Review Article

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Prevalence of hypovitaminosis D in India & way forward

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Deficiency of vitamin D or hypovitaminosis D is widespread irrespective of age, gender, race and geography and has emerged as an important area of research. Vitamin D deficiency may lead to osteoporosis (osteomalacia in adults and rickets in children) along with calcium deficiency. Its deficiency is linked with low bone mass, weakness of muscles and increased risk of fracture. However, further research is needed to link deficiency of vitamin D with extra-skeletal consequences such as cancer, cardiovascular disease, diabetes, infections and autoimmune disorders. The causes of vitamin D deficiency include length and timing of sun exposure, amount of skin exposed, latitude, season, level of pollution in atmosphere, clothing, skin pigmentation, application of sunscreen, dietary factors and genetic factors. The primary source is sunlight, and the dietary sources include animal products such as fatty fish, food items fortified with vitamin D and supplements. Different cut-offs have been used to define hypovitaminosis D and its severity in different studies. Based on the findings from some Indian studies, a high prevalence of hypovitaminosis D was observed among different age groups. Hypovitaminosis D ranged from 84.9 to 100 per cent among school-going children, 42 to 74 per cent among pregnant women, 44.3 to 66.7 per cent among infants, 70 to 81.1 per cent among lactating mothers and 30 to 91.2 per cent among adults. To tackle the problem of hypovitaminosis D in India, vitamin D fortification in staple foods, supplementation of vitamin D along with calcium, inclusion of local fortified food items in supplementary nutrition programmes launched by the government, cooperation from stakeholders from food industry and creating awareness among physicians and the general population may help in combating the problem to some extent.

Key words Fortification - 25-hydroxyvitamin D - hypovitaminosis D - India - prevalence

Introduction

The deficiency of vitamin D or hypovitaminosis D has emerged as an important area of research. Inadequate levels of vitamin D are widespread irrespective of age, gender, race, and geography[1]. Vitamin D a fat soluble vitamin also functions as a hormone. It is involved in maintaining the integrity of skeletal system as it regulates parathyroid hormone, calcium and phosphorous metabolism[2]. It is also essential for calcium homoeostasis and musculoskeletal health[3,4]. The level of 25-hydroxyvitamin D [25(OH)D] is considered as the most reliable index for assessing an individual's vitamin D status[4,5].

Skeletal consequences of hypovitaminosis D

Deficiency of vitamin D and calcium may lead to osteoporosis. Deficiency of vitamin D can cause low bone mass (rickets in children and osteomalacia in adults) and muscle weakness, thus increasing the risk of fracture[6,7]. The intestinal calcium absorption reduces to as low as 10-15 per cent in vitamin D-deficient state, whereas it is 30-80 per cent in vitamin D-sufficient state[8]. Adequate intake of calcium together with vitamin D can help in maintaining peak bone mass[7]. Adequate levels of vitamin D during adolescence can be helpful in reducing the risk of osteoporosis during adulthood[7].

Extra-skeletal consequences of hypovitaminosis D

The presence of vitamin D receptors and enzymes which produce the active form of vitamin D (*i.e.* 1,25-dihydroxyvitamin D) in the skin have highlighted the potential role of vitamin D in reducing risk of chronic diseases, such as carcinomas, autoimmune diseases, infectious diseases and cardiovascular diseases[2]. However, the Institute of Medicine Committee in its report on dietary requirements for calcium and vitamin D has concluded that there are inconclusive and inconsistent data that vitamin D and calcium lower the risk of cancer, cardiovascular disease, diabetes, infections, autoimmune disorders and other extra-skeletal consequences[9].

Vitamin D deficiency is prevalent in India. Factors such as length and timing of sun exposure, amount of skin exposed, latitude, season, level of pollution in atmosphere, clothing, skin pigmentation, application of sunscreen, dietary factors and genetic factors may lead to hypovitaminosis D[4,7,8,10]. Other factors which may cause lower levels of vitamin D include changing food habits, consuming only vegetarian food, less intake of vitamin D-fortified foods, high fibre diet-containing phosphates and phytates, cultural and traditional practices such as '*burqa*' and '*pardah* system', and repeated, unplanned and unspaced pregnancies[4,7,11]. Association between modifiable factors such as sun exposure, sunscreen use, geographic allocation (latitude and altitude), atmospheric pollution, clothing, melanin pigmentation, ageing and vegetarian diet and decreased vitamin D synthesis has been reported[12,13].

