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ORIGINAL ARTICLE

Prevalence of Vitamin D Deficiency in Children (6–18 years) Residing in Kullu and Kangra Districts of Himachal Pradesh, India

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Abstract

Objective To assess the prevalence of Vitamin D deficiency (VDD) and associated risk factors amongst children in the age group of 6–18 y residing at an altitude of 1000 mts and above.
Methods A community based cross-sectional study was conducted in the year 2015–2016. Two districts (namely: Kangra and Kullu) of Himachal Pradesh state, India was selected for the present study. In each district thirty clusters/schools were identified using Population Proportionate to Size (PPS) sampling methodology. In the identified school, all the children in schools were enlisted. Twenty children per school were selected by using random number tables. A total of 1222 children (Kangra: 610; Kullu: 612) in the age group of 6–18 y were enrolled. The data on socio economic status, physical activity and sunlight exposure was collected. The blood samples were collected and serum 25-hydroxyvitamin D, intact parathyroid hormone, serum calcium, phosphorous, albumin and alkaline phosphate were assessed using standard procedures.
Results Eighty one percent (Kangra) and 80.0% (Kullu) of school age children were found Vitamin D deficient as per serum 25(OH) D levels (less than 20 ng/ml).
Conclusions A high prevalence of VDD was found in children residing in 2 districts located at high altitude regions of Himachal Pradesh, India.

Keywords Vitamin D deficiency · Parathyroid hormone · Children · India

Introduction

The World is currently facing an unrecognized and untreated pandemic of Vitamin D Deficiency (VDD) [1]. VDD is a significant health problem in developed as well as developing countries [2], including India [3]. In the recent past, high prevalence of VDD (85–98%) has been reported in Indian children and adolescents in plain regions of India especially in those residing in urban indoor [4–8]. Vitamin D is required for calcium absorption and bone development in children [9]. Vitamin D is also involved in various physiological and pathological processes [10]. Recently, role of Vitamin D in functioning of immune system [11], cardiovascular, endocrine, neuro-psychological, neuromuscular, cellular differentiation [12] and anticancer actions has been documented [13–19].

The common risk factors associated with VDD in India are low exposure to sunshine, atmospheric pollution, indoor confinement of children during the day, high rise buildings and

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low physical activity [20–23]. These risk factors are not present at high altitude regions as compared to plains areas.

There is limited data on prevalence of VDD amongst children in the age group of 6–18 y from high altitude regions. The authors showed a high prevalence of VDD in their earlier published data on prevalence of VDD amongst children residing in the high altitude district Shimla, Himachal Pradesh [24]. The present study was conducted to assess the prevalence of VDD and associated risk factors amongst children in the age group of 6–18 y residing at an altitude of 1000 mts and above in the other two districts of Himachal Pradesh, India namely: Kangra and Kullu. It was hypothesized that school age children residing at an altitude of 1000 mts and above the sea level will have low prevalence of VDD due to higher exposure to sunlight, absence of high rise buildings, lower air pollution and more physical activity.

Material and Methods

A community based cross-sectional study was conducted in the year 2015–2016. The study was undertaken in the state of Himachal Pradesh, India, which has three geographical regions namely: (i) Kangra, (ii) Mandi, and (iii) Shimla. One district was selected randomly from geographical regions namely: Kangra and Mandi, *i.e.,* Kangra (Kangra region) and Kullu (Mandi region). District Kangra is situated in western himalayas at latitude of 32°0 N and longitude of 76.3°E. The district Kullu is situated at latitude of 31.8° N and longitude of 77.4° E. The schools which were located at 1000 mts and above were only included in the study.

The authors adopted school based approach for data collection for the study. More than 90% of children in the age group of 6–18 y residing in the villages attended the school (as per records of Department of Education, Himachal Pradesh Government, India) in the Kangra and Kullu districts selected; hence, authors considered the children studying in the school as a proxy of the children residing in the community. All the middle and senior secondary schools in the district were enlisted along with their enrollment. In each district, 30 clusters (schools) were identified by using Population Proportionate to Size (PPS) sampling methodology. In each school, all children in the age group of 6–18 y were enlisted. From this list, a minimum of 20 children in the age group of 6–18 y were selected with the help of random number tables.

