

Original Communication

Poor Vitamin D Status in Healthy Population in India: A Review of Current Evidence

Geeta Trilok Kumar¹, Reema Chugh¹, and Manfred Eggersdorfer²¹Department of Biochemistry, Institute of Home Economics, University of Delhi, India²DSM Nutritional Products Ltd, Kaiseraugst, Switzerland

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Abstract: Vitamin D deficiency is associated with rickets in children, with osteoporosis in the elderly, is thought to increase the risk of certain cancers and of cardiovascular diseases, and may have an impact on many other health conditions. Asians are reported to have a poor vitamin D status in spite of adequate sunshine in their regions. Data on the extent of vitamin D deficiency at the population level from most Asian countries, including India, are limited. Part of the reason for paucity of data on vitamin D status is the absence of clear recommendations on optimal vitamin D intakes and status as well as clear consensus on the cut-offs for deficiency. With a large country covering several latitudes, ethnicities, cultures, traditions, and attitudes, the current data on vitamin D status in India is inadequate and classified in different ways, making interpretation difficult, and is unrepresentative as it comes only from four states, with about half the data from Delhi. Poor vitamin D status is almost universally reported across all age groups with as many as 95.7 % neonates, 75 % adults and 67 % pregnant women having serum 25 hydroxy vitamin D levels <50 nmol/L (deficient). Children and adults exposed to sunlight, living in rural or less polluted areas have been reported to have a better vitamin D status especially in summer months. Lack of conclusive information emphasizes the need for state-specific data on the vitamin D status and the extent of sun exposure to make recommendations for vitamin D intake in the country.

Key words: vitamin D, vitamin D status, 25-hydroxy vitamin D, 25(OH)D, India, population, prevalence

Introduction

Vitamin D has been recognized for several decades for its role in growth and maintenance of the skeletal system as well as for the regulation of serum calcium levels. Its deficiency has been known to cause improper bone mineralization, resulting in rickets in children and osteopenia in adults. Recent scientific evidence indicates an emerging role for vitamin D in a variety of physiological functions, including cell differentiation, insulin production, and immune function [1]. Next to the established role of vitamin D in bone

mineralization and muscle strength, inadequate status may be associated with increased risk of high blood pressure [2], infectious diseases including tuberculosis [3], some cancers, multiple sclerosis, cardiovascular disease, type I diabetes, neurodevelopmental disorders, and several other health conditions [4–7].

The interest in vitamin D status has increased substantially over the past decade because of the many roles of vitamin D in physiological functions; the reported worldwide prevalence of vitamin D deficiency [8–10] including countries with sufficient sunshine and lack of enough evidence on the impact of inadequate

and deficient status on public health. In Asia, vitamin D deficiency is widespread and a prevalence of more than 70 % deficiency has been reported in the general Indian population [11]. Although there is no national data describing the extent of vitamin D deficiency in India, studies conducted in various regions of the country across all age groups indicate poor vitamin D status. Historically, the main source of vitamin D for Indians has always been via synthesis in the skin resulting from exposure to UVB light from the sun. Lack of sun exposure due to lifestyle changes, darker skin colour, high pollution levels, overcrowded residences with very little or no sunlight and almost no consumption of foods containing vitamin D are some of the risk factors for a poor vitamin D status in the healthy Indian population.

This review aims to collate the current data available on vitamin D status in the healthy population and to understand the extent of vitamin D deficiency in India across all age groups.

Methods

Criteria for identification and selection of studies

To identify relevant articles, we searched Pubmed and EmBase databases for terms such as vitamin D, vitamin D deficiency and prevalence, hypovitaminosis D, cross-sectional studies, vitamin D status, bone mineral density, and India. We restricted the search to selected peer-reviewed articles in English from 2000 to 2015 (as of 28 February 2015) conducted on apparently healthy populations reporting serum or plasma 25(OH)D levels. We excluded case control and randomized controlled studies and case reports. Baseline vitamin D levels in observational studies conducted on healthy populations were included (Figure 1).

Vitamin D status

The most well-accepted indicator of vitamin D status in humans is the level of 25(OH)D in serum or plasma and it is traditionally used to measure vitamin D status. There is, however, no worldwide consensus on the levels of 25(OH)D that are adequate or optimal for maintenance of bone health or for other health-related outcomes, and various studies have used different cut-offs for deficiencies. Lips classified the 25-hydroxyvitamin D levels into four stages

[12, 13]: severe deficiency (<12.5 nmol/L), deficiency (12.5–25 nmol/L), insufficiency (25–50 nmol/L), repletion (>50 nmol/L). Subsequently, the U.S. Institute of Medicine (IOM) in 2011 suggested that an RDAs of 600 IU/d for ages 1–70 years and 800 IU/d of vitamin D for ages 71 years and older that corresponded to a serum 25(OH)D level of at least 20 ng/mL (50 nmol/L) was sufficient to meet the requirements for at least 97.5 % of the population for bone health outcome [14, 15], indicating that 20 ng/mL (50 nmol/L) of 25(OH)D was adequate. However, no recommendations were made on extraskeletal outcomes due to lack of enough evidence.

