ORIGINAL ARTICLE

PREVALENCE AND FACTORS ASSOCIATED WITH VITAMIN D DEFICIENCY IN INDIAN CHILDREN: A HOSPITAL BASED CROSS SECTIONAL STUDY

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Abstract

Aim: To determine the prevalence and clinical, socio-economic and demographic factors determining hypovitaminosis D in children aged 6 months and 18 years.

Material and methods: Hospital based Cross-sectional study, conducted in pediatric outpatient department (OPD) of a tertiary care hospital. A sample of 230 children between 6 months and 18 years attending OPD, who met the inclusion criteria were included in the study by systematic random sampling. The relevant socio-demographic, clinical, and biochemical parameters (including serum calcium, phosphorus, alkaline phosphatase and 25 hydroxy Vitamin D3 levels) of the study population were assessed using standardized questionnaire and laboratory investigations.

Results: The prevalence of hypovitaminosis D was 62.2%. However, only 7(3%) had overt rickets.The odds ratio of hypovitaminosis D were 1.3(95% CI 0.7-2.4), 1.8 (95% CI 0.8-4)and 5.3(95% CI 0.6-44.3) times higher in 5 to 9 years, 10 to 14 years and above 15 years respectively, compared with children below 5 years. Female children were 1.9 (95% CI 1.3 to 4.0) times more at risk of having vitamin D deficiencywhen compared to males. The odds of hypovitaminosis D were 1.8 (95% CI 0.8 to 3.8, p-value 0.12), 4.2 (95% CI 2.1 to 8.5, p-value< 0.01), and 6.9 (95% CI 2.3 to 20.5, p-value< 0.05) times more in lower middle, upper middle and upper socio economic groups respectively when compared with lower socio economic status children.The odds of hypovitaminosis D were 1.3 (95% CI 0.2 to 7.7, p-value 0.74), 2.6 (95% CI 0.9 to 7.5, p-value 0.07), and 6.3 (95% CI 1.5 to 25.4, p-value 0.01) times more children with mother's educated up to primary school, graduation and post graduation when compared to children of illiterate mothers.

Conclusion: The prevalence of hypovitaminosis D was very high in Indian children. Female sex, higher socio economic status, higher educational status of the mother were the factors with strong positive association with hypovitaminosis D.

Introduction

Scientific evidence indicates that calcium and vitamin D play a key role in bone health. (1) Vitamin D is a prohormone that is essential for the normal absorption of calcium in the gastrointestinal tract. Deficiency of vitamin D leads to hypocalcemia and hypophosphatemia with resultant rickets in children and osteomalacia in adults. Although a majority of pediatric patients are asymptomatic, less severe deficiency has been associated with a number of negative skeletal consequences including secondary hyperparathyroidism, increased bone turn over, enhanced bone loss and risk of fracture with minor trauma. (3,4) Studies also highlight the association of vitamin D receptor (VDR) genotype with leprosy and association between single nucleotide polymorphism in the VDR and tuberculosis. (5,6)

Vitamin D is primarily made in the skin after exposure to ultraviolet radiation and less than 10 % is derived from dietary sources. (7) Hence deficiency of vitamin D in a land of ample sunshine such as India provokes disbelief and appears to be a paradox. However vitamin D deficiency is present in a significant proportion of general population in India as per findings from hospital based studies. (8,9) However except for a few studies (10,11), data are scarce in the pediatric population in South India, which receives abundant sunlight throughout the year. We thus undertook this study to assess the prevalence of vitamin D deficiency and its association with various socio demographic, clinical and biochemical parameters in pediatric population.