The inclusion criteria adopted was: i) Healthy children in the age group of 6–18 y and ii) Written consent from parents. The exclusion criteria adopted was: i) Children suffering from any disease/factor that could influence the Vitamin D status like systemic illness and endocrine disorders ii) Subjects consuming drugs which may alter Vitamin D status in the body *e.g.,* phenobarbital, phenytoin, isoniazid, steroids, calcium and Vitamin D supplements during last six months and iii) Subjects recently (2015–2016) shifted their residence from the plain areas to hilly areas.

A pre-tested structured questionnaire was administered to each child to elicit information on identification data and socio-demographic profile. Socio-economic status (SES) was assessed using modified Kuppuswamy's socioeconomic status scale [25].

The standing height was recorded with bare foot, using a standard stadiometer (SECA 213) to the nearest 1 mm. The body weight was assessed using a clinical balance (SECA 813) to the nearest 0·1 kg, wearing minimal clothing and without shoes. Body Mass Index (BMI) was calculated as weight (kg)/height (m^2).

All the subjects were examined for clinical signs of VDD. Subjects were requested to walk and movements of limbs were assessed for the diagnosis of bow leg (genu varum) and knock knee (genu valgum). The forehead was examined for frontal bossing. The subjects were also observed while getting up from a sitting position and *vice-versa* for the diagnosis of muscle weakness.

Physical activity assessment was done by administering a detailed oral questionnaire. The data on the type of physical activity performed along with duration (in minutes) in the last 24 h of the survey was collected during school and home. The physical activities were then categorized as light, moderate or heavy activity based on metabolic equivalent of task (MET) values. The physical activity level (PAL) value for each subject in the age group of 12–18 y was calculated by using standard methodology [26].

An oral questionnaire was administered to collect data on time spent in sunshine during last 24 h of survey. The sunshine exposure of the subjects was calculated with the help of Wallace' Rule of Nine [27]. The operational flow diagram of the study is depicted in Fig. 1.

Blood samples were collected by venipuncture from median cubital vein. After collection, blood samples were centrifuged within two hours and serum samples were stored at −20 °C until transported to central laboratory, All India Institute of Medical Sciences, New Delhi, India. In central lab the serum was stored at −70 degree until analysis.

The biochemical estimation of serum 25-hydroxyvitamin D ((25OH) D) and intact parathyroid hormone (iPTH) was done using chemiluminescence immunoassay (CLIA) using kits (DiaSorin Co., Italy).

25(OH) D levels in serum were measured by direct competitive chemiluminescence immunoassay on LIAISON (Diasorin) analyzer. The lower limit of quantitation of the assay was 4.0 ng/ml. The intrassay and interassay CV was less than 4% and 8% respectively.

Serum concentration of parathyroid hormone (PTH) was measured by two site sandwich chemiluminescence immunoassay that uses two polyclonal antibodies for capture and detection of intact PTH on LIAISON (Diasorin) Analyzer. The

