REVIEW

Modern India and the vitamin D dilemma: Evidence for the need of a national food fortification program

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India is located between 8.4 and 37.6°N latitude with the majority of its population living in regions experiencing ample sunlight throughout the year. Historically, Indians obtained most of their vitamin D through adequate sun exposure; however, darker skin pigmentation and the changes which have accompanied India's modernization, including increased hours spent working indoors and pollution, limit sun exposure for many. Inadequate sun exposure results in reduced vitamin D synthesis and ultimately poor vitamin D status if not compensated by dietary intake. Dietary vitamin D intake is very low in India because of low consumption of vitamin D rich foods, absence of fortification and low use of supplements. All these factors contribute to poor vitamin D status as measured by low circulating levels of 25-hydroxy vitamin D. Our review searches the published literature specific to India for evidence that would confirm the need to fortify food staples with vitamin D or stimulate public health policies for vitamin D supplementation and dietary guidelines tailored to the Indian diet. This review documents findings of widespread vitamin D deficiency in Indian populations in higher and lower socioeconomic strata, in all age groups, in both genders and people in various professions. Moreover, poor vitamin D status in India is accompanied by increased bone disorders including osteoporosis, osteomalacia in adults and rickets and other bone deformities in children. Without a concerted national effort to screen for vitamin D status, to implement policies or guidelines for vitamin D fortification and/or supplementation and to re-assess recommended dietary intake guidelines, dramatic increase in the number of bone disorders and other diseases may lie ahead.

Keywords:
Fortification / India / Sun exposure / Skin Pigmentation / Vitamin D deficiency

1 Introduction

An explosion of recent scientific literature clearly documents the global prevalence [1–3] of vitamin D insufficiency as determined by low circulating levels of 25(OH)D. Adequate circulating 25(OH)D concentrations are critical in maintaining the health and function of the metabolic, immune, reproductive, muscular, skeletal, respiratory and cutaneous systems of men and women of all ages and race/ethnicity [4, 5]. Historically, our vitamin D needs were met by production in human skin exposed to UV light (UVB 290–315 nm) [6], and during periods of inadequate UVB light for skin production, dietary sources of vitamin D could meet these needs [5]. To assess vitamin D status, we measure the circulating levels of the intermediary metabolite, 25(OH)D produced by the hepatic hydroxylation of both dietary and skin sources of vitamin D (vitamin D_3 or cholecalciferol and vitamin D_2 or ergocalciferol) [6]. It is well established that severely low circulating 25(OH)D concentrations (<10–25 nmol/L) are associated with bone disorders, rickets in children [7] and osteomalacia in adults [8]. A

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Abbreviations: BMC, bone mineral content; **VDR,** vitamin D receptor

growing number of reports indicate that concentrations of 25(OH)D less than 50 nmol/L may be associated with the measured risk of chronic diseases affecting systems other than bone and calcium homoeostasis [9]. There is considerable controversy surrounding the threshold levels for circulating 25(OH)D, indicative of vitamin D sufficiency as illustrated in Fig. 1 [9]. For the purpose of this review, we considered 37.5 nmol/L 25(OH)D as a conservative cut off for vitamin D insufficiency and levels below 50 nmol/L to be a more realistic threshold for vitamin D insufficiency.

Factors contributing to the worldwide prevalence of vitamin D insufficiency vary among countries, but in all cases involve limitations in either or both cutaneous synthesis and dietary sources of vitamin D. High prevalence of vitamin D insufficiency seemingly has no socioeconomic or geographic boundaries based on recent reports of dramatic decreases in serum 25(OH)D levels in the US population [10], in European countries [2] and in some of the most sun-drenched countries of Asia and the Near East [1, 11–13]. We are only beginning to understand the importance of dietary sources of vitamin D in maintaining healthy vitamin D status in different countries, particularly those with ample sunshine year round, such as India.

To assure adequate dietary intake of vitamin D, some countries allow optional fortification of specific foods with vitamin D which is left to the discretion of the manufacturer. In the US and Canada, fortification of fluid milk is required and the addition of vitamin D to milk and some optional food categories is strictly regulated [14]. However, in India, there is neither an official recommendation for adequate dietary vitamin D intake nor a national food fortification program [15]. It is the combined impact of the absence of vitamin D fortification, low dietary intake [15, 16] and low sun exposure due to working indoors with the modernization of India [15, 17–19] that have contributed to lower vitamin D status. Modernization has resulted in increased pollution, which also effectively blocks sunlight causing reduced vitamin D synthesis [20]. Higher skin pigmentation among most of the Indian population will require longer sun exposure to achieve better vitamin D synthesis [21, 22]. A large number of Indians consume predominantly vegetarian diets with very little vitamin-D-rich foods such as fish and meats that may result in vitamin D insufficiencies or deficiencies, especially in the absence of fortification or supplementation [1, 18, 19, 23]. This review will focus on these factors contributing to vitamin D deficiency and associated health problems in various parts of India and will offer some practical ways of correcting this situation.