Subsequent to the IOM report, in the past few years, several studies on the role of vitamin D in skeletal and non-skeletal outcomes have been published and it is clear that the minimum level of serum 25(OH)D required for preventing non-skeletal diseases is higher than that for skeletal diseases [16]. However, the threshold for serum 25(OH)D levels that is sufficient for various non-skeletal outcomes is not yet clear. Although some recent reports suggest that thresholds for required serum 25(OH)D vary according to outcomes and subgroups [17] or are disease-dependent [16], more data from larger studies are needed to make any recommendations on preventive and therapeutic doses.

For the purpose of this review we have used Lips classification for severe deficiency, deficiency and insufficiency because many articles from India used these cut-offs. The 25(OH)D levels <50 nmol/L were used as cut-offs for deficiency according to Lips classification. Although most studies that we selected had reported their results in ng/mL, we converted 25(OH)D levels from ng/mL to nmol/L, which is currently the more accepted unit.

Results

A total of 41 studies that matched our selection criteria were selected. Vitamin D status of Indian children, adolescents, pregnant women, adults and elderly from lower as well as upper socioeconomic strata and from rural or urban areas are listed in the following tables (Tables I–III).

The data cover many parts of the country but are not representative for all states. Latitudes, where mentioned, have been reported in tables. Use of vitamin D supplements was either absent or not reported in the majority of the studies.

Vitamin D status of infants, children and adolescents could not be tabulated separately because the

Table 1: Vitamin D deficiency in infants, children and adolescents.

Publication	Age Mean (SD)	n (Sex)	Place	Latitude (North)	Season	Vitamin D use	Assay method	Mean (SD) 25(OH) D nmol/L	% in each category based on 25(OH)D levels (nmol/L)				
									<12.5	12.5 ≤ 25	25 ≤ 50	50 ≤ 75 other ^y	
Sachan et al. 2005 [22]	Neonates (cord blood samples)	117	Lucknow	26.8°N	Sept–Nov	Unknown	Radioimmunoassay	21.0 (14.2)	–	–	95.7 (0 ≤ 50 nmol/L)	–	–
Bhalala et al. 2007 [23]	At birth (cord blood)	42	Mumbai	18.9°N	–	–	Radioimmunoassay	48.4 (24.0)	–	–	–	–	(0 ≤ 62.5 nmol/L)
	At 3 mo	35 (M/F)						45.5 (24.2)					62.0 80.0
Agarwal et al. 2012 [24]	Within 48 h of birth	220 (LBW) 116 (NBW)	Delhi		–	–	Radioimmunoassay	LBW 16.2 (10.0–136.2) [§] NBW 14.5 (10.0–66.5) [§]	LBW 33.8 NBW 44.0	–	–	–	(0 ≤ 37.5 nmol/L) LBW 87.3 NBW 88.8 (<50 nmol/L) LBW 93.0 NBW 94.8
Goswami et al. 2000 [25]	Newborn	29 (16 M, 13 F)	Delhi	28.35°N	Apr–Jul	Unknown	Radioimmunoassay	41.7 (12.5)	–	–	–	–	–
Seth et al. 2009 [26]	2–24 wks*	180 (99 M, 81 F)	Delhi		Apr–Mar		Radioimmunoassay	29.0 (20.7)	47.2	22.8	21.1	–	–
Marwaha et al. 2011 [27]	6–8 wks*	340 (M/F)	Delhi		Apr–Oct (1.5 yrs)	–	Radioimmunoassay	22.2 (10.2)	16.3	44.5	38.0	–	–
Agarwal et al. 2010 [28]	10 wks	179 (M/F) 96 AGA, 83 SGA	Delhi		–	–	Radioimmunoassay	31.5 (21.0)	–	–	–	–	–