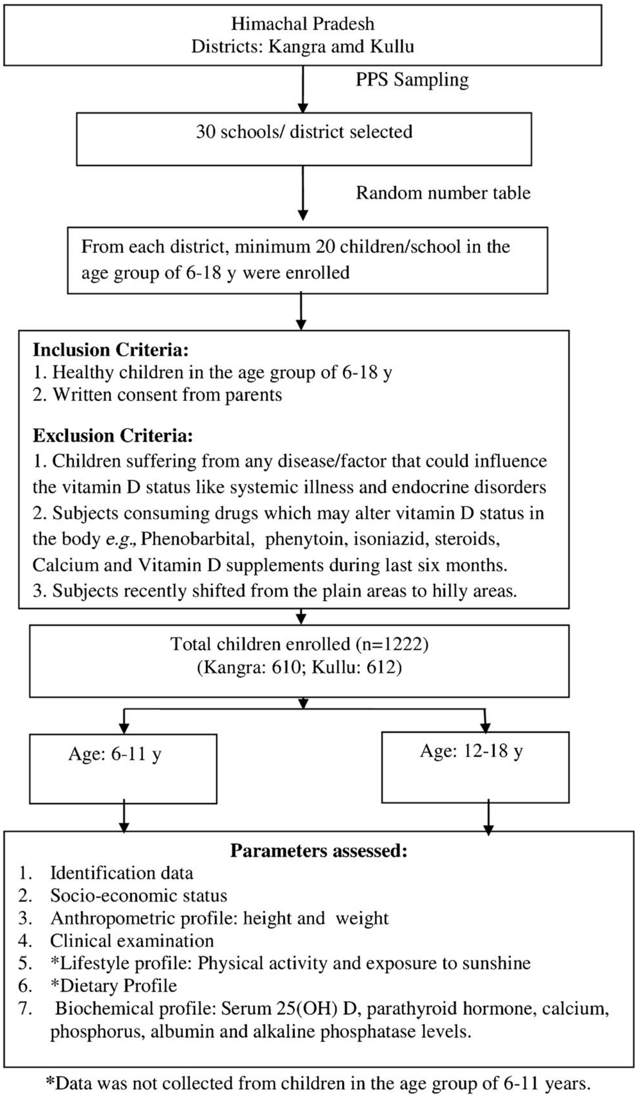

Fig. 1 Operational flow diagram for the study

intrassay CV was less than 5% and inter assay CV was less than 8%.

The biochemical estimation of serum total calcium, serum inorganic phosphorus, serum albumin and serum alkaline phosphatase (ALP) was done on autoanalyzer (ROCHE Modular P 800, Germany) using standard methods. Serum total calcium was estimated by o-cresolphthalein method. Serum inorganic phosphorus estimation was done by molybdate method. Serum albumin was measured by bromo-cresol green (BCG) method and serum alkaline phosphatase was estimated using p-nitrophenyl phosphate (PNPP) method.

The United States Endocrine Society [28] and Lips, P. Classification [29] were utilized for the determination of VDD amongst children. The subjects with serum 25(OH) D level of <20 ng/ml and 20 ng/ml and above, were classified as deficient and sufficient respectively.

The study was approved by ethical committee of All India Institute of Medical Sciences, New Delhi. The written consent was obtained from the parents of each child prior to data collection.

The sample size of the study was calculated keeping in view the anticipated prevalence of Vitamin D deficiency as 25%, a confidence level of 75%, absolute precision of 5.0 and a design effect of 2.0. A total sample size of 600 was calculated for each district.

Statistical Package for Social Sciences (SPSS) version 19.0 was used for statistical analysis of the data. Quantitative data [serum 25 (OH) D] values expressed in Mean ± SD; quantitative data was expressed in frequency and percentage. Chi-square test/Fischer exact test was used to establish the association between different parameters with Vitamin D levels. The $p < 0.05$ was considered as statistical significant.

Results

A total of 1222 children (Kangra: 610; Kullu: 612) in the age group of 6–18 y were enrolled. Of the 610 children enrolled in district Kangra 303 (49.6%) were boys and 307 (50.4%) were girls. The distribution was similar in district Kullu with 304 (49.6%) boys and 308 (50.4%) girls. The mean age of the subjects enrolled was 13.1 ± 3.2 y (boys) and 13.0 ± 3.3 y (girls) in Kangra district and 12.9 ± 3.4 y (boys) and 13.0 ± 3.3 y (girls) in Kullu district. The relationship between serum Vitamin D levels with different socio economic profiles is depicted in Table 1.

Subjects belonging to middle SES had higher prevalence of VDD, compared to children from upper SES in both the districts (Table 1).

The mean BMI in children of 6–11 y and 12–18 y was 18.8 ± 2.9 kg/m^2 and 18.9 ± 2.9 kg/m^2 (Kangra) and 16.4 ± 2.5 kg/m^2 and 17.3 ± 2.3 kg/m^2 (Kullu) respectively. No significant association was found between Vitamin D deficiency and BMI of subjects studied.

In district Kangra; according to BMI for age z scores, 18.4% of children were severely thin (< -3SD), 27.2% were thin (< -2SD), 53.0% were normal, 0.8% were overweight (> +1SD) and 0.7% were obese (> +2SD). In district Kullu; 4.2% of children were severely thin (<-3SD), 15.7% were thin (<-2SD), 77.6% were normal, 2.1% were overweight (> + 1SD) and 0.2% were obese (> + 2SD).

All children were assessed for the clinical symptoms of VDD. In district Kangra, 92 (15.1%) of children and in Kullu, 40 (6.5%) children reported backpain, 64 (10.5%) children reported joint pain in Kangra district and the figure was 49 (8.0%) in Kullu district. Muscle pain was present in 42 (6.9%) children in Kangra and 31 (5.1%) in Kullu. The symptoms such as muscle pain, back pain, and joint pain were found higher in children who had lower serum Vitamin D level (< 20 ng/ml) as compared to children with sufficient Vitamin D levels.