2 Evidence of widespread prevalence of vitamin D deficiency in India

Theoretically, the Indian subcontinent located between 8.4°N and 37.6°N gets plenty of sunlight throughout the year and should not experience poor vitamin D status. Nonetheless, there are many reports of widespread vitamin D deficiency/insufficiency in India, which include various socioeconomic groups, ages, both genders and different race/ethnicities as well as specific disease states, such as primary hyperparathyroidism [1, 24]. These findings are summarized in Table 1, which presents studies reporting 25(OH)D levels (measures of circulating levels of 25(OH)D) in various populations, including different ages, socioeconomic groups, genders, volunteers from different professions, pregnant and postmenopausal women from urban and rural areas of India that have been published since year 2000. Most of the studies showed circulating 25(OH)D levels well below 50 nmol/L (Table 1) with the exception of paramilitary men and women whose vitamin D levels were considered adequate, 46 ± 13.25 and 63.25 ± 18.5 nmol/L 25(OH)D, respectively [16]. The paramilitary men and women were more likely to be exposed to adequate sun and consumed nutritionally balanced diets. There was no consistent correlation between lower socioeconomic position and 25(OH)D levels. Many studies showed that rural populations, as well as males in general

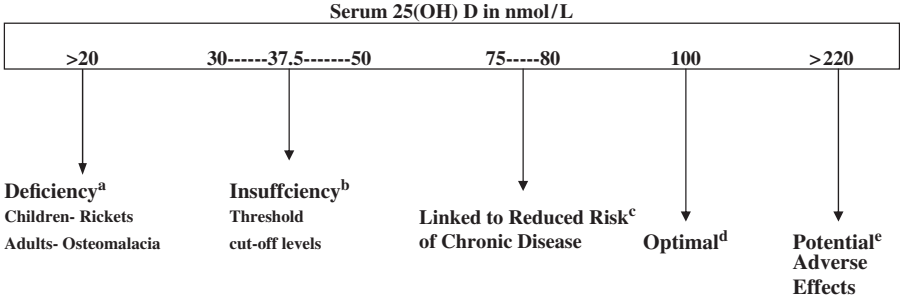

Figure 1. Classification of vitamin D status by serum 25(OH)D concentration. [a]*Deficiency*. The level below which frank skeletal abnormalities are observed, such as rickets in children and osteomalacia in adults [8, 40]. [b]*Insufficiency*. Is the range of 25(OH)D not associated with clinical rickets or osteomalacia but defined as at risk for other chronic disease conditions [94, 95]. [c]*Serum 25(OH)D range linked to the reduced risk of chronic disease* and it is the threshold for vitamin D dependent calcium absorption [96]. [d]*Optimal*. Vitamin D status defines the serum level at which substrate availability does not limit cellular 1–25, $(OH)_2D$ synthesis, the active metabolite of vitamin D [9, 74]. [e]*Potential adverse effects* can occur at levels above 220 nmol/L, including hypercalcemia, irritability, coma and kidney stones [97].

Table 1. Vitamin D intake/status in different geographic areas of India

Reference	Population, age	Location, latitude	Type of diet	Sun exposure, mean ± SD (min/day)	Socioeconomic status	Vitamin D intake, (IU/day)[a]	Plasma 25(OH)D, mean ± SD (nmol/L)[b]
Arya *et al.* [27]	67 F, 25 M, 34.2 ± 6.7 years	Lucknow, 26.55°N	Unknown	5–25	Hospital staff	No data	30.75 ± 27.25
Balasubra-manian *et al.* [98]	24 children with rickets (33 months) and 34 controls (27 months) 16 adolescents with rickets (16.5 years) and 19 adolescent controls (13 years)	Lucknow, 26.55°N	Mostly vegetarian diet with occasional meat and fish consumption	55 ± 28min × m^2/day 56 ± 23min × m^2/day 16 ± 15min × m^2/day 27 ± 17min × m^2/day	Low and middle socioeconomic status and lived in crowded dwellings	Insignificant vitamin D intake with no data	50 ± 38.9 61.3 ± 35.9 12.6 ± 7.1 46 ± 45.4
Sachan *et al.* [26]	207 urban and rural pregnant women, 24.04.1 years	Lucknow, 26.55°N	Unknown	Sun × BSA[c] 7.5 ± 5.6 h/day 11.6 ± 8.4 h/day	Low and middle socioeconomic groups	5-day diet record 16.4 16.5	 35 ± 23.75 35.25 ± 22.25
Sahu *et al.* [18]	139 pregnant women, 26.7 ± 4.1 years 121 adolescent girls, 14.3 ± 2.7 years 34 boys, 14.0 ± 3 years 28 girls, 14.4 ± 2.7 years	Lucknow, 26.55°N	Rice and wheat diet with seasonal fruits and vegetables Low milk and fish intake	32.4 ± 21.9 (S) 29.9 ± 19.8 (W) 35.4 ± 15.9 (S) 26.8 ± 8.1 (W) 49.1 ± 15.7 (S) 30.5 ± 20.7 (S) h/dx%BSA	LSES	No data	37.8 ± 19.8 33.3 ± 16 67.5 ± 29 31.3 ± 13.5
Khandare *et al.* [28]	Control-1443 High fluoride-240 8.7 ± 2.6 years (control) 9.4 ± 2.4 years (no deformities) 7.9 ± 2.4 years (with deformities)	Bihar villages, 25°N	Rice, potatoes, milk, some varieties of vegetables	Adequate but no specific data	Mostly lower socioeconomic strata in high fluoride villages	No data	Control: 108.75 ± 66 ($N = 7$) no deformities − 55.513 ($N = 10$) with deformities − 35 ± 20.25 ($N = 13$)
Goswami *et al.* [43]	Soldiers – 31 M, 25 ± 5 years, W Physicians and nurses – 11 M, 8 F, 23 ± 5 years, W Depigmented – 10 M, 5 F, 43 ± 16 years, W Physicians and nurses – 11 M, 8 F, 24 ± 4 years, S Pregnant women – 29, 23 ± 3 years, S Newborns – 16 M, 13 F, S	Delhi, 28.38°N	Predominantly vegetarian diet, meat 2–3 times/wk, fish was rarely included	370 ± 30 25 ± 5 5 ± 5 25 ± 5 25 ± 5	Pregnant women were from low socioeconomic group – annual i ncome <$1000	No data	47.17 ± 11.73 7.98 ± 3.49 18.2 ± 11.23 17.97 ± 7.98 21.9 ± 10.73 16.72 ± 4.99
Tandon *et al.* [16]	40 M, 22.7 ± 2.8 years 50 F, 23.4 ± 3.1 years	Delhi, 28.38°N	Unknown	Score 12 (M) 12 (F)	Staff paramilitary	No data	46 ± 13.25 63.25 ± 18.5

