low 25(OH)D levels was absent in half of the patients of the study. Also there was no correlation of BMD(Bone marrow density) with 25(OH)D.

The editorial by Vishwanath P et al<sup>(30)</sup> expresses that there may have been overestimation of vitamin D deficiency in our country and have also emphasized that population based studies need to be done to first establish reference ranges for India as till now the ranges used are those specified by the companies supplying kits or are based on international standards. This is a very similar opinion as ours.

According to Harinarayan<sup>(31)</sup> also a vast intensive programme is required covering the whole country to establish acceptable reference ranges after taking into account the numerous factors that determine vitamin D levels and its synthesis in an individual. Therefore it is imperative to review the reference ranges to be followed in our country. It is possible that Indians may require lower levels of vitamin D to maintain homeostasis as compared to the western world.

### 5. Conclusion

There is an urgent need to review the reference ranges followed for vitamin D in our country to label an individual as vitamin D deficient. Further well planned studies on a vast scale on a larger population are required alongwith carefully thought of measureable parameters to help determine reference ranges for India. After doing so if vitamin D deficiency still seems widely prevalent in our country, then supplementation and food fortification will have to be resorted to in order to check the rising epidemic of vitamin D deficiency.

### References

- [1] Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, El-Hajj Fuleihan G, Josse RG, Lips P, Morales-Torres J. Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int.* 2009;20(11):1807-1820.
- [2] Londhey V, Editorial: Vitamin D deficiency: Indian Scenario, *J Assoc Physicians India.* 2011;59:695-696.
- [3] Kanekar A, Sharma M, Joshi VR. Vitamin D deficiency- A Clinical Spectrum: Is There a Symptomatic Nonosteomalacic state? *International J Endocrinology.* 2010;10:1-6.
- [4] Goswami R, Mishra SK, Kochupillai N. Prevalence & potential significance of vitamin D deficiency in Asian Indians. *Indian J Med Res.* 2008;127:229-238.
- [5] Goswami R, Gupta D, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr.* 2000;72:472-475.
- [6] Arya V, Bhambri R, Godbole MM, Mithal A. Vitamin D status and its relationship with bone mineral density in healthy Asian Indians. *Osteoporos Int.* 2004;15:56-61.