Methods & Materials

This cross sectional study was conducted in the pediatric outpatient department (OPD) in a tertiary care teaching hospital situated in sub urban metropolitan area, Chennai over a period of nine months between June 2012 to March 2013.Considering the anticipated prevalence of vitamin D deficiency of 75%, to fall within 5% of true prevalence with 95% confidence, the required sample size was 204.To account for refusals and drop outs, it was decided to recruit a total of 250 children in to the study.Systematic random sampling was used to select the study participants. The average monthly attendance of the clinic of the institute was 200. The estimated total OPD attendance for the study period of 9 months was 1800. Dividing the estimated OPD attendance with the required sample size yielded a sampling interval of 7. So every 7thchild registered in the outpatient department was included in the study till the proposed sample size was reached. All childrenbetween 6 months and 18 years were included in the study. Patients with serious illness requiring intensive care unit (ICU) admission and patients with other skeletal disease(fractures,osteogenesis imperfecta) were excluded from the study.The study protocol was approved by the Institute's human ethics committee of Chettinad Hospital and Research Institute. Informed written consent was obtained from the parents /guardian of the children providing all the necessary information about the study.Four ml of venous blood was drawn for estimation of hemoglobin, serum calcium, phosphate, alkaline phosphatase, 25-hydroxy vitamin D [25(OH) D].Hemoglobin estimation was done by patented Coulter principle using a lytic reagent that converts hemoglobin to a stable pigment. This pigment solution was measured at 525nm. Serum was separated in a centrifuge and stored at -20 degree Celsius until analyzed. Alkaline phosphatase was estimated in the serum by the pNPP (para nitro phenyl phosphate) method. 25 (OH) D levels were measured by an immunochemiluminometric assay in ADVIA Centaur auto analyzer with an assay range of 3.7-150ng/ml. As per the US Institute of Medicine classification, 25(OH)D levels of > 20 ng/ml indicated vitamin D sufficiency, levels of <15ng /ml were considered as deficiency and 5ng/ml or less were considered as severe deficiency. (12) The laboratory reference range for alkaline phosphatase was 150-470 U/L, for serum calcium was 8.8-10.2 mg/dl and for serum phosphorus was 2.5-4.9mg/dl. Anemia was defined as hemoglobin less than 11gm/dl.Clinical vitamin D deficiency was diagnosed if the subject had frontal bossing,epiphyseal widening, rachitic rosary or genu varum or genu valgum,the latter being defined as intercondylar and intermalleolar distances >6cm and>8cm respectively.

Statstical Methods

Statistical analysis was carried out using IBM SPSS statistical software (version 21).Various degrees of hypovitaminosis were taken as outcome variable. Socio demographic parameters like age, sex, socio economic status, mother's education, clinical parameters like concurrent illnessand body mass index(BMI) were considered as explanatory variables. Descriptive analysis of explanatory and outcome variables was done. After confirming the distribution of normality, association between the explanatory and outcome variables was analyzed by calculating unadjusted odds ratios using binary logistic regression. The variables with statistically significant association in univariate analysis were included in the multivariate analysis to compute adjusted Odds ratios and their 95% CI and p - value.

Results

A total of 250 children were approached and 20 children refused to participate,so the non-participation rate was 8% in the study. A total of 230 children were included in the final analysis. Vitamin D deficiency was seen in 87 (37.4%), Vitamin D insufficiency was seen in 57 (24.8%) and 86 (37.8%). Out of the total study subjects, 114 (49.6 %) were below five years, 71(30.9 %) were between five to 9 years, 37(16%) were between 10 to 14 years and the remaining 8 (3.5 %) were above 15 years of age. Male: female ratio was 118:112. According to the modified Kuppuswamy's socio economic status scale (13), 29(12.6%) belonged to upper, 86 (37.4%) to upper middle, 54(23.5%) to lower middle, 59(25.7%) to upper lower and remaining 2 (0.9%) to the lower socio economic class. Eighteen mothers (7.8%) were illiterate, 7(3%)had completed primary school,104(45.2%) went to school from 6 to 12 years, 72(31.3%) were graduates and 29(12.6%) were post graduates.In 50 (21.7%) children the milk consumption was below 150 ml/day, the proportion of children with daily consumption levels between 150 ml to299 ml,300 ml to 449 ml, 450 ml to 599 ml and above 600 ml were 74(32.2%),52(22.6%), 46(20%) and 8 (3.5 %) respectively.Seventy-nine children (34.3%) were underweight, 134 (58.3%)had normal nutrition and the remaining 17 (7.4%) were overweight. The proportion of subjects with anemia was 36 (15.7%) in study population. Infections other than skin and soft tissue infections (SSTI) were seen in 43 (18.7%), recurrent abdominal pain (RAP) in 16 (7%), asthma/bronchiolitisin 15(6.5%), allergies in 11 (4.8%), neurodevelopmental problems in 7 (3%), seizures in 4 (1.7%), skin & soft tissue infections in 3 (1.3%) children. Clinical vitamin D deficiency was present only in 7 (3%) children. Table 1 gives association with various socio-economic parameters and vitamin D levels. Multivariate logistic regression analysis was conducted by including all the socio demographic variables which have demonstrated statistically significant association in univariate analysis in the equation which is depicted in Table 2. Table 3 gives association of various biochemical parameters with different vitamin D groups.