Table 1. Continued

Reference	Population, age	Location, latitude	Type of diet	Sun exposure, mean ± SD (min/day)	Socioeconomic status	Vitamin D intake, (IU/day)[a)]	Plasma 25(OH)D, mean ± SD (nmol/L)[b)]
Tiwari and Puliyel [99]	196 children (9–30 months of age)	Delhi, 28.38°N	Mostly vegetarian	Unknown	Poor, children from three slums	No data	17.8 ± 22.4 to 96.3 ± 25.7, >80% had < 35nmol/L, with the exception of one slum which had 2% < 35nmol/L
Marwaha *et al.* [17]	5137 school children 3089 LSES 2048 USES 760 children evaluated for biochemical markers	Delhi, 28.38°N	Unknown	≥30	USES LSES	No data	LSES – 26 ± 1 USES – 34.25 ± 1
Puri *et al.* [25]	3127 school girls 12.4 ± 3.2 years (193-LSES) 12.3 ± 3 years (211-USES) 404 girls evaluated for biochemical markers	Delhi, 28.38°N	55.7% vegetarians, 9.7% egg eaters, 34.5% non-vegetarians	45 25+ sunscreen (28%)	USES LSES	24 hr diet record 60 ± 52 112 ± 56	33.61 ± 17.43 29.38 ± 12.69
Agarwal *et al.* [20]	15 M, 11 F – high pollution, 16 ± 4 months 15 M, 16 F – low pollution 15.9 ± 3.8 months	Delhi, 28.38°N	Hindu, vegetarians	Children were mostly indoors	LSES	No data	31 ± 17.5 67.75 ± 17.5
Goswami *et al.* [100]	32 M (42.8 ± 16.6 years), 25 F (43.4 ± 12.6 years);	Rural parts of Delhi, 28.38°N	Unknown	>300 for rural and 25 for urban population	LSES	No data	44.2 ± 24.4 (M) 26.9 ± 15.9 (F)
Harinarayan *et al.* [15]	191 healthy subjects, 44 ± 1.03 years (rural) 125 healthy subjects, 45.5 ± 0.95 years (urban)	Tirupati, 13.26°N	Vegetarian diet, meat once/wk in urban and once/2 wk in rural areas	Rural – 8–10 h/day Urban-not reported	Students, staff of SVIMS and their relatives constituted urban subjects	No data	52.5 ± 1.15 33.8 ± 1.48
Harinarayan [23]	164 postmenopausal women, 54 ± 8 years Severe def Moderate def Insufficiency Normal level	Tirupati, 13.26°N	Mostly vegetarian diet with occasional meat consumption	4–6 h/day	Unknown	No data	8.4 ± 2.75 (6 or 4%) 20 ± 3.75 (43 or 26%) 37.5 ± 7 (85 or 52%) 63.75 ± 11.25 (30 or 18%)
Harinarayan *et al.* [19]	134 urban M, 46 ± 0.43 years 109 rural M, 43 ± 1.01 years 807 urban F, 46 ± 0.43 years 96 rural F, 43 ± 1.01 years	Tirupati, 13.26°N	Mostly vegetarian diet with occasional meat consumption	Rural-8–10 h/day Urban – not reported	Urban subjects were medical & paramedical staff	No data	46.35 ± 2 59.33 ± 2 38.75 ± 0.75 47.5 ± 2.23

Table 1. Continued

Reference	Population, age	Location, latitude	Type of diet	Sun exposure, mean ± SD (min/day)	Socioeconomic status	Vitamin D intake, (IU/day)[a)]	Plasma 25(OH)D, mean ± SD (nmol/L)[b)]
Harinarayan *et al.* [38]	30 urban boys 34 rural boys 39 urban girls 36 rural girls	Tirupati, 13.26°N	Mostly vegetarian diet with occasional meat consumption	Urban and rural children had arms, legs, face and forearms exposed to sun	Unknown	No data	38.93 ± 3.03 42.5 ± 3.25 46.25 ± 4.15 47.5 ± 3.98

F, females; M, males; W, winter; S, summer; depigmented, vitiligo universalis or albinism; LSES, lower socioeconomic strata; USES, upper socioeconomic strata.
a) To convert International units (IU) of vitamin D to μg, divided by 40.
b) To convert ng/mL from SI units, divided by 2.54.
c) BSA = % body surface area exposed.

