Vitamin D evaluation based on demographics and calcium supplement intake in children suffering from acute febrile illness admitted in as tertiary care center

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ABSTRACT

Background: Vitamin D or sunshine vitamin is a vital steroid group of vitamins with its deficiency being common, especially among children. The literature establishing the correlation of dietary habits with Vitamin D levels in Indian population is scarce. **Objective:** This study aims to evaluate serum 25-hydroxyvitamin D (25(OH)D) level in the hospitalized children suffering from acute febrile illness (AFI) and find its correlation with calcium intake and demographic characters. **Materials and Methods:** The study was conducted at the pediatric department of a tertiary hospital of Maharashtra, over a period of 6 months in the children between the age groups of 1 month and 12 years, admitted with AFI and with or without clinical or biochemical evidence of rickets. After detailed history, evaluation of Vitamin D status was done in all children within 48 h of admission to the hospital using early morning sample of 2 ml of serum using chemiluminescent immunoassay method. We correlated Vitamin D levels with socioeconomic status (SES) along with various other parameters like serum calcium (S. calcium). **Results:** It was observed that with the improvement of SES, the Vitamin D deficiency (VDD) did not improve. The biochemical parameters such as S. calcium and alkaline phosphatase revealed a significant correlation with Vitamin D status. S. calcium level was significantly low in children with VDD. Radiological evidence of rickets was seen only in 40.5% of cases of VDD and 14.3% of cases of Vitamin D insufficiency and thus was not a diagnostic hallmark for rickets. **Conclusion:** The data suggested that VDD is very common among children aged 1 month–12 years and it is not correlated with SES and calcium intake. Efforts need to be made to improve the Vitamin D status by creating awareness among people.

Key words: *Acute febrile illness, Rickets, Serum calcium, Vitamin D*

Vitamin D is a fat soluble, steroid group of vitamins, which is crucial for the absorption and metabolism of calcium and phosphorous and overall calcium homeostasis in humans. Vitamin D deficiency (VDD) has reached pandemic proportions today, severely affecting the general bone health in children and adolescents. Various studies in Indian population have shown a very high prevalence of nutritional VDD not only in adults but also in adolescents, children, infants, neonates, and pregnant and lactating mothers [1-5]. Normal reference range of 25-hydroxyvitamin D (25(OH)D) and exact cutoffs for deficiency and insufficiency remains controversial [4,6]. Threshold at which 25(OH)D induces an increase in plasma parathyroid hormone concentration in adults ranges from 10 to 32 ng/ml [7].

It has been well established that VDD and poor dietary intake of calcium have a prominent role in defective mineralization of bone, leading to diseases such as rickets in children and osteomalacia in adults. Studies by Chapuy *et al*. [8] and Dawson-Hughes *et al*. [9] have shown that the individuals which are supplemented with both calcium and Vitamin D have comparatively low chances of non-vertebral fractures and age-related bone losses. The literature establishing the relationship of dietary habits with Vitamin D in Indian population is scarce. A study was conducted in healthy South Indian population [10].

Another major factor affecting Vitamin D level is the socioeconomic status (SES) which is usually defined by the income of the family, number of family members, and educational status. There are very few studies based on correlation between both these parameters [11]. It is well established that Ca^{2+} metabolism is dependent on Vitamin D, parathormone, and calcitonin levels, and intestinal absorption of Ca^{2+} is stimulated by Vitamin D which also regulates the serum concentration of calcium for skeleton mineralization [12]. This study aims to evaluate Vitamin D status in the hospitalized children suffering from acute febrile illness (AFI) and find its correlation with calcium intake and demographic characters.

MATERIALS AND METHODS

A prospective observational case-cohort study was conducted at the pediatric department of a tertiary hospital of Maharashtra after approval of protocol by the Institutional Ethics Committee. A method of universal sampling was used. All children between 1 month and 12 years of age admitted consecutively over a period of 6 months to our unit with AFI and with or without clinical or biochemical evidence of rickets were included in the study. Children younger than 1 month and older than 12 years, children with disorders known to affect Vitamin D metabolism, namely, chronic liver disease, chronic kidney disease, prolonged medications like anticonvulsants, children ongoing Vitamin D therapy, especially in mega doses, and children admitted directly to pediatric intensive care unit were excluded from the study.