The primary source of vitamin D is sunlight. Vitamin D is synthesized in the skin by conversion of 7-dehydrocholesterol to cholecalciferol (vitamin D_3) when it is exposed to ultraviolet B radiation (wavelength: 290-320 nm)[4,14]. Dietary sources of vitamin D include animal products such as fatty fish, food items fortified with vitamin D and supplements[9,14]. Adequate levels of vitamin D can be achieved by exposure to sunlight[1]. Exposing skin (arms and face area) to sunlight without applying sunscreen for half an hour (between 1000 and 1400 h) every day is considered adequate to avoid hypovitaminosis D[7]. However, even in tropical countries like India which get plenty of sunshine, a high prevalence of hypovitaminosis D (70-100%) has been observed among healthy individuals due to socio-economic and cultural constraints[1].

An individual's serum concentration of 25(OH) D of at least 20 ng/ml (50 nmol/l) is considered sufficient, levels >30 ng/ml (75 nmol/l) are not related with benefits, and levels >50 ng/ml (125 nmol/l) have been associated with some risks[9]. Distinct cut-offs have been used to define hypovitaminosis D and the level of severity of its deficiency by different experts in their studies. Table I lists some of the diagnostic cut-offs.

Prevalence of hypovitaminosis D among different age groups in India

Vitamin D deficiency has been observed in countries which are 'sunshine deficient' and 'sunshine sufficient'[14]. It is considered as a public health problem in India. Even though Indians receive abundant sunshine throughout the year, hypovitaminosis D is still considered as a growing problem[19,20]. A high prevalence (50-90%) of vitamin D deficiency along with low dietary calcium intake has been documented in Indian population[3].

A review of literature was carried out to identify studies conducted to assess the prevalence of vitamin D deficiency in India among different age groups. Selected

Table I. Some diagnostic cut-offs for serum 25-hydroxyvitamin D [25(OH)D] concentrations for the detection of hypovitaminosis D

Reference	Diagnostic cut-offs for serum 25(OH)D concentrations (ng/ml)
Lips, 2001[15]	10-20: Mild hypovitaminosis D 5-10: Moderate hypovitaminosis D <5: Severe hypovitaminosis D
Consensus by Dawson-Hughes *et al*, 2005[16]; Grant and Hollick, 2005[17] and Hollis, 2005[18]	<20: Vitamin D deficient 20-30: Vitamin D insufficient >30: Vitamin D sufficient

Table II. Selected studies on the prevalence of hypovitaminosis D among different age and physiological groups in India

Reference	Locale	Age group	Sample size	Criteria for defining hypovitaminosis D based on serum 25(OH)D levels (ng/ml or nmol/l)	Method of analysis	Prevalence of hypovitaminosis D (%)
School going children						
Kapil *et al*, 2017[21]	Shimla, Himachal Pradesh	6-18 yr	626	Sufficient: ≥30 ng/ml Insufficient: 20-29 ng/ml Deficient: <20 ng/ml	Chemiluminescence	Sufficient: 1.1 Insufficient: 5.9 Deficient: 93
Khadgawat *et al*, 2012[22]	New Delhi (hospital-based)	6-17 yr (obese adolescents)	62	<20 ng/ml	Radioimmunoassay	100 <5 ng/ml: 17.7 5-<10 ng/ml: 48.3 ≥10-<20 ng/ml: 33.8
Marwaha *et al*, 2005[23]	New Delhi	10-18 yr	5137 LSES: 3089 (1079 boys, 2010 girls) USES: 2048 (968 boys, 1080 girls)	<20 ng/ml	Radioimmunoassay	LSES: 92.6 USES: 84.9
Infants, pregnant and lactating mothers						
Sahu *et al*, 2009[24]	Lucknow	Adolescent girls: 10-20 yr Pregnant women: Not mentioned	121 adolescent girls; 139 pregnant women in the second trimester	<50 nmol/l	Radioimmunoassay	Adolescent girls: 88·6 Pregnant women: 74
Agarwal *et al*, 2010[25]	Delhi	Exclusively breastfed infant-mother pairs	179 infant-mother pairs (96 AGA (Group 1) and 83 SGA infants (Group 2) recruited at 10 wk) At 6 months: 52 (Group 1) and 45 (Group 2) evaluated	<11 ng/ml	Radioimmunoassay	Infants at 10 wk: 55.67 (total), 55.77 (AGA), 55.26 (SGA) Infants at 6 months: 44.33 (total), 38.46 (AGA), 57.11 (SGA) Mothers: 70
Jain *et al*, 2011[26]	New Delhi	Infants aged 2.5-3.5 months and their mothers	98 infants and their mothers [47 enrolled in winter (November-January) and 51 in summer (April-June)]	Deficiency: ≤15 ng/ml Insufficiency: 15-20 ng/ml, severe deficiency: <5 ng/ml	Radioimmunoassay	Deficiency: Infants: 66.7; mothers: 81.1 Insufficiency: Infants: 19.8; mothers: 11.6 Severe deficiency: Infants: 27.1; mothers: 23.2
Dasgupta *et al*, 2012[12]	North-Eastern India	20-40 yr	50 pregnant females studied during first trimester of pregnancy 50 age- and BMI-matched females taken as controls	Not mentioned	Radioimmunoassay	Cases: 42% had vitamin D deficiency and 14% had vitamin D insufficiency Controls: 20% had vitamin D deficiency and 24% had vitamin D insufficiency (P=0.0375)