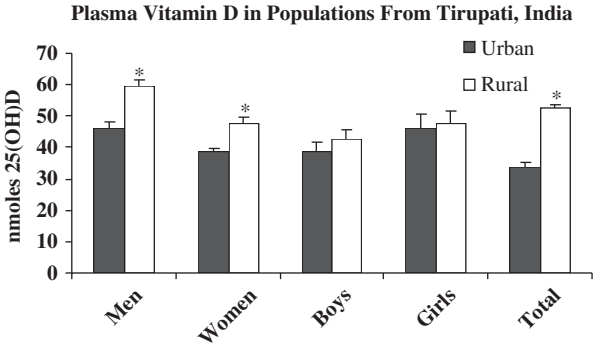

Figure 2. Compiled from studies conducted in Tirupati, India 13.26°N latitude [15, 19, 38]. Each bar represents mean ± SEM for that population. The * on the bars shows that the rural adult population had significantly higher plasma 25(OH)D than their urban counterparts with $p < 0.001$. There was no significant difference in plasma 25(OH)D between rural and urban boys and girls.

(children and older adults), had slightly higher 25(OH)D levels presumably due to higher sun exposure. The advantages to greater sun exposure in rural populations is clearly illustrated in Fig. 2, where in all cases, the rural residents at this Southern latitude had higher circulating levels of 25(OH)D than their urban counterparts [15, 19, 23]. Dietary vitamin D was measured in only two of the studies, and it was extremely low in both upper and lower socioeconomic groups and in urban and rural populations [25, 26]. Some of these studies have reported biochemical osteomalacia characterized by increased parathyroid hormone, reduced bone mineral density of the spine, femur and forearm and bone deformities [17, 26–28].

Postmenopausal women residing in Southern India showed varying degrees of vitamin D status, as shown in Fig. 3 [23]. These ranged from severely deficient to just adequate with 52% of the population showing a mean level of 37.5 nmol/L, a conservative cut-off level for vitamin D insufficiency used by many American and Canadian investigators [29]. More importantly, none of these women residing in sunny India had serum 25(OH)D concentrations in the optimal range associated with reduced levels of chronic diseases including osteoporosis.

3 Evidence of bone disorders associated with vitamin D deficiency

In addition to low plasma levels of vitamin D, there have been several reports of bone disorders associated with vitamin D and/or calcium deficiency. These studies are summarized in Table 2. Most important among these studies were a huge national survey conducted by Teotia and Teotia [30] and a case control study from villages in the Indian state of Bihar (25°N), showing increased bone deformities, including Genu valgum, Genu varum and anterior bowing of legs in young children, examples of

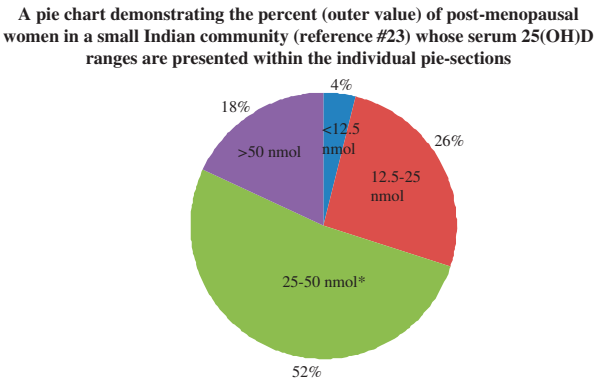

Figure 3. Vitamin D status measured by level of 25(OH)D (nmol/L) in a population of 164 postmenopausal women living in Southern India (13.26°N) are shown as a pie chart using data taken from Ref. [23]. The vitamin D concentrations are shown in the pie wedge, and the percent of the population with this value is shown on the outside of the pie chart. 52% of the women had serum 25(OH) D level at 37.5 nmol/L; 26% were at 20 nmol/L; 18% exceeded the cut-off value for vitamin D insufficiency used in the US NHANES III survey [95] (50 nmol/L), and 4% of the population was severely deficient at 8.4 nmol/L.

which are shown in Fig. 4 [28]. Although dietary calcium was low, serum calcium was within normal range, suggesting that calcium homeostasis was maintained, but it does not preclude the possibility that poor vitamin D status may also be a contributing factor to the observed bone deformities. Teotia and Teotia describe the widespread vitamin-D-deficiency-associated bone disorders that are observed in the Indian population [30]. This large population survey conducted between 1963 and 2005, involved 338 million people residing in 390 000 villages in 22 of the 28 states of India. The findings show that greater than 400 000 survey participants experienced bone disorders. Among these were 75 600 cases of vitamin-D-deficiency-related osteomalacia and 16 300 cases of frank rickets. Vitamin D deficiency was primarily attributed to reduced sun exposure combined with almost negligible dietary intake [30]. Teotia and Teotia [30] also reported that women with severe vitamin D deficiency gave birth to babies with rickets, which was not corrected by one mega dose of vitamin D3 (7.5 mg given intravenously) to the mothers prior to giving birth. It was only corrected in the infants when a second dose was given to the mother, underscoring the importance of first correcting the vitamin D levels in nursing mothers. With sufficient vitamin D treatment to mother and infant, it was possible to cure the rickets in these infants, even if they were exclusively breast fed [30].