Table 1: Continued

Publication	Age Mean (SD)	n (Sex)	Place	Latitude (North)	Season	Vitamin D use	Assay method	Mean (SD) 25(OH) D nmol/L	% in each category based on 25(OH)D levels (nmol/L)			
									<12.5	12.5 ≤ 25	25 ≤ 50	50 ≤ 75 other*
Jain et al. 2011 [29]	10-14 wks* 13.6 (2.2) wks	98 (57 M, 41 F)	Delhi	28.38°N	Nov-Jan (Winter)	Drops of 125 IU D2 to 1/3	Radioimmu- noassay	22.0 (6.2- 95.0)§	-	-	-	(12.5-37.5 nmol/L) 39.6
Agarwal et al. 2002 [30]	9-24 mo* High pollution 16 (4.1) mo	26 (15 M, 11 F)	Delhi	28.35°N	Mar-Apr	Unknown	HPLC	31.0 (17.5)	Delhi 11.5	Delhi 53.8	-	Delhi (<30 nmol/L) 34.6
Tiwari et al. 2004 [31]	15.9 (3.8) mo Low pollution	31 (15 M, 16 F)	Gurgaon					67.7 (17.5)				Gurgaon (>30 nmol/L) 100.0
	9-30 mo*	196 (M/F) 47	Delhi	-	Jan	-	ELISA	96.5 (26.0)	-	-	-	(0 ≤ 35 nmol/L) 2.0
		49	Sunder- nagari		Feb			23.7 (27.0)				82.9
		48	Colony Rajiv		Aug			17.7 (22.5)				84.0
		52	Colony Gurgoan		Aug			19.2 (20.2)				82.0
Ekbote et al. 2010 [32]	2.6 (0.7) yrs	110 Sun exposed 50 (25 M, 25 F)	Pune	18.34°N	Sept	unknown	Radioimmu- noassay	96.0 (91.7) M- 130.5 (67.7) F	-	-	-	(0 ≤ 30 nmol/L) 0.0
					Dec			14.0 (32.0) M- 5.2 (21.0) F				77.0
Ekbote et al. 2011 [33]	2-3 yrs* 2.8 (0.6) yrs	71 (36 M, 35 F)	Pune	-	-	-	Radioimmu- noassay	30.0 (31.5)	57.0	-	-	-

Table I: Continued

Publication	Age Mean (SD)	n (Sex)	Place	Latitude (North)	Season	Vitamin D use	Assay method	Mean (SD) 25(OH) D nmol/L	% in each category based on 25(OH)D levels (nmol/L)				
									<12.5	12.5 ≤ 25 ≤ 50	50 ≤ 75 other ^x		
Puri et al. 2008 [34]	6–18 yrs* LSES 193 USES 211	404 F	Delhi	28.37°N	Jul	No supple- ments used	Radioimmu- no assay	Overall 32.0 (15.5) LSES 34.7 (17.5) USES 29.5 (12.7)	5.2	25.4	59.0	–	–
Marwaha et al 2007 [35]	7–17 yrs* 12.8 (2.7)	F LSES 369 USES 295	Delhi	–	–	–	Radioimmu- no assay	Overall 28.5 (14.5) LSES 27.7 (13.0) USES 29.5(16.0)	–	–	–	–	–
Harinarayan et al. 2008 [36]	Urban 11–13.6 yrs* 12.5 (0.5) Rural 11.6–13.3 yrs* 12.6 (0.4)	146 Urban (30 M, 39 F) Rural (34 M, 36 F)	Tirupati, Andhra Pradesh	13.4°N	Not men- tioned	–	Radioimmuno- assay	Urban M: 39.0 (3.0) (32.5–45.0)# F: 46.2 (4.2) (37.5–55.0)# Rural M: 42.5 (3.2) (35.0–50.0)# F: 47.5 (4.0) (40.0–55.0)#	–	–	(0 ≤ 50 nmol/L) 14.8 81.5 25.7 11.4	–	(>75 nmol/L) 3.7
Garg et al. 2014 [37]	13.3 (2.5) yrs	1829 (816 M, 1013 F)	Delhi	28.35°N	–	–	Radioimmuno- assay	20.7 (13.0)	27.7	43.7	25.5	2.6	0.5
Sahu et al. 2009 [38]	14.3 (2.7) yrs	121 F	Bara- banki District, Uttar Pradesh	26.8°N	Summer & winter months	Unknown	Radioimmuno- assay	33.2 (16.0)	–	(0 ≤ 25 nmol/L) 34.0	(0 ≤ 50 nmol/L) 88.6	–	–
	14 (3.0) yrs	34 M						67.5 (29.0)		(0 ≤ 25 nmol/L) 3.0			

Table I: Continued

Publication	Age Mean (SD)	n (Sex)	Place	Latitude (North)	Season	Vitamin D use	Assay method	Mean (SD) 25(OH) D nmol/L	% in each category based on 25(OH)D levels (nmol/L)				
									<12.5	12.5 ≤ 25	25 ≤ 50	50 ≤ 75	other [‡]
Khadilkar et al. 2010 [39]	14–15 yrs* 14.7 (0.7) yrs	50 F	Pune	18.34°N	Feb–Apr (1.16 yrs)	–	Radioimmuno- assay	23.4 (13.5– 31.9) [§]	–	–	–	–	(70.0
Marwaha et al. 2005 [40]	10–18 yrs* 14.7 (0.7) yrs	760 LSES 430 (167 M, 263 F) USES 330 (158 M, 172 F)	Delhi	28°N	Not men- tioned	Unknown	Radioimmuno- assay	LSES 26.0 (1.0) USES 34.2 (1.0)	LSES 11.2 USES 4.9	LSES 39.5 USES 25.5	LSES 57.6 USES 36.3	–	–
								TOTAL 11.3	TOTAL 25.5	TOTAL 57.6	TOTAL 36.3	TOTAL 43.5	

[§]Median (interquartile range).