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Reference	Locale	Age group	Sample size	Criteria for defining hypovitaminosis D based on serum 25(OH)D levels (ng/ml or nmol/l)	Method of analysis	Prevalence of hypovitaminosis D (%)
Adults						
Harinarayan 2005[27]	Tirupati	-	164 post-menopausal women	Deficiency: <10 ng/ml Insufficiency: 10-20 ng/ml Normal: >20 ng/ml	Radioimmunoassay	Deficiency: 30 Insufficiency: 52 Normal: 18
Harinarayan *et al*, 2007[28]	Tirupati	-	943 (urban) 205 (rural)	Deficiency: <20 ng/ml Insufficiency: 20-30 ng/ml Sufficiency: >30 ng/ml	Radioimmunoassay	Deficiency: Rural - men: 44; women: 70 Urban - men: 62; women: 75 Sufficiency: Rural - men: 39.5; women: 29 Urban - men: 26; women: 19 Insufficiency: Rural - men: 16.5; women: 1 Urban - men: 12; women: 6
Zargar *et al*, 2007[29]	Kashmir	18-40 yr	92 (64 men; 28 NPNL women)	Deficiency: <50 nmol/l Mild: 25-50 nmol/l, Moderate: 12.5-25 nmol/l Severe: <12.5 nmol/l	Radioimmunoassay	Deficiency: 83 Mild deficiency: 25 Moderate deficiency: 33 Severe deficiency: 25
Goswami *et al*, 2009[30]	Delhi	16-60 yr	642 (244 males; 398 females)	≤25.0 nmol/l	Radioimmunoassay	87
Shivane *et al*, 2011[31]	Mumbai	25-35 yr	1137	Severe deficiency: <5 ng/ml Moderate deficiency: 5-10 ng/ml Mild deficiency: 10-20 ng/ml Sufficiency: >20 ng/ml Optimal status: >30 ng/ml	Radioimmunoassay	Severe deficiency: 2.9 Moderate deficiency: 16.45 Mild deficiency: 51.45 Sufficiency: 30.78 Optimal status: 7.2
Marwaha *et al*, 2011[32]	Delhi	≥50 yr	1600 adults	<20 ng/ml	Radioimmunoassay	Deficiency: 91.2
Goswami *et al*, 2015[33]	New Delhi	-	194 male adults further categorized into: Outdoor (n=88) Mixed outdoor-indoor (n=32) Indoor (n=74)	Deficient: ≤20.0 ng/ml Insufficient: 20.1-30 ng/ml Sufficient: >30.0 ng/ml	Chemiluminescence	Deficient: 14.8 (outdoors), 62.5 (mixed), 97.3 (indoors) Insufficient: 45.4 (outdoors), 34.4 (mixed), 2.7 (indoors) Sufficient: 39.8 (outdoors), 3.1 (mixed), 0 (indoors)

LSES, lower socio-economic schools; USES, upper socioeconomic schools; BMI, body mass index; AGA, appropriate-for-gestational age; SGA, small-for-gestational age; NPNL, non-pregnant non-lactating