Geographical differences in prevalence of vitamin D deficiency and bone disorders were also evident. People in northern parts of India had more severe vitamin D deficiency than those living south of Mumbai (18.56°N) [30]. This is attributed to the narrow angle and shorter duration of sunlight in northern compared with southern states [1]. People in northern states require longer duration of sun exposure to synthesize vitamin D. There is paucity of information to directly prove an increase in bone disorders among North Indians compared with those living in the southern states, an observation which merits further research.

In osteoporotic postmenopausal Indian women with low serum 25(OH) D, bone mineral content (BMC) of lifetime lacto-ovo vegetarians was compared with that of non-vegetarians revealing higher BMC in the vegetarians. This finding suggests that the vegetarian diets were likely adequate in calcium, and in this case, the known low vitamin D content of the diet did not place an additional burden on bone mineral status [30]. Earlier, it was believed that the high prevalence of vitamin D deficiency among Asians living in sun-deprived England was due to their typical high fiber intake from whole-wheat flour chapattis [31]. However, other studies have proved that the high fiber, phytate or specifically eating chapattis do not exacerbate vitamin D deficiency [19, 25, 32–38]. Among the general non-Asian population in the UK, the observed higher BMC of lifetime vegetarians consuming low phytate Western diets may relate more to the adequacy of their calcium intake [39]. The high phytate/calcium ratio reported for the typical Indian diet is associated with low calcium and low 25(OH)D levels which accelerates bone loss in most populations [1].

Compared with the US dietary guidance for calcium intake [40], the Indian Council of Medical Research considers a lower level of calcium adequate for various populations in India (Table 3). The Council has not proposed a dietary recommended intake level(s) for vitamin D [15]. These nutritional factors, namely lower dietary calcium and vitamin D, are known to adversely affect bone homeostasis [15] and likely contribute to the observed increase in bone disorders, such as osteomalacia in adults and rickets in children in India. Recent reviews estimate there are over 25 million people in India with osteoporosis, which is expected to reach about 36 million by 2013 [41, 42]. The extent of vitamin D deficiency's contribution in the development of osteoporosis is unclear. Serum vitamin D levels or bone mineral densities were not tested in these individuals diagnosed with osteoporosis due to lack of resources and the unwillingness of the insurance companies to bear the costs of these laboratory measures. Osteoporosis was attributed to reduced calcium and vitamin D intake owing to the increased cost of calcium rich foods in India, such as milk, yogurt, cheese, nuts and certain types of fish, absence of vitamin D fortification of food staples, as well as darker skin pigmentation and limited sun exposure which limit skin synthesis of vitamin D.

4 Evidence of effects of skin pigmentation and body exposure to sun on vitamin D status

Strong association between body exposure to sun and 25(OH)D levels in India have been documented very

Table 2. Bone diseases associated with vitamin D deficiency in India

Reference	Population	Location, Latitude	Clinical indicators of bone disorders	Calcium intake	Serum calcium and vitamin D (mean ± SD)
Teotia and Teotia [30]	213 760 patients with nutritional bone disease	Surveyed 22 states in India	75 600 Osteomalacia 16 300 vitamin D deficiency rickets	86 800 participants had low Ca intake	14 205 participants had calcium and vitamin D deficiency
Paul *et al.* [101]	150 ambulatory postmenopausal women	Vellore, Tamil Nadu, 12° 55′ N	Osteoporosis – 48% at the lumbar spine, 16.7% at the femoral neck and 50% at any site	398.76 ± 190.13 mg/d	Calcium: 9.41 ± 0.47 mg/dL 25(OH)D: 52.13 ± 21.58 nmol/L
Bhambri *et al.* [102]	19 F, 7 M, 39 ± 15 years	Delhi, 28.38°N	Difficulty walking (27%), bed-ridden (15%), muscle weakness (69%), pseudo fractures or loozer's zones (46%), fractures (15%), tetany (4%)	Unknown	Calcium: 8.2 ± 1 mg/dL 25(OH)D: 9.5 ± 7.5 nmol/L
Sachan *et al.* [26]	207 pregnant women	Delhi, 28.38°N	None had clinical osteomalacia, 14% had biochemical osteomalacia – heat labile alkaline phosphatase >125 IU/L PTH: 127 pg/mL – subjects with osteomalacia 74 pg/mL – subjects no osteomalacia	813 ± 435 mg/day – subjects with osteomalacia 737 ± 466 mg/day – subjects without osteomalacia	25(OH)D: 30.25 ± 2 nmol/L in osteomalacia 35.75 ± 23.25 nmol/L in subjects without osteomalacia
Arya *et al.* [27]	67 F and 25 M, healthy volunteers	Lucknow, 26.55°N	Bone mineral density of femur and forearm was lower compared with normal Caucasians; serum PTH was higher (75.5 pg/mL) in eight subjects with low 25(OH)D	438.6 ± 125.5 mg/day	25(OH)D: 30.75 ± 27.25 nmol/L
Harinarayan [23]	164 postmenopausal women	Tirupati, 13.26°N	Alkaline phosphatase – 126 ± 67 IU/L PTH 26 ± 20 pg/mL	322 ± 66 mg/day	Serum calcium: 9.7 ± 0.6 mg/dL 25(OH)D: 36.5 ± 17.5 nmol/L
Khandare *et al.* [28]	240 subjects from HFV 1443 subjects from control village (C)	Bihar, 25°N	Genu valgum, Genu varum and anterior bowing of legs, enlargement of epiphyses, neuro-muscular signs were observed in children 1–18 years old	346 ± 169.5 mg/day – HFV 409 ± 165.5 mg/day (C)	Calcium: 10.3 ± 0.6 mg/dL (C) 10.5 ± 0.7 mg/dL (no deformities) 9.4 ± 1.2 mg/dL (with deformities) Vitamin D (Table 1)