Detailed history was recorded of the present complaints, duration of illness, history of any form of recurrent illnesses, or hospitalization in a predesigned pro forma. Antenatal, natal, and postnatal history, including gestational age at birth, birth weight, any antenatal, perinatal, or postnatal events, were recorded. Vitamin D supplementation if given, its dose and duration were also noted. A thorough history of dietary intake including adequacy of calories, protein, and calcium was recorded. A direct question regarding sun exposure was asked and its adequacy in terms of duration of exposure, area of skin exposed, and timing of the day was deduced as per recommendations. Major aspects such as socioeconomic history and family history of any illnesses were recorded.

All the children were thoroughly examined. Detailed anthropometric evaluation in terms of weight, height, and head circumference measurement was done. Body mass index was calculated as weight/(height in m^2) [13]. These growth parameters were plotted on Agarwal *et al*. growth charts [14] and standard deviation score adjusted for age and sex was calculated based on these Indian reference standards.

Detailed evaluation of the presenting illness was done on admission. Assessment of vital parameters, severity of illness, stigmata of nutritional deficiency states, including pallor, and signs of other vitamin deficiencies were made. Assessment was done for signs of rickets in the form of wide open anterior fontanel, frontoparietal bossing, craniotabes, delayed dentition, rib beading, Harrison's sulcus, wrist widening, double malleoli, bony deformities (bowing of limbs, knock-knees), and pot belly with visceroptosis.

Laboratory investigations such as complete hemogram, renal function tests, liver function tests (to rule out liver or kidney diseases), bacteriology cultures, radiography, and sonography were done as per indications. Serum calcium (S. calcium), serum phosphorous, and alkaline phosphatase (ALP) levels were evaluated in all patients. All these tests were carried out in our in-house laboratory automated ERBACEN 5+ biochemistry machine. Standardized reference values were taken.

Radiograph of wrist was done to look for evidence of rickets in the form of cupping, splaying, and fraying of distal ends of metaphysis, increased distance between epiphysis and metaphysis due to accumulation of unmineralized osteoid, bony deformity, and osteopenia and pseudofractures. Evaluation of Vitamin D status was done in all children within 48 h of admission to the hospital using early morning sample of 2 ml of serum. 25(OH)D levels were determined at a standardized referral laboratory with validated reference data using chemiluminescent immunoassay method.

In our study, serum 25(OH) D level of less than 10 ng/ml was considered as VDD, level between 10 and 30 ng/ml was considered as Vitamin D insufficiency, and levels more than 30 ng/ml were considered as Vitamin D sufficiency.

Children found to be deficient or insufficient in Vitamin D were treated with cholecalciferol (Inj. Arachitol®) given IM to all these children as per unit protocol. All the children including those who had sufficient 25(OH)D levels were advised to take a daily maintenance dose of 400 units of cholecalciferol orally. Chi-square tests, Pearson's Chi-square test, and one-way ANOVA test were used for statistical analysis.

RESULTS

A total of 90 subjects were included. Based on the levels of Vitamin D, 20% (n=18) of children were found to be Vitamin D sufficient and 80% (n=72) of them were either VDD (n=37) or Vitamin D insufficient (n=35). Comparison of Vitamin D levels in AFI children based on birth weight, religion, sunlight exposure, and SES is given in Table 1. Out of 18 low birth weight children, only 2 (11.1%) had adequate levels of Vitamin D. However, in the normal birth weight group, 16 out of 72 children (22.2%) had adequate levels. Out of the 90 children, 69 (76.7%) belonged to Hindu community, 18 (20%) were Muslims, while 3 (3.3%) were of other community, however, this difference was non-significant. When 25(OH)D levels were correlated with the SES, VDD was found in 76.2% of children in low-income group and 81.2% of children in high-income group. On correlating the adequacy of sunlight exposure with 25(OH)D levels, 13 (81.3%) had levels ≤30 ng/ml. A total of 67.8% (n=61) of children had no exposure to sunlight and 80% of them were either VDD or Vitamin D insufficient. However, the correlation was statistically non-significant (Table 1).