Table 1 Relationship between serum Vitamin D levels with different socio-demographic profiles

Parameters	Kangra			Kullu		
	Deficient (<20) N (%)	Insufficient/ Sufficient (≥20) N (%)	*p*-value	Deficient (<20) N (%)	Insufficient/ Sufficient (≥20) N (%)	*p*-value
Age Groups						
6–11 y	156 (31.5)	31 (27.0)	0.37	151 (30.6)	36 (30.3)	1.00
12–18 y	339 (68.5)	84 (73.0)		342 (69.4)	83 (69.7)	
Gender						
Male	217 (43.8)	86 (74.8)	<0.001	208 (42.2)	96 (80.7)	<0.001
Female	278 (56.2)	29 (25.2)		285 (57.8)	23 (19.3)	
Socio-economic status						
Upper	146 (43.2)	38 (44.7)	0.01	80 (23.3)	12 (14.6)	0.174
Middle	192 (56.8)	44 (51.8)		261 (76.1)	70 (85.4)	
Lower	0	3 (3.5)		2 (0.6)	0	

Children with high physical activity level had lower prevalence of VDD in both the districts. Children who were exposed to sunlight for less than 150 min had higher prevalence of VDD in both the districts studied (Table 2).

The percentage of non vegetarian subjects was 78.5% (Kangra) and 65.6% (Kullu). The Eggetarian children were 7.8% (Kangra) and 13.7% (Kullu). It was found that in district Kangra, higher percentage of vegetarian (89.6%) subjects were VDD followed by eggetarian (81.8%) and non vegetarian (78.1%) subjects. In district Kullu, higher percentage of eggetarian (91.3%) subjects were VDD followed by vegetarian (81.8%) and non vegetarian (77.8%) subjects.

Prevalence of VDD in the age group of 6–11 y and 12–18 y in the two districts is depicted in Tables 3 and 4. Girls had higher prevalence of VDD compared to boys.

PTH levels were found within normal range amongst subjects having sufficient serum Vitamin D levels (≥ 20 ng/ml). In district Kangra, 0.3% and; in district Kullu, 0.6% of children had PTH levels of more than 87.1 pg/ml indicating possible involvement of skeletal system (Table 5).

No significant difference was observed in serum inorganic phosphorous, serum albumin and serum alkaline phosphatase with Vitamin D status amongst children surveyed in both the districts. Whereas, a significant difference ($p < 0.05$) was observed between serum total calcium levels and Vitamin D status amongst children surveyed in both the districts (Table 5).

Discussion

In the present study, 81.0% of children in district Kangra and 80.0% children in Kullu district were Vitamin D deficient (< 20 ng/ml). A similar study conducted earlier amongst children of district Shimla, the other district from Himachal Pradesh reported the prevalence of VDD as 93.0% [24]. Another study conducted in high altitude region in India also reported similar results. It was found that 83% of the subjects had VDD, however this study was conducted in 18–40 y of age group [30]. Studies conducted in plain areas amongst

Table 2 Relationship between serum Vitamin D levels with sunlight exposure and physical activity

Parameters	Kangra			Kullu		
	Deficient (< 20) N (%)	Insufficient/ Sufficient (≥ 20) N (%)	*p*-value	Deficient (< 20) N (%)	Insufficient/ Sufficient (≥ 20) N (%)	*p*-value
Sunlight exposure time (min)						
≤ 150	205(60.3)	20 (23.5)	0.29	203(59.4)	40 (48.2)	0.04
> 150	135(39.7)	40 (47.1)		139(40.6)	43 (51.8)	
Physical Activity Level (PAL)						
Low physical active lifestyle (<1.4)	269 (79.4)	56 (66.7)	0.04	266 (77.8)	51 (61.4)	<0.001
Sedentary life style (1.4–1.54)	40 (11.8)	15 (17.9)		53 (15.5)	17 (20.5)	
Physically active lifestyle (≥1.55)	30 (8.8)	13 (15.5)		23 (6.7)	15 (18.1)	

Table 3 Prevalence of Vitamin D deficiency according to age and gender of the children 6–18 y in districts Kangra ($n = 610$) and Kullu ($n = 612$) (According to Endocrine Society Classification)