HFV, high fluoride village; PTH, parathyroid hormone.

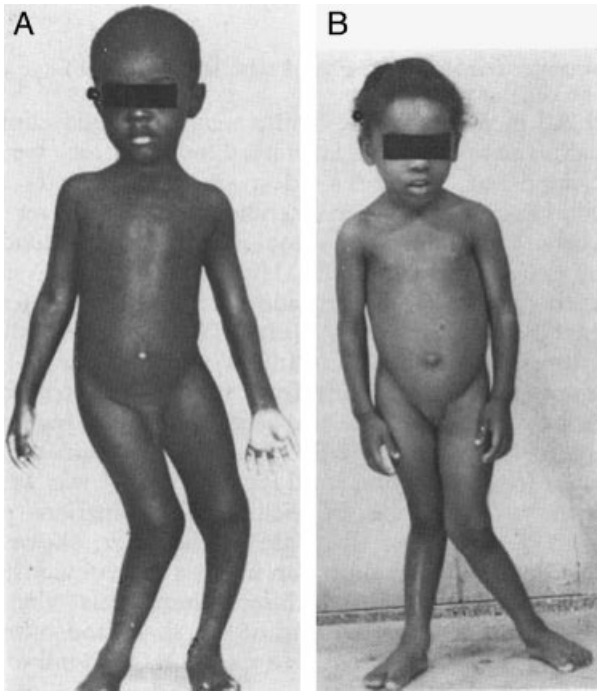

Figure 4. Vitamin D deficiency rickets in dark complexioned children living in the West Indies. (A) Jamaican boy with inadequate exposure to sunlight presenting with 'wind swept legs' or Genu varum. (B) Jamaican girl presenting with bilateral Genu valgum on admission to the hospital. Photograph reproduced with permission from C. G. Miller and W. Chutkan (*Arch. Dis. Childhood* 1976, *51*, 214–218). It is important to note that these conditions of wind swept legs are not exclusive to poor vitamin D status and may be due to calcium deficiency or a combination of both.

recently. For example, Sahu *et al.* have shown greater sun exposure among boys especially in summer months resulting in higher serum 25(OH)D levels [18]. Goswami *et al.* have shown much higher serum 25(OH)D in soldiers with longer sun exposure than in physicians, nurses, de-pigmented people (vitiligo universalis or albinism) and pregnant women [43]. Similarly, Zargar *et al.* have shown a direct correlation between sun exposure and serum 25(OH)D levels among farmers compared with government employees, people who spend most of the time inside their homes/offices, medical professionals and students [44]. This subject merits further discussion toward possible action to educate people about the relationship between safe sun exposure and optimal vitamin D levels. Regrettably, this action alone might not be sufficient as evidenced by the fact that more than 70% of the farmers were vitamin D insufficient (<50 nmol/L), with an average sun exposure of 25.1 h/wk [44]. Reduced 25(OH)D levels may also be due to darker skin pigmentation in most Indians, which is known to be an effective sunscreen blocking vitamin D synthesis [21, 22]. Skin types classified according to the level of melanin, the sun blocking pigment, require different durations of sun exposure to synthesize the same amount of vitamin D [45]. The majority of Asians indigenous to India range in skin type from IV to V and may require from two to three times longer exposure duration than lighter skinned Europeans (types I, II and III) to synthesize the same level of vitamin D [45]. These estimates are also based on considerable skin exposure (face, arms and legs), which may often be concealed by the modest traditional dress in India. Goswami *et al.* [43] showed that people without pigmentation had lower serum 25(OH)D levels in winter months and attributed this to the clothing covering most of their body surface (90%), thus limiting the sun exposure. Social and

Table 3. Dietary guidelines for calcium and vitamin D intake in India and the United States

Population	Calcium		Phosphorus		Vitamin D	
	Adequate intake (mg/day)		RDA (mg/day)		RDA (mg/day)	
	India	USA	India	USA	India	USA
Infants (0–6 months)	500	500		100	No guidelines	200[a]
Infants (6–12 months)	500	750		275		200
1–9 years (boys and girls)	400	800		460–500		200
4–12 years[b]	–	–	1000			200
10–15 years (boys and girls)	500	1200–1300		1250		200
16–18 years (boys and girls)	500	1200–1300		1250		200
Men	400	800–1000	400[c]	700		200 → 600[d]
Women	400	800–1000	400	700		200 → 600[d]
Pregnant and lactating	1000	1200–1300		1250		200

a) In 2008, the American Academy of Pediatrics (AAP) revised their 2003 guidelines on vitamin D supplementation. The AAP recommended an increase from 200 to 400 IU/day in infants consuming less than 500 mL formula *per* day [72].
b) Ref. [103].
c) Ref. [104].
d) Recommended intake increases with age.