*Age group.

[‡]25(OH)D cut-offs expressed in any way other than <12.5, 12.5 ≤ 25, 25 ≤ 50, 50 ≤ 75 nmol/L are included in 'other'; cut-off range included in the same cell.

[#]Range for 25(OH)D levels.

To convert to nmol/L multiply by 2.5.

studies included have used different age ranges and age cut-offs, with no clear rationale for selecting the age ranges. In absence of homogeneity in age ranges used by various authors, we have reported all studies covering the age groups from birth to 18 years in Table I, those with participants aged >18 years have been reported in Table III, and vitamin D status of pregnant women is shown in Table II.

Both age group and mean ages have been reported in our tables because large age ranges were used in most studies where medians were not calculated and means held little value. We have reported medians wherever available.

Radioimmunoassay was the most commonly used method for assessment of 25(OH)D in serum or plasma, but a few articles reported using electrochemiluminescence, high performance liquid chromatography (HPLC) and enzyme-linked immunosorbent assay (ELISA). Various assays for determining 25(OH)D levels are available, but standardization and harmonization of these 25(OH)D measurements is an issue. Serum 25(OH)D levels vary depending on the assay used [18–21]. To address these issues, many laboratories participate in quality and surveillance programs to enable standardized 25(OH)D values. None of the studies reported being enrolled in any external quality control program. Most studies reported the vitamin D status as mean 25(OH)D levels while a few used median with interquartile range; those reporting proportions that were vitamin D-deficient used various cut-offs for deficiency. Use of vitamin D supplements is not reported in the majority of studies.

Vitamin D status in infants, children and adolescents

Table I lists all studies conducted on infants, children, and adolescents arranged in ascending order of age for better understanding. However, different assay methods used, serum 25(OH)D values reported either as medians or as means 25(OH)D, varying cut-offs for deficiency, insufficiency and sufficiency and inconsistent reporting on seasonality and vitamin D use made comparisons of the studies difficult.

The mean values for 25(OH)D ranged from 17.7 (22.5) nmol/L [31] to 130.5 (67.7) nmol/L [32], showing large variability. Considerable heterogeneity was also seen in vitamin D status between studies conducted on the same age group and within the same city, for e.g. mean serum vitamin D levels from Delhi in the first two months after birth ranged between to 29.0

Table II: Vitamin D status in pregnant women.

Publication	Age (yrs) Mean (SD)/ range	Number	Place	Latitude	Season	Vitamin D use	Assay method	Mean (SD) 25(OH)D (nmol/L)	% in each category based on 25(OH)D levels (nmol/L)				
									<12.5	12.5 ≤ 25	25 ≤ 50	50 ≤ 75	other [‡]
Goswami et al. 2000 [25]	23 (3)	29	Delhi		Apr–Jul	–	Radioimmunoassay	22.0 (10.5)	–	–	–	–	–
Sachan et al. 2005 [22]	24 (4.1)	207	Lucknow	26.8°N	Sep–Nov	–	Radioimmunoassay	35.0 (23.2)	–	42.5	–	–	(25–37.5 nmol/L) 24.2
Bhalala et al. 2007 [23]	20–35*	42	Mumbai	18.9°N	–	–	Radioimmunoassay	57.5 (27.2)	–	–	–	–	(37.5–56.2 nmol/L) 17.3 (<62.5 nmol/L) 50.0
Sahu et al. 2009 [28]	26.7 (4.1) 2nd trimester	139	Barabanki district, Lucknow	26.8°N	–	–	Radioimmunoassay	37.7 (19.7)	–	(0 ≤ 25 nmol/L) 32.0	42.0	–	–
Farrant et al. 2009 [44]	20–26* 23.7 30 (2) wks of gestation	559	Mysore	–	–	156 women taking vit D and Ca supplements (500–1250 mg Ca and 100–250 IU vit D)	Radioimmunoassay	37.7 (24.0–58.5) [§]	–	–	(0 ≤ 50 nmol/L) 66.0	–	–
Marwaha et al. 2011 [27]	19–30* 24.6 (2.8)	541 1st trimester, 156 2nd trimester, 218 3rd trimester, 167	Delhi	–	Apr–Oct (1.5 yrs)	–	Radioimmunoassay	23.2 (12.0) 23.5 (11.2)	17.7	41.8	36.8	–	–
Krishnaveni et al. 2011 [46]	23.9 ± 4.3 28–32 wks of gestation	568	Mysore	–	–	–	Radioimmunoassay	39.0 (24.0–58.0) [§]	–	–	(0 ≤ 50 nmol/L) 67.0	–	–