	Boys		Girls		Total
	6–11 y	12–18 y	6–11 y	12–18 y	
Kangra					
Deficient (< 20 ng/ml)	71 (11.6)	146 (23.9)	85 (13.9)	193 (31.6)	495 (81.1)
Insufficient (20-29 ng/ml)	16 (2.6)	51 (8.4)	10 (1.6)	16 (2.6)	93 (15.2)
Sufficient (30 and above ng/ml)	4 (0.6)	15 (2.5)	1 (0.2)	2 (0.2)	22 (3.6)
Kullu					
Deficient (< 20 ng/ml)	73 (11.9)	135 (21.6)	78 (12.7)	207 (33.8)	493 (80.5)
Insufficient (20-29 ng/ml)	21 (3.4)	72 (11.8)	11 (1.8)	10 (1.6)	114 (18.6)
Sufficient (30 and above ng/ml)	2 (0.3)	1 (0.2)	2 (0.3)	0	5 (0.8)

children and adolescents have documented VDD as 96.9% [4], 90.8% [5], 93.7% [6], 92.3% [7] and 87% [8]. The prevalence reported in the present study is less than that reported in plain areas.

Girls had higher prevalence of VDD compared to boys in the present study. Similar results have been reported by an earlier study conducted in district Shimla of Himachal Pradesh [24]. This could be due to the higher coverage of body in girls due to religious and social constraints which leads to lower sun exposure compared to boys. Further, girls usually are permitted to have limited outdoor activities compared to boys which leads to lower exposure to sunshine. An earlier study from northern India has also found lower Vitamin D levels amongst adolescent school girls compared to boys [7].

On comparing Vitamin D status in different socio economic strata it was found that higher percentage of children with VDD were from middle SES followed by subjects from upper SES. The possible factors for low Vitamin D status could be due to less time spent on outdoor physical activity and greater indulgence in indoor activities like watching television, computer gaming, indoor tuition and other recreational activities [6]. An earlier study has reported no difference ($p = 0.07$) in the prevalence of VDD in school children from lower (LSES) and upper SES (USES) [7].

Physical activity increases local bone mass, reduces calcium excretion and raises absorption efficiency [31], thus increasing serum calcium, which results in sparing serum Vitamin D. The authors found that children with low physical activity had higher prevalence of VDD compared to children with higher physical activity. Similar results have been reported by earlier studies [24, 32].

The high prevalence of VDD status is assumed to be a result of inadequate sun exposure. Exactly how much sun exposure is needed for healthy people to maintain normal serum 25(OH) D is not clear. Other factors such as age, skin pigmentation, season, latitude and UV index also affect the Vitamin D status of the population. In the present study, it was found that children who were exposed to sunlight for less than 150 min had higher prevalence of VDD in both the

Table 4 Prevalence of Vitamin D deficiency according to age and gender of the children 6–18 y in districts Kangra (n = 610) and Kullu (n = 612) (according to LIPS Classification)

	Boys		Girls		Total
	6–11 y	12–18 y	6–11 y	12–18 y	
Kangra					
Less than 5.0 (ng/ml) (Severe deficiency)	5 (0.8)	4 (0.6)	16 (2.6)	40 (6.5)	65 (10.6)
5.0- <10.0 (ng/ml) (Moderate deficiency)	28 (4.6)	37 (6.1)	26 (4.3)	78 (12.8)	169 (27.7)
10.0- <20.0 (ng/ml) (Mild deficiency)	38 (6.2)	105 (17.2)	43 (7.0)	75 (12.3)	261 (42.8)
20- <30.0 (ng/ml) (Insufficient)	16 (2.6)	51 (8.4)	10 (1.6)	16 (2.6)	93 (15.2)
30 and above (ng/ml) (Sufficient)	4 (0.6)	15 (2.5)	1 (0.2)	2 (0.2)	22 (3.6)
Kullu					
Less than 5.0 (ng/ml) (Severe deficiency)	1 (0.2)	0	0	2 (0.3)	3 (0.5)
5.0- <10.0 (ng/ml) (Moderate deficiency)	7 (1.1)	13 (2.1)	15 (2.4)	66 (10.8)	101 (16.5)
10.0- <20.0 (ng/ml) (Mild deficiency)	65 (10.6)	122 (19.9)	63 (10.3)	139 (22.7)	389 (63.6)
20- <30.0 (ng/ml) (Insufficient)	21 (3.4)	72 (11.8)	11 (1.8)	10 (1.6)	114 (18.6)
30 and above (ng/ml) (Sufficient)	2 (0.3)	1 (0.2)	2 (0.3)	0	5 (0.8)