religious customs that require people to wear concealing clothing, veiling and traditional attire, such as the ''Burqa'' and to a lesser extent the ''salvar kameez'' and sari significantly prevents sun exposure [44, 46, 47]. Puri *et al.* [25] have shown that school girls from lower socioeconomic strata in Delhi had slightly better serum 25(OH)D than those from upper socioeconomic strata, because 28% of their body surface was exposed to sun for about 45 min/day, compared with 15% body surface exposed to 25 min/day in the higher socioeconomic group.

5 Evidence of widespread vitamin D deficiency in exclusively breast-fed Indian infants

Breastfeeding is highly recommended for the first 6 months of an infant's life span to protect against the development of asthma, eczema, infectious diseases, sudden infant death syndrome, type 1 and type 2 diabetes and enhanced cognitive development [48, 49]. Despite the modernization of India and adoption of many Western practices, breastfeeding practices remain unchanged and its use is preferred by the vast majority of Indian women [50, 51]. However, exclusive breastfeeding by mothers who are vitamin D deficient can lead to higher incidence of infantile or nutritional rickets characterized by stunted growth, protruding abdomen, bowlegs and knock-kneed legs [52]. Poor vitamin D status in infants has also been linked to infections and impaired immune functions [53] as well as asthma and respiratory infections [54, 55]. Vitamin D is a critical nutrient in breast milk, whose level is very sensitive to maternal diet and sun exposure [56]. Mothers with adequate circulating vitamin D levels during pregnancy may provide sufficient vitamin D in milk for up to 8 wk after delivery [57]. Reflecting the poor vitamin D status of mothers worldwide, human breast milk is usually very low in vitamin D, containing approximately 25 IU/L vitamin D (>0.5 μg/L). A typical infant consumes about 800–1000 mL/day [58], which makes sun exposure the main source of vitamin D for infants who are exclusively breast fed and not receiving supplements. Exclusive breastfeeding has been shown to cause vitamin D deficiency in infants across the world [59–70]. It is possible to prevent vitamin D deficiency by supplementing the infants with 200 IU (5 μg) vitamin D/day [71]. Widespread practice of exclusive breastfeeding in India clearly contributes to greater vitamin D deficiency in infants [50, 52], particularly when the mothers or infants are not supplemented with vitamin D. Evidence for the adverse effects of unsupplemented exclusive breastfeeding to vitamin D status in Indian populations residing in India or other sunny Near East countries is summarized in Table 4. The growing evidence for increased vitamin D deficiency in infants manifested as rickets or other bone deformities will hopefully motivate the policy makers to initiate much needed guidelines for vitamin D supplementation and/or fortification.

In 2008, the American Academy of Pediatrics revised their 2003 guidelines on vitamin D supplementation, recommending an increase from 200 to 400 IU/day for children aged 2 months of age through adolescence [72]. The Academy expressed confidence in the safety of doubling the guidelines based on the fact that children in the US do not consume enough fish or vitamin-D-fortified milk, nor do they receive sufficient exposure to sunlight due to sunscreen use, pollution, protective clothing, living in northern latitudes, urban communities or having darker skin pigmentation [72].

6 Concluding remarks

We believe that the evidence presented in this review demonstrates a significantly high prevalence of vitamin D deficiency/insufficiency throughout India, affecting all ages, genders and socioeconomic classes. Widespread vitamin D deficiency in India among adults and children is evident from the average circulating 25(OH) D levels, which were 34.8 and 46.3 nmol/L, respectively. These levels are far below the levels of circulating 25(OH)D associated with reduced chronic disease risk [3]. In general, men and boys had better vitamin D status than their female counterparts, and rural populations were slightly better than those living in urban areas, possibly due to higher sun exposure. From all the reports, it is clear that the dietary intake of vitamin D is negligible due to low consumption of foods rich in vitamin D and the absence of fortification or supplementation. Most of the Indian population has darker skin and therefore need longer duration of sun exposure for optimal vitamin D synthesis. As the modern Indian work force spends more time indoors and continues the current preference for traditional clothing covering most of the body, Indians will face a growing trend for reduced sun exposure. We believe we have demonstrated sufficient evidence to stimulate discussion and possible action toward improving vitamin D content of the general Indian food supply.