Table II: Continued

Publication	Age (yrs) Mean (SD)/ range	Number	Place	Latitude	Season	Vitamin D use	Assay method	% in each category based on 25(OH)D levels						
								Mean (SD) 25(OH)D (nmol/L)	<12.5	12.5 ≤ 25	25 ≤ 50	50 ≤ 75	other [‡]	
Jani et al. 2015 [47]	26.8 ± 4.1 20–35 yrs* 32–36 wks	150	Mumbai	–	Feb–May (spring– summer)	–	Chemilumin- escent microparticle immunoassay	29.5 (27.0–32.3) [§]	–	–	–	–	–	6
		68 affluent 82 non affluent						24.5 (22.8–26.5) [§]						

[§]Median (interquartile range).

*Age group.

[‡]25(OH)D cut-offs other than <12.5, 12.5 ≤ 25, 25 ≤ 50, 50 ≤ 75 nmol/L are included in 'other'; cut-off range included in the same cell.

To convert to nmol/L multiply by 2.5.

[#]Range for 25(OH)D levels.

(20.7) nmol/L [26], 22.2 (10.2) nmol/L [27] and 31.5 (21.0) nmol/L [28]. Vitamin D status at birth was poor, with nearly 95 % of newborn children having deficient levels of 25(OH)D (mean 25(OH)D below 50 nmol/L; table 1). Pollution appeared to have an appreciable effect on vitamin D levels, with children from less polluted areas having half the levels of mean 25(OH)D when compared those in highly polluted areas [31.0 (17.5) vs 67.7 (17.5) nmol/L] [30]. Living in rural areas [36] as well as playing outdoors rather than staying indoors [32] resulted in better vitamin D status. Seasonal variation in 25(OH)D levels was observed in most studies that included summer and winter months in their methods [29, 31, 38], with mean 25(OH)D levels higher in the summer months. However, none of the authors applied any statistical tests of significance to show the extent of variation due to season.

Vitamin D status of pregnant women

Vitamin D status of pregnant women is important in India because undernutrition of the mother prior to and during pregnancy is a risk factor for low birth weight, which is common in India. However, the role of vitamin D during pregnancy is not clearly defined [41, 42]. Vitamin D deficiency in pregnancy has been associated with a spectrum of adverse pregnancy and birth outcomes [43], including gestational diabetes [44], preeclampsia [43] preterm birth [45] as well as cardio-metabolic risks [46]. Little is known about vitamin D status in Indian pregnant women and whatever literature is available is not very consistent. Table 2 gives available data on vitamin D status of pregnant women in India. The publications covered are from different parts of the country. Eight studies fulfilled our inclusion criteria and were conducted on women aged 19–40 years.

With a lot of disparity in gestation time, cut-offs of 25(OH)D, season of assessment, as well as mean 25(OH)D levels, it is difficult to compare data from various studies reported in this article. Mean (SD) 25(OH)D levels ranged from 22.0 (10.5) to 57.5 (27.2) nmol/L, and the proportion of women with serum levels of 25(OH)D < 50 nmol/L (classified as deficient) varied from 20 to 67 % (Table II).

Vitamin D status of adults and elderly

A total of 23 studies on healthy adults were short-listed under this section (Table III). Due to very wide age ranges used by various investigators and

Table III: Vitamin D status in adults.