Table III. Selected randomized controlled trials on vitamin D in India

Reference	Locale	Age group	Sample size	Dose and duration	Criteria for defining hypovitaminosis D based on serum 25(OH)D levels (ng/ml or nmol/l)	Results
Harinarayan *et al*, 2015[36]	-	-	132 (n=41, 35 and 56 each at baseline and 8 wk; n=41, 23, 30 at 20 wk)	Protocol 1 (intensive regimen): 60,000 IU oral cholecalciferol once/week for 2 months+ elemental calcium (1 g/day)+ supervised monitoring Protocol 2 (parenteral regimen): single dose cholecalciferol 600,000 IU+elemental calcium 1 g/day. Oral cholecalciferol 600,000 IU/ fortnight+elemental calcium 1 g/day for 3 months Protocol 3: Similar to Protocol 1+No supervised monitoring	Sufficiency: >30 ng/ml Deficiency: <20 ng/ml	Baseline Deficiency: 98% (Protocol 1), 100% (Protocol 2), 96.5% (Protocol 3) 8 wk 17% (Protocol 1), 6% (Protocol 2), 46% (Protocol 3) 20 wk 24% (Protocol 1), 0% (Protocol 2), 23% (Protocol 3)
Goswami *et al*, 2012[37]	Delhi	≥21 yr (females)	153	4 groups: double placebo (n=37), calcium/placebo (n=38), cholecalciferol/placebo (n=39) and cholecalciferol/calcium (n=39) Cholecalciferol: 60,000 IU/wk for 8 wk followed by 60,000 IU/ fortnight Elemental calcium: 500 mg twice/day for 6 months	Not mentioned	An increase of 20.6±8.73 and 17.5±8.61 was seen in serum 25(OH) D (ng/ml) levels in cholecalciferol/placebo and cholecalciferol/ calcium group, respectively
Khadgawat *et al*, 2013[38]	National Capital Region of Delhi	10-14 yr	n=713 (boys-300; girls-413)	All groups received 200 ml milk/ day Group A (n=237): unfortified milk Group B (n=243): milk fortified with 600 IU (15 µg) of vitamin D Group C (n=233): milk fortified with 1000 IU (25 µg) of vitamin D for 12 wk	<20 ng/ml	Baseline serum 25(OH) D level (ng/ml) Group A: 11.74±5.23 Group B: 11.42±5.24 Group C: 11.94±5.62 Endline serum 25 (OH) D level (ng/ml) Group A: 10.83±5.24 Group B: 22.87±6.75 (P<0.001) Group C: 27.67±8.47 (P<0.001)
Garg *et al*, 2013[39*]	New Delhi	10-15 yr	482	Group 1 (n=238), Group 2 (n=139) and Group 3 (n=134) each given 60,000 IU of vitamin D_3 granules (cholecalciferol)/wk along with unfortified milk (200 ml) daily for 4, 6 and 8 wk, respectively Groups 2 and 3 received fortified milk (200 ml) (fortified with 600 IU of vitamin D3) daily for 12 wk	Sufficiency: >75 nmol/l (>30 ng/ml) Deficiency: <50 nmol/l (<20 ng/ml)	In all 3 groups, >90% subjects attained vitamin D sufficiency

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Reference	Locale	Age group	Sample size	Dose and duration	Criteria for defining hypovitaminosis D based on serum 25(OH)D levels (ng/ml or nmol/l)	Results
Agarwal *et al*, 2013[13^]	New Delhi	40-73 yr (Post-menopausal women)	64	Group A (control): 1000 mg calcium carbonate (n=21) Group B: 1000 mg calcium carbonate+500 IU vitamin D (n=25) Group C: 1000 mg calcium carbonate+1000 IU vitamin D (n=18) for 3 months	Deficiency: <20 ng/ml (50 nmol/l) Insufficiency: 20-30 ng/ml (525-725 nmol/l) Normal:>30 ng/ml	Baseline: 83.7% (deficiency), 8.7% (insufficiency) and 7.6% (normal) Post-intervention: Normal: 0 (Group A), 4% (Group B), 22% (Group C) Sufficiency: Group A (4.7%), 12 % (Group B), 38.9% (Group C)
Marwaha *et al*, 2010[40]	Delhi	6-17 yr	290 healthy schoolgirls (LSES-124; USES-166)	Cholecalciferol granules (sachets) 60,000 IU of cholecalciferol granules given as follows Two-monthly D_3 Group: 1000 IU/day every 2 months One-monthly D_3 group: 2000 IU/day every month for one year	Not mentioned	Serum 25(OH)D (nmol/l) LSES Two-monthly D_3 group (n=60) Baseline: 31.20 (1.68) 6 months: 39.53 (2.01)* 12 months: 53.0 (3.05)#,$ One-monthly D_3 group (n=64) Baseline: 32.93 (1.37) 6 months: 43.90 (1.50)* 12 months: 59.33 (2.64)#,$ USES Two-monthly D_3 group (n=81) Baseline: 29.13 (1.54) 6 months: 39.55 (1.24)* 12 months: 38.25 (2.13)# One-monthly D3 group (n=85) Baseline: 30.80 (1.39) 6 months: 46.81 (1.45)* 12 months: 49.94 (2.01)# *P<0.05 for baseline vs 6 months #P<0.05 for baseline vs 12 months $$P$<0.05 for 6 months vs 12 months