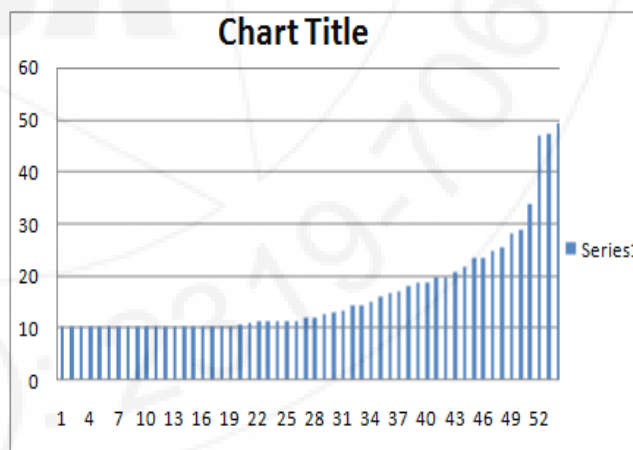
- [7] Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr.*2005;81:1060-1064.
- [8] Harinarayan CV. Prevalence of vitamin D deficiency in postmenopausal south Indian women. *Osteoporos Int.*2005;16:397-402.
- [9] Marwaha RK, Tandon N, Reddy DRHK, Aggarwal R, Singh R, Sawhney RC, et al. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr.*2005;82:477-482.
- [10] Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PV, Sarma KV, et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *Am J Clin Nutr.*2007;85:1062-1067
- [11] Harinarayan CV, Joshi SR. Vitamin D status in India-Its implications and Remedial measures. *J Assoc Physicians India.*2009;57:40-48.
- [12] Marwaha RK, Sripathy G. Vitamin D and bone mineral density of healthy school children in northern India. *Indian J Med Res.*2008;127:239-244.
- [13] Babu US, Calvo MS. Modern India and the vitamin D dilemma: evidence for the need of a national food fortification program. *Mol Nutr Food Res.*2010;54:1134-1147.
- [14] Grant WB, Holick MF. Benefits and Requirements of Vitamin D for Optimal Health: A Review. *Altern Med Rev.*2005;10(2):94-111.
- [15] Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int.*2005;16(7):713-6.
- [16] Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D insufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr.*2005;135:317-322.
- [17] Bolland MJ, Grey A, Gamble GD, Reid IR. The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis. *Lancet Diabetes Endocrinol.*2014;2(7):573-580.
- [18] Bischoff-Ferrari HA, Conzelmann M, Dick W, et al. Effect of vitamin D on muscle strength and relevance in regard to osteoporosis prevention. *Z Rheumatol.*2003; 62:518-521. [Article in German]
- [19] Specker B. Vitamin D requirements during pregnancy. *Am J Clin Nutr.*2004;80:1740S-1747S.
- [20] Purvis RJ, Barrie WJ, MacKay GS, et al. Enamel hypoplasia of the teeth associated with neonatal tetany: a manifestation of maternal vitamin-D deficiency. *Lancet.*1973;2:811-814.
- [21] Garland FC, Garland CF, Gorham ED, Young JF. Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. *Prev Med.*1990;19: 614-622.
- [22] Hanchette CL, Schwartz GG. Geographic patterns of prostate cancer mortality. Evidence for a protective effect of ultraviolet radiation. *Cancer.*1992;70:2861-2869.
- [23] Lefkowitz ES, Garland CF. Sunlight, vitamin D, and ovarian cancer mortality rates in US women. *Int J Epidemiol.*1994;23:1133-1136.
- [24] Freedman DM, Dosemeci M, McGlynn K. Sunlight and mortality from breast, ovarian, colon, prostate, and non-melanoma skin cancer: a composite death certificate based case-control study. *Occup Environ Med.*2002;59:257-262.
- [25] Holick MF. The photobiology of vitamin D and its consequences for humans. *Ann N Y Acad Sci.*1985;453:1-13.
- [26] Holick MF. Environmental factors that influence the cutaneous production of vitamin D. *Am J Clin Nutr.*1995;61:638S-645S.
- [27] Holick MF. Photosynthesis of vitamin D in the skin: effect of environmental and life-style variables. *Fed Proc.*1987;46:1876-1882.
- [28] Holick MF. Vitamin D and bone health. *J Nutr.*1996;126:1159S-1164S.
- [29] Marwaha RK, Tandon N, Garg MK et al. Vitamin D status in healthy Indians aged 50 years and above. *J Assoc Physicians India.*2011;59:703-707.
- [30] Vishwanath P, Kulkarni P, Prashant A. Editorial: Vitamin D deficiency in India: Are we overconcerned? *Int J Health Allied Sci.*2014;3:77-78.
- [31] Harinarayan CV. The multiple roles of vitamin D. *NFI Bulletin.*2014;35(3):1-8.

**Table 1:** Minimum/maximum/mean/SD values

	vit D	CALCIUM	PHOS	ALP	TPR	ALB	CHOL
	nmol/L	mg/dl	mg/dl	U/L	gm/dl	gm/dl	mg/dl
min	10.5	8.4	3.5	69	7	3.8	140
max	49.19	10.1	5.3	185	8.9	4.9	290
mean	16.88	8.99308	4.2962	104.9	7.992	4.35	173.6
S.D	9.68	0.33595	0.4463	24.98	0.367	0.251	24.88

**Table 2:** Correlations between different parameters

	P value	Significance
Ca & Vit D	0.8636	NS
Ca & Alb	0.4052	NS
Vit D & ALP	0.7541	NS



**Graph 1:** Graph Showing Vitamin D Levels in Patients (10.5-49.19 nmol/L)