Publication	Age range*/ Number mean (SD) yrs	Place	Latitude	Season	Vitamin D use	Assay method	Mean (SD) 25(OH)D or range (nmol/L)	% in each category based on 25(OH)D levels (nmol/L)				
								<12.5	(12.5 ≤ 25	25 ≤ 50	50 ≤ 75 other ^y	
Goswami et al. 2000 [25]	23.0 (5.0)	Delhi	-	Winter	-	Radioimmunoassay	8.0 (3.5)	-	-	-	-	
	24.0 (4.0)						19 (11 M, 8 F)	18.0 (8.0)	-	-	-	
	25.0 (5.0)						19 (11 M, 8 F)	47.2 (11.7)	-	-	-	
	43.0 (16.0)						31 (M)	18.2 (11.2)	-	-	-	
Tandon et al. 2003 [48]	M 22.7 (2.8)	Paramilitary soldiers	-	-	-	Radioimmunoassay	-	-	-	-	-	
	F 40 M, 50 F						46.0 (13.2)	-	-	-	-	
	23.4 (3.1)						63.2 (18.5)	-	-	-	-	
Arya et al. 2004 [49]	24-53*	Lucknow	26.55 °N	Jan-Feb	-	Radioimmunoassay	30.7 (27.2)	20.6	27.2	-	(25-37.2 nmol/L)	
	34.2 (6.7)						92 (25 M, 67 F)	(<12.5-160)#	-	-	-	18.5 (>37.5 nmol/L)
Harinara-yan et al. 2004 [50]	Rural	Multiple locations in Tirupati	-	Jan-Jul (3.5 yrs)	-	Radioimmunoassay	52.5 (1.2)	combined	-	-	(>50 nmol/L)	
	44.0 (1.0)						191 rural	33.7 (1.5)	1.0	14.0	54.0	31.0
	Urban						125 urban	-	-	-	-	-
Vupputuri et al. 2006 [51]	43.3 (9.7)	Delhi	28.35 °N	-	-	Radioimmunoassay	24.5 (15.0)	-	-	(0 ≤ 50 nmol/L)	(50-80 nmol/L)	
	51 M, 54 F)						105 (51 M, 54 F)	94.3	4.8	(>80 nmol/L)	0.9	
Zargar et al. 2007 [52]	18-40*	Kashmir	320	1 yr	-	Radioimmunoassay	-	-	-	-	-	
	28.2 (4.9)						92	37.7 (30.0)	14.1	26.5	35.9	23.4
	64 M						64 M	13.7 (11.0)	50.0	46.4	0.0	3.6
	28 F	28 F	50°N				combined	25.0	33.0	25.0		

Table III: Continued

Publication	Age range*/ mean (SD) yrs	Number	Place	Latitude	Season	Vitamin D use	Assay method	Mean (SD) 25(OH)D or range (nmol/L)	% in each category based on 25(OH)D levels (nmol/L)					
									<12.5	(12.5 ≤ 25	25 ≤ 50	50 ≤ 75 other [†]		
Harinarayan et al. 2008 [36]	Urban	1146	Tirupati, Andhra (134 M, 807 F) Pradesh	13.4°N	-	-	Radioimmu- noassay	Urban	-	(0 ≤ 50 nmol/L)	(>75 nmol/L)			
	45-47*	Urban						M: 46.2(2.0) F: 38.7(0.7)	M: 42.5-50.0# (37.2-40.0)#	62.0	26.0	12.0		
	Rural							Rural	-	(0 ≤ 50 nmol/L)	(>75 nmol/L)			
	41-45*	Rural						M: 59.2(2.0) F: 47.5(2.2)	(55.0-62.5)# (43.7-52.5)#	75.0	39.5	16.5		
Goswami et al. 2008 [53]	M	57	Uttar Pradesh	28.5°N	Winter		Radioimmu- noassay	Overall	36.5	-	-	(>50 nmol/L)		
	42.8 (16.6)	32 M 25 F						44.5 (24.5) 27.0 (16.0)				31.5		
Goswami et al. 2009 [54]	15-60*	642	New Delhi	-	Nov-Mar	-	Radioimmu- noassay	Urban	17.5 (10.2)	(0 ≤ 25 nmol/L)	-	-		
	33.7 (13.5)	(244 M, 398 F)						87.0						
Multani et al. 2010 [55]	M	214	Mumbai	-	May-Aug		Radioimmu- noassay	Overall	32.0 (19.7)	Combined	12.0	30.5	44.5	13.0
	F	26.3 (1.6)						(174 M, 40 F)	27.2 (11.2)					
Marwaha et al. 2011 [27]	50-84*	1346	Delhi	28.35°N	-	Some taking 500 mg Ca and few 200-400 IU vit D	Radioimmu- noassay	Overall	24.5	27.9	34.0	29.4	6.8	
	58.0 (9.5)	643 M 703 F						(19.0)	25.8	34.2	31.3	7.3		
								24.5 (17.0) 24.5 (18.2)	29.9	33.7	27.6	6.4		