*Open label non-randomized prospective trial; ^Open label study; LSES, lower socio-economic strata; USES, upper socio-economic strata

studies (since 2005) on the prevalence of vitamin D deficiency have been tabulated for different age groups such as school-going children; infants, pregnant and lactating mothers and adults in this review article. Selected randomized controlled trials on vitamin D conducted in India have also been tabulated. Studies reviewed have been divided into the following:

Prevalence studies

Several studies conducted to assess hypovitaminosis D in different age groups in India reveal a widespread prevalence of vitamin D deficiency among all age groups, such as school-aged children, pregnant and lactating mothers, their neonates and adults (Table II). It should be noted that based on selected studies included

in Table II, the prevalence of hypovitaminosis D ranged from 84.9 to 100 per cent among school-going children, 42 to 74 per cent among pregnant women, 44.3 to 66.7 per cent among infants, 70 to 81.1 per cent among lactating mothers and 30 to 91.2 per cent among adults. Hypovitaminosis D was present in all obese children aged 6-17 yr[22]; in 93 per cent children aged 6-18 yr[21] and in 93 and 85 per cent children (aged 10-18 yr) belonging to lower and upper socio-economic groups, respectively[23]. A high prevalence of vitamin D deficiency (>65%) was reported among infants, pregnant and lactating mothers[24-26]. One study reported 42 per cent prevalence of vitamin D deficiency among pregnant women[12]. It is important that pregnant women have adequate levels of vitamin D as undernutrition in pregnant women has been linked with birth of low birth weight babies[34]. Similarly, a high prevalence of vitamin D deficiency has been reported among adults[27-33]. All studies included in this Table used radioimmunoassay and only two studies[21,33] used chemiluminescence to measure serum 25(OH)D levels. A high prevalence of deficiency of vitamin D among healthy Indian population, irrespective of age, gender, menopausal status and urban/rural areas, was also reported in a systematic review[35].

Randomized controlled trials

Selected randomized controlled trials on vitamin D supplementation conducted in India have been listed in Table III. In most of these studies, cholecalciferol was given as a supplement. Calcium supplementation was also provided along with vitamin D supplementation. The duration of intervention ranged from three months to one year. Some studies mentioned the percentage of vitamin D-deficient individuals, whereas some only presented the mean/median values of 25(OH)D levels before and after the intervention.

Way forward: Management of hypovitaminosis D

In India, fortifying staple foods with vitamin D can be a feasible population-based strategy[1]. It is vital that calcium supplementation should also be provided along vitamin D supplementation[41]. Evidence suggests that fortification of milk with vitamin D is an efficient and safe way of improving serum 25(OH)D levels in India[38]. It is also suggested that supplementary nutrition programmes launched by the government should include local food items fortified with micronutrients including vitamin D to address this issue. Stakeholders from food industry can also help in making fortification programmes successful in India[1]. Creating awareness among physicians and the general population will also help in combating the problem to some extent.

Conclusion

Hypovitaminosis D is prevalent among Indian population, irrespective of age, physiological status and geographical location. In India, fortifying staple foods with vitamin D, supplementing vitamin D along with calcium and inclusion of local food items fortified with vitamin D in supplementary nutrition programmes launched by the government may help in improving the problem of hypovitaminosis D.

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