Discussion

We found a high prevalence of hypovitaminosis D in our study group which is similar to that reported in previous Indian studies. (14-15). Skin pigmentation determines the duration of sun exposure necessary to achieve a concentration of vitamin D. Overall, an Asian Indian is thought to require 3 times and darker skinned person 6-10 times as much as ultraviolet B exposure as a light skinned person to achieve equivalent vitamin D concentration. (16) The high vitamin D prevalence reported in India could be due to decreased cutaneous synthesis owing to higher skin pigmentation and less sun exposure. Other contributing factors are a high fiber diet containing phosphates and phytates which can deplete vitamin D stores and increase calcium requirement (17), genetic factors like having increased 25 hydroxyvitaminD – 24- hydroxylase which degrades 25 hydroxy vitamin D to inactive metabolites (18) and increased pollution which hampers cutaneous vitamin D synthesis. (19) However, clinical manifestations of hypovitaminosis D were seen in a very small fraction in our study which proves that overt rickets is only the tip of the iceberg of hypovitaminosis D. (2)

Female children had a higher risk of vitamin D deficiency in our study. More clothing of the body and lesser participation in outdoor activities leading to decreased cutaneous vitamin D synthesis could be a contributing factor.In a study of schoolgirls from India,90.8% were found to have vitamin D deficiency (20).

Adolescents are prone to vitamin D deficiency because of greater mineral demands of their growing bones. (21)The current study found increased risk of vitamin D deficiency in children aged 10 and above. In children,few studies have examined whether childhood vitamin D status is associated with obesity or insulin resistance. (22)In the current study, obese children were at a greater risk of developing vitamin D deficiency.It has been proposed that higher body fat leads to increased sequestration of vitamin D in adipose tissue,resulting in lower serum vitamin D levels that lead to insulin resistance and metabolic syndrome. (22)

Though there are some studies reporting association of pneumonia and asthma with vitamin D deficiency

Table 1: Association between various socio demographic parameters and hypovitaminosis D (N=230)

Parameter	Normal vitamin D (N = 87) (%)	Insufficient N= 57 (%)	Deficient N= 86 (%)	Unadjusted Odds Ratio (95%CI)	P value
Age group					
Below 5 yrs	49(43.0%)	27(23.7%)	38(33.3%)		
5 to 9 yrs	26(36.6%)	22(31.0%)	23(32.4%)	1.3(0.7 to 2.4)	0.39
10 to14 yrs	11(29.7%)	6(16.2%)	20(54.1%)	1.8 (0.8 to 4.0)	0.15
15 and above	1(12.5%)	2(25.0%)	5(62.5%)	5.3(0.6 to 44.3)	0.12
Gender					
Male	33(29.5%)	30(26.8%)	49(43.8%)		
Female	54(45.8%)	27(22.9%)	37(31.4%)	1.9 (1.2 to 3.5)	0.01
Socio Economic status					
Lower/ Upper lower	36(59.0%)	11(18.0%)	14(23.0%)		
Lower middle	24(44.4%)	14(25.9%)	16(29.6%)	1.8 (0.8 to 3.8)	0.12
Upper middle	22(25.6%)	23(26.7%)	41(47.7%)	4.2 (2.1 to 8.5)	<0.001
Upper	5(17.2%)	9(31.0%)	15(51.7%)	6.9 (2.3 to 20.5)	<0.001
Education of mother					
Illiterate	9(50%)	3(16.7%)	6(33.3%)		
Upto primary	3(42.9%)	1(14.3%)	3(42.9%)	1.3 (0.2 to 7.7)	0.74
Primary to +2	51(49%)	28(26.9%)	25(24%)	1.0 (0.4 to 2.9)	0.94
Graduate	20(27.8%)	17(23.6%)	35(48.6%)	2.6(0.9 to 7.5)	0.07
Post graduate	4(13.8%)	8(27.6%)	17(58.6%)	6.3(1.5 to 25.4)	0.01
Milk Consumption					
Below 150	28(56%)	8(16%)	14(28%)		
150 to299	24(32.4%)	21(28.4%)	29(39.2%)	2.6 (1.3 to 5.6)	0.01
300 to 449	20(38.5%)	9(17.3%)	23(44.2%)	2 (0.9 to 4.5)	0.07
450 to 599	14(30.4%)	17(37%)	15(32.6%)	2.9(1.2 to 6.7)	0.01
600 and above	1(12.5%)	2(25%)	5(62.5%)	8.9(1.0 to 77.9)	0.04
Body Mass Index (BMI)					
Under weight	34(43%)	19(24.1%)	26(32.9%)		
Normal	48(35.8%)	34(25.4%)	52(38.8%)	1.4(0.8 to 2.4)	0.29
Overweight & obesity	5(29.4%)	4(23.5%)	8(47.1%)	1.8(0.6 to 5.6)	0.30
Anemia					
Anemia	16(44.4%)	11(30.6%)	9(25%)		
No anemia	71(36.6%)	46(23.7%)	77(39.7%)	1.4(0.7 to 2.8)	0.37
Morbidity					
Well child	16(26.7%)	16(26.7%)	28(46.7%)	2(1 to 3.8)	0.04
Any morbidity	71(41.8%)	41(24.1%)	58(34.1%)		