Table 5 Relationship between serum Vitamin D levels with different biochemical parameters

Parameters	Kangra			Kullu		
	Deficient (< 20) N(%)	Insufficient/ Sufficient (≥ 20) N (%)	*p*-value	Deficient (< 20) N(%)	Insufficient/ Sufficient (≥ 20) N (%)	*p*-value
Serum intact PTH						
PTH (≤ 87.1 pg/ml)	467 (94.3)	113 (98.3)	<0.0001	452 (91.7)	114 (95.8)	<0.0001
PTH (> 87.1 pg/ml)	28 (5.7)	2 (1.7)		41 (8.73)	5 (4.2)	
Serum total calcium						
Calcium (8.10–10.4 mg/dl)	346 (69.9)	68 (59.1)	0.03	375 (76.1)	79 (66.4)	0.03
Calcium (>10.4 mg/dl)	149 (30.1)	47 (40.9)		118 (23.9)	40 (33.6)	
Serum inorganic phosphorus						
Phosphorus (< 2.5 mg/dl)	12 (2.4)	1 (0.9)	0.20	–	–	0.55
Phosphorus (2·5–4·8 mg/dl)	448 (90.5)	110 (95.7)		426 (86.4)	100 (84.0)	
Phosphorus (> 4.8 mg/dl)	35 (7.1)	4 (3.5)		67 (13.6)	19 (16.0)	
Serum albumin						
Albumin (< 4.0 g/dl)	33 (6.7)	7 (6.1)	1.00	10 (2.0)	1 (0.8)	0.70
Albumin (4.0–5.5 g/dl)	462 (93.3)	108 (93.9)		483 (98.0)	118 (99.2)	
Serum alkaline phosphatase						
Alkaline phosphatase (<180 IU/l)	100 (20.2)	21 (18.3)	0.69	129 (26.2)	27 (22.7)	0.48
Alkaline phosphatase (180–1200 IU/l)	395 (79.8)	94 (81.7)		364 (73.8)	92 (77.3)	

districts studied. However, no significant association was found between Vitamin D status and sun exposure. Similar results of sun exposure with VDD have been reported in the earlier studies from India [24, 32–35].

The well recognized function of 1, 25 $(OH)_2$ D involves regulation of calcium and phosphorus balance for bone mineralization and remodeling. Biochemical evidence of suboptimal bone health includes elevated PTH (secondary hyperparathyroidism) and alkaline phosphates which are considered as surrogate markers of increased bone turnover. In the present study a significant association of PTH with Vitamin D status was observed in both the districts ($p < 0.0001$). Significant difference was also reported with respect to calcium levels in Vitamin D deficient and sufficient categories in Kangra ($p = 0.03$) and Kullu ($p = 0.03$) districts. Similar observations have been made in an earlier study conducted amongst children which reported significant association of PTH ($p < 0.01$) and calcium levels ($p < 0.01$) with Vitamin D status [36].

An earlier study conducted amongst school age children of Shimla district, Himachal Pradesh reported no association of Vitamin D status with phosphorous, albumin and alkaline phosphatase [24]. Another similar study conducted on children and adolescent reported no significant association of Vitamin D status with alkaline phosphatase [37]. However, a significant association of Vitamin D status with serum calcium, phosphorus and alkaline phosphatase has been reported earlier [36].

The present study revealed high prevalence of VDD in areas at high altitude of 1000 mts and above. The prevalence of VDD in high altitude areas was similar to plain areas of the country.

Limitations of the study include: the subjects in the age group of 6–11 y were not included for the assessment of socioeconomic status, physical activity, sunlight exposure and dietary pattern as these children were unable to provide valid information on these parameters. Data on sun exposure was based on questionnaire administered, which may have subject's recall bias. Dietary intake of Vitamin D was not calculated because the Vitamin D content of Indian foods is not available.

Contributions UK: Concept, design, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review; RMP: Concept, design, data analysis, statistical analysis and manuscript review; BS: Concept, design, data acquisition, manuscript editing and manuscript review; LR: Concept, design, literature search, data acquisition, data analysis, manuscript editing and manuscript review; NS: Literature search, data acquisition and manuscript review; GS: Literature search manuscript editing and manuscript review; NehaS: Literature search, manuscript preparation, manuscript editing and manuscript review. UK will act as guarantor for this paper.

Compliance with Ethical Standards

Conflict of Interest None.

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