The vitamin D situation in India is very similar to that in Jordan which gets plenty of sunlight throughout the year but 87% of the Jordanian women between ages 18 and 70 suffer from vitamin D deficiency (mean <50 nmol/L) (http://www.jordantimes.com/?news = 14125, last accessed April 22, 2009). Jordanian women wear traditional clothing concealing most of their bodies and both Indians and Jordanians have darker skin which blocks vitamin D synthesis. Until recently, neither Jordan nor India had national fortification or supplementation policies. In both the countries, most babies are exclusively breast fed for the first few months, which increases the chances of vitamin D deficiency among children unless they receive supplements. To rectify the problem with widespread poor vitamin D status, Jordan has created a policy and program to fortify their bread with vitamin D, a common staple consumed by

Table 4. Vitamin D levels of breast fed children in the near east and India

Reference	Age of infants	Duration of breast feeding, country of origin	Serum 25(OH)D (nmol/L), mean ± SD
Sachan *et al.* [26]	Cord blood	N/A	Mothers with osteomalacia: 20.25 ± 18.5 Mothers without osteomalacia: 21.25 ± 13.5
Girish and Subramaniam [52]	6.5 months ($N = 20$)	Exclusively breast fed for 6 months, Nagpur, India	Clinically diagnosed with rickets but no serum 25(OH)D data
Bhalala *et al.* [50]	3 months ($N = 35$)	Exclusively breast fed, India	Infants: 45.48 ± 24.35
Balasubramanian *et al.* [105]	3-6 months ($N = 13$)	Exclusively breast fed, Chennai, India	Infants: 9.65 ± 5.18
Dawodu *et al.* [106]	Mother–infant pair study, median age – 6 weeks ($N = 90$)	Exclusively breast fed, United Arab Emirates	Median values of serum 25(OH)D: Mothers – 21.75, Infants – 11.5
Andiran *et al.* [107]	Mother–infant pair study, 19.5 ± 4.4 days ($N = 54$)	Exclusively breast fed, Turkey	Mothers – 29.11 ± 10.47, Infants – 18.62 ± 8
Atiq *et al.* [108]	Mother–infant pair study 5.1 ± 2.7 months ($N = 62$)	Breast fed up to 4 months, Pakistan	USE mothers ($N = 37$): 26.5 ± 24.1 Infants ($N = 37$): 22.46 ± 16.4 LSE mothers ($N = 25$): 39.76 ± 15.7 Infants ($N = 25$): 52.34 ± 28.78

LSE, lower socioeconomic class; USE, upper socioeconomic class.

all but the very youngest Jordanians (http://www.jordantimes.com/news = 14125, last accessed April 22, 2009).

India would be well suited to follow Jordan's lead by fortifying wheat flour with vitamin D. Wheat flour is the major component of chapattis, a bread staple consumed by vegetarians as well as omnivores, by all ages, socioeconomic backgrounds and by the rural and urban populations. Others have shown the stability of vitamin D fortification of grain products to long shelf life, stability to high baking temperatures and excellent bioavailability [33, 73–75]. Unlike pasteurized, fortified milk which is not widely consumed in India, flour fortification with vitamin D requires no refrigeration or special distribution and processing and is cost effective [73]. To date, studies examining the potential for correcting vitamin D insufficiency through fortification of bread and other grain products have used only modest levels of vitamin D (400 IU or 10 μg vitamin D_3 in three slices of bread) [33, 75]. However, recently, Mocanu *et al.* demonstrated both the efficacy and safety of fortifying bread with 5000 IU (125 μg) of vitamin D_3 *per* daily serving consumed by sun-deprived nursing home residents in Romania (latitude: 47°N). Fortification of bread with this highest level resulted in higher serum concentrations (>75 nmol/L) and significantly improved bone density measures [76]. To improve the vitamin D status, a nationwide program to monitor the circulating levels of 25(OH)D needs to be initiated. Sound national recommendations for Indian dietary intakes based on age, gender and other factors such as pregnancy or other medical conditions need to be established. From these guidelines, India can develop national policies for supplementation of pregnant women and infants.

There is growing evidence for the critical role of vitamin D adequacy in the prevention of serious chronic diseases beyond osteoporosis [77], osteomalacia [76] and rickets [78]. Vitamin D nutritional status most likely works in coordination with specific genetic predispositions in relation to the development of diseases, such as cancer and diabetes. According to the National Cancer Institute breast and prostate cancer cohort consortium (2009), vitamin D is hypothesized to reduce the risk of breast cancer by inhibiting cell proliferation *via* the nuclear vitamin D receptor (VDR) [79]. Nucleotide polymorphisms (SNP) in the VDR gene have been inconsistently associated with breast cancer risks; however, Chakraborty *et al.* show significant association of the VDR polymorphism with breast cancer risk in North Indians [80]. The VDR gene polymorphisms are also suspected in type 2 diabetes mellitus. Bid *et al.* have shown an increased risk of type 2 diabetes mellitus in North Indians with a specific combination of VDR gene polymorphisms, FFBbtt [81]. The interaction between vitamin D nutritional status and unique VDR gene polymorphisms in susceptibility to diseases in India needs further study. Vitamin D nutritional status works in concert with genetics; nevertheless, vitamin D adequacy by itself has been shown to be associated with reduced mortality [82–84] as well as reduced morbidity due to cancer [85], cardiovascular diseases [86], diabetes [87] and others [88, 89]. Efficacy of vitamin D fortification of foods to increase circulating 25(OH)D is well established [90, 91]. Given the rising prevalence of coronary heart disease and diabetes in India [92, 93], correction of widespread vitamin D deficiency/insufficiency through fortification of flour or development of supplementation programs could signifi-

cantly impact future health care costs and incidence of chronic disease in all Indians.

The findings and conclusions presented in this review are those of the authors and do not necessarily represent the views or opinions of the US Food and Drug Administration. Mention of trade names, product labels or food manufacturers does not constitute endorsement or recommendation for use by the US Food and Drug Administration.

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