Table 2: Multivariate logistic regression analysis of association between Hypovitaminosis D and various socio demographic and clinical parameters

Parameter	Adjusted OR	P- value	95% CI for OR	
			Lower	Upper
I. Sex				
Male (Base line)				
Female	2.1	.014	1.2	3.9
II.Socioeconomic status				
Upper lower &lower (Base line)				
Lower middle	1.7	0.18	0.8	3.9
Upper Middle	3.5	0.00	1.4	8.9
Upper	4.5	0.03	1.1	18.0
III. Mother's education				
Illiterate (Base line)				
Upto primary	1.6	0.62	0.3	9.9
Primary to +2	0.7	0.55	0.2	2.1
Graduate	0.8	0.76	0.2	3.0
Post graduate	1.7	0.54	0.3	8.6
IV. Milk consumption				
Below 150 (Base line)				
150 t0 299	2.0	0.07	0.9	4.6
300 to 449	1.3	0.54	0.5	3.2
450 to 599	2.1	0.12	0.8	5.6
600 and above	4.2	0.21	0.4	41.9

Table 3: Summary of various bio chemical parameters in different Vitamin D status groups

Vitamin D status	Serum Calcium(mg/dl)	Serum Phosphorus (mg/dl)	Serum Alkaline Phosphatase (U/L)
Sufficient(N= 87)	9.67±0.43	5.34±0.69	239.69±59.48
Insufficient (N=57)	9.80±0.50	5.30±0.79	241.12±71.43
Deficient (N=86)	9.61±0.62	5.33±0.75	245.65±78.12
Total (N=230)	9.68±0.53	5.33±0.73	242.27±69.63
p value	0.12	0.95	0.84

(23), the current study did not find an association with any co-morbidity. However, contrary to expectations, children with increased intake of milk had a higher incidence of vitamin D deficiency. As the vitamin D content of cow's milk is only 3-40 IU/litre(24), sunlight exposure is the primary determinant of vitamin D status in humans. Secondly a potential limitation of the current study is that the estimated dietary milk intake and sunlight exposure information was self report.

The present study found that children from the higher socio economic group were at greater risk of hypovitaminosis D. This is contrary to the study by Marwah et al. (9) LInhares et al did not find any significant differences in the mean vitamin D concentration between the two socio economic groups. (25) However the difference we foundis supported by observations that other biochemical parameters like serum calcium , phosphorus and alkaline phosphatase concentrations did not differ significantly in both groups whereas the sun light exposure (as obtained by self report) was more in the low socio economic groups. This could also probably explain why children with better educated mothers had a higher risk of vitamin D deficiency; the time spent in outdoor activities in such children was less compared to children with poorly educated mothers.

Serum alkaline phosphatase has been reported to be a useful screening test for hypovitaminosis D. (26) In the present study, there was no correlation between serum alkaline phosphatase and serum vitamin D levels. This in contrast to several studies in which serum alkaline phosphatase showed a significant but inverse correlation with vitamin D level in children with hypovitaminosis D. (26,27) However the results of the study are consistent with those of Shaheen et al (28) and Siddiqui et al(29). This could be explained on the basis of the fact that serum alkaline phosphatase rise has been documented in patients with known rickets or osteomalacia. However rickets with florid manifestations is only a fraction of the total prevalence of vitamin D deficiency. (2) Most of the cases diagnosedwith vitamin D deficiency/ insufficiency in the present study did not have signs of rickets. Hence in subclinical vitamin D deficiency, rise in serum alkaline phosphatase is insufficient or inconsistent enough to pick up hypovitaminosis D.

Conclusion

There is a very high prevalence of vitamin D deficiency in the pediatric population, more so in adolescents, female children and obese children. It is more prevalent in upper socio-economic strata, probably linked to lesser sunlight exposure. Serum alkaline phosphatase is not a good screening tool to detect vitamin D deficiency. In view of this high prevalence of hypovitaminosis D, importance has to be given to adequate vitamin D supplementation in the Indian population even though vitamin D is a sunshine vitamin.

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