Table III: Continued

Publication	Age range*/ Number mean (SD) yrs	Place	Latitude	Season	Vitamin D use	Assay method	Mean (SD) 25(OH)D or range (nmol/L)	% in each category based on 25(OH)D levels (nmol/L)			
								<12.5	(12.5 ≤ 25	25 ≤ 50	50 ≤ 75 other [†]
Harinarayan et al. 2011 [56]	150 Reproduc- tive 37.4 (0.7) Post-meno- pausal 53.3 + 0.7	Tirupati	13.4°N	-	NO	Radioimmu- noassay	39.3 (3.5)	76	16.5	7.5	(>75 nmol/L)
Majumdar et al. 2011 [57]	441 18-75* 39.7 (12.8) 237 M 204 F	Bangalore	-	-	-	Enzyme im- munoassay	5.5-181.5 [#] 40.2 (18.0) 43.7 (19.0)	0	-	-	(12.5-50 nmol/L) 65.6 (50 ≤ 100 nmol/L) 31.1 (100 ≤ 250 nmol/L) 0.5
Shivane et al. 2011 [58]	1137 25-35* 30.4 (3.5)	Mumbai	18°56'N	May-Jun	-	Radioimmu- noassay	43.5 (22.7)	2.9	16.5	51.5	(>75 nmol/L) 7.2
Ramakris- hnan et al. 2011 [59]	329 (M/F) 18-25* 237 (M/F of same cohort)	Chandi- garh	-	Summer	-	-	132.2 (84.2)	-	-	-	(>75 nmol/L) 72.5
Baidya et al. 2012 [60]	40 29-80* 52.2 (10.9) (3.9 M, 1 F)	Calcutta	-	Dec	-	Electro chemilumine- scence	32.5 (12.0) 30.5 (17.0-80.5) [§]	0.0	30.0	62.5	(>75 nmol/L) 2.5
Beloyart- seva et al. 2012 [11]	2063 42.7 (6.8) (1516 M, 603 F)	Multicen- tric (18 Indian cities)	-	Dec-Mar	-	Radioimmu- noassay	36.0 (26.5) 29.7 (3.7-299.2) [§]	0.0	(0 ≤ 50 nmol/L) 79.0	15.0	(>75 nmol/L) 6.0

Table III: Continued

Publication	Age range*/ Number mean (SD) yrs	Place	Latitude	Season	Vitamin D use	Assay method	Mean (SD) 25(OH)D or range (nmol/L)	% in each category based on 25(OH)D levels (nmol/L)			
								<12.5	(12.5 ≤ 25	25 ≤ 50	50 ≤ 75 other [‡]
Marwaha et al. 2012 [61]	>50 67.5 (7.5) 62.6 (6.3)	Delhi	28.35°N	-	Some were Radioimmu- using Ca (500 mg) and vit D (200-400 IU)	Radioimmu- noassay	25.0 (17.0) 24.2 (18.7)	-	-	-	-
Agarwal et al. 2013 [62]	50-84* 62.6 (7.6)	Varanasi	-	Jan-Sept (1.65 yrs)	-	Radioimmu- noassay	47.5 (25.5) (7.5-122.5) [#]	(0 ≤ 25 nmol/L) 24.5	33.5	28.5	(>75 nmol/L) 13.5
Garg et al. 2014 [37]	58.0 (9.5) 1346 (643 M,703 F)	Delhi	28.35°N	-	-	Radioimmu- noassay	24.5 (19.0)	28.0	29.3	6.8	(>75 nmol/L) 1.9
Shetty et al. 2014,[63]	51-74* 55.8 (11.8)	South India	-	-	-	Chemilumi- nescence	51.0 (20.8) (10-145) [#]	(0 ≤ 25 nmol/L) 7	46		
Agarwal et al. 2014 [64]	56.3 (7.6) 71 F years	Delhi	28.38°N	-	-	Radioimmu- noassay	31.8 (19.1)	(0 ≤ 50 nmol/L) 87.3	7		(>75 nmol/L) 5.6
Bachhel et al. 2015 [65]	17-68* 36 75 F)	North- West Punjab	-	-	-	Radioimmu- noassay	-	(0 ≤ 25 nmol/L) 40.0	(25 ≤ 75 nmol/L) 50.0		(>75 nmol/L) 10.0

[§]Median (interquartile range).

*Age range.

[‡]25(OH)D cut-offs other than <12.5, 12.5 ≤ 25, 25 ≤ 50, 50 ≤ 75 nmol/L are mentioned in 'other'. Cut-off range included in the same cell. To convert to nmol/L multiply by 2.5.

[#]Range for 25(OH)D levels.

some articles including the elderly in adults, data on elderly have been included in this table.

The age ranges included in this table are from 18 to 80 years with most authors reporting either age range or mean age. A few have reported median and interquartile ranges.

Overall mean 25(OH)D levels reported were between 8.0 (3.5) nmol/L [25] and 132.2 (84.2) nmol/L [59]. Mean 25(OH)D values were higher in males when compared to females, respectively [37.7 (30.0) vs 13.7 (11.0) [52]], [44.5 (24.5) vs 27 (16.0) [53]], [32 (19.7) vs 27.2 (11.2) [55]]. The urban population had lower mean 25(OH)D when compared to the rural population [33.7 (1.5) vs 52.5 (1.2) nmol/L] [50], and being in the paramilitary forces resulted in higher vitamin D status both in winter and summer [46.0 (13.2) nmol/L, winter; 63.2 (18.5) nmol/L, summer] [48]. The seasonal variation was also reported to influence vitamin D status in other studies and mean 25(OH)D values were higher in summer as compared to winter [25, 48, 59]. Proportions of adults deficient or sufficient with respect to vitamin D status were reported based on different cut-offs for deficiency and thus no comparisons could be made.

Discussion

This is a review of studies conducted in the Indian population to determine the vitamin D status either assessed by mean or median 25(OH)D vitamin D or on the proportions deficient based on various cut-offs. All studies show poor vitamin D status based on mean or median 25(OH)D levels irrespective of age. In absence of an accepted definition of vitamin D deficiency, we used the cut-offs for deficiency as defined by various authors. We found that vitamin D deficiency is highly prevalent in India despite being a country which has sunshine throughout the year. However, due to a large variation in vitamin D status in studies conducted within the same city as well as within the same groups and different cut-offs used to define deficiency, it was difficult to draw clear-cut conclusions on the extent of vitamin D deficiency in India.

High prevalence of poor vitamin D status as reported above may be attributed to a combination of factors related to geographical location, urbanization, skin pigmentation, changing lifestyle, diet, religious beliefs, air pollution, use of sunscreen and other ways of sun protection or possibly a genetic predisposition to vitamin D deficiency reported amongst Asian people [66].

Air pollution due to industrial and vehicular emissions forms a cover and absorbs UV radiation preventing it to reach the earth's surface. Pollution has been shown to affect vitamin D status in India [30] and coupled with darker skin pigmentation of Indians [67] can add to the risk of vitamin D deficiency. This is compounded by the desire for a white skin resulting in use of sunscreens, staying indoors during the day, using umbrellas and covering most of the body parts to protect them from sun exposure. Covering of the face and body parts either due to religious or cultural reasons [68–70], or as a protection from the extreme heat of the sun could be one of the main reasons attributable to the low vitamin D status of Indians. Urbanization has resulted in large-scale migration to cities and living in settlements with small cramped homes with very little sunlight. It has also resulted in change in lifestyle of the middle class and the affluent who stay indoors in air-conditioned homes and offices with no direct exposure to sunlight, leading to poor vitamin D status.

The main source of vitamin D in India is sun exposure. Diets are very low in vitamin D and currently characterized by absence of vitamin D-fortified foods in India [71]. Oily fish are almost non-existent in the Indian diet and meat, which has vitamin D [72], is consumed by a small proportion of people due to exorbitant costs. Thus, any factor interfering with adequate sun exposure could potentially affect vitamin D status. The sun-protecting behaviour of Indians coupled with the urban lifestyle and limited outdoor activity could be the key determinants for a large proportion of population categorized deficient or insufficient, and this needs further investigation. All deficiency levels, including insufficiency and so-called mild deficiency, can be prevented by focused supplementation, but consumption of supplements in India is not common.

This review provides an overview of studies in which the vitamin D status is reported. However, it has a number of potential limitations. Firstly, most studies were conducted in cities and a larger proportion of them in Delhi, so the results are not representative of the population in the country, where more than half of the population still lives in villages. Secondly, with a country as large as India and covering several latitudes, more data is needed from other parts of the country, especially from the eastern and western states as well as rural areas, to draw inferences. Thirdly, barring a few, almost all studies used radioimmunoassay for assessment of plasma or serum 25(OH)D and large variations were seen between methods and between laboratories using the same methods. Quality control procedures in most studies have not been de-

scribed and there could be a possibility of imprecision in classifying participants who are deficient. Fourthly, with no data on the amount of sunlight exposure in a country with sun protective behaviour it is difficult to determine whether it is the unavailability of enough UVB light due to pollution or other atmospheric covers or simply a behavioural or lifestyle change that is a determinant for the widespread deficiency. Finally, the different cut-offs used to describe deficiency in each study and the heterogeneity in results make it very difficult to draw clear conclusions on the extent of vitamin D deficiency in India.

Conclusion

This publication provides an overview of 25(OH)D status in India. It reveals large gaps in information on vitamin D status of populations living in rural areas and also lacks sufficient data on different age groups. It is, however, evident from the published literature that vitamin D deficiency is common in India and prevalent in all age groups and can be of public health concern. More studies are needed to understand the extent of vitamin D deficiency at the population level and among the important groups at risk so that policy decisions can be made.

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Conflict of interest

Dr. Manfred Eggersdorfer is employed by DSM Nutritional Products. The other authors have no conflict of interest to declare.

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Geeta Trilok Kumar

Department of Biochemistry
Institute of Home Economics
University of Delhi
F-4 Hauz Khas Enclave
Delhi 110016
India
Tel.: +911146018108
Fax: +911126510711
geetatrilockumar@gmail.com