The mean daily calcium intake did not differ among the various Vitamin D status groups (Table 2).

In our cohort, S. calcium level was significantly low in children with VDD (8.34±1.25 mg/dl) as compared to those with insufficient (8.95±0.82 mg/dl) or sufficient (9.43±0.85 mg/dl) levels of 25(OH) D levels (p=0.001). ALP levels were significantly higher in VDD (1003.2±1210 IU/L) children as

Table 1: Vitamin D levels compared between AFI children based on birth weight, religion, sunlight exposure, and SES

Vitamin D status	Birth weight (kg)		Religion		Sunlight exposure		SES	
	<2.5	≥2.5	Hindu	Muslim	Adequate	Inadequate	Low income^	High income^^
	(n=18) (%)	(n=72)	(n=70)	(n=20)	(n=16)	(n=74)	(n=21)	(n=69)
Deficient[#]	16 (88.8)	56 (77.78)	60 (85.71)	14 (70)	13 (81.25)	59 (79.72)	16 (76.19)	56 (81.16)
Sufficient[##]	2 (11.1)	16 (22.2)	12 (14.29)	6 (30)	3 (18.75)	15 (20.28)	5 (23.81)	13 (18.84)
p-value	0.2994		0.1074		0.8903		0.6201	

[#]Vitamin D levels ≤30 ng/ml [##]Vitamin D levels >30 ng/ml. ^Kuppuswamy SES score ≤15, ^^Kuppuswamy SES score ≥16. AFI: Acute febrile illness, SES: Socioeconomic status compared to those with Vitamin D insufficient or sufficient status (Table 3).

When the correlation between Vitamin D levels and radiological features for rickets was assessed, only 40.5% of children in the VDD group showed radiological features of rickets. In the insufficient group, 14.3% showed evidence of rickets on X-rays (Table 4).

DISCUSSION

In the present study, a total of 90 children were assessed. We found that the mean 25(OH)D level was 17.53±15.48 ng/ml. Only 20% of children had sufficient levels of Vitamin D, whereas there were higher proportion, i.e., 80% who were categorized as VDD (n=37) or Vitamin D insufficient (n=35). The data are supported by the findings of Seth *et al*. who found a high prevalence of VDD in lactating mothers and their exclusively breastfed infants [3]. In a large school-based study of girls by Puri *et al*., biochemical VDD was found in 90.8% of girls [15].

On correlation of 25(OH)D levels with the SES of the children, the percentage of total children who were VDD did not decrease as the SES improved and the difference between Vitamin D levels was not statistically significant (p=0.6177). Influence of affluence on Vitamin D status has not been consistently proven in the literature [16]. However, Al-Agha *et al*. concluded that SES did not affect Vitamin D levels in children [17].

Table 2: Correlation of adequacy of calcium intake with Vitamin D status

Vitamin D status	Calcium intake*		Total, n (%)
	Adequate, n (%)	Inadequate, n (%)	
Deficient	10 (43.5)	27 (40.3)	37 (4.1)
Insufficient	9 (39.1)	26 (38.8)	35 (38.9)
Sufficient	4 (17.4)	14 (20.9)	18 (20)
Total	23	67	90
Chi-square tests	Df	p-value	Association
Pearson's Chi-square	2	0.929	Not significant

Mean daily calcium intake in this group of children was 314±155.3 mg/day. The mean daily intake of calcium in VDD (303±165.3 mg/dl), insufficient (341.5±150 mg/dl), and sufficient (282.7±143 mg/dl) children was low as compared to recommended dietary allowance of calcium intake recommended by the Indian Council of Medical Research [18-21]. This result is in accordance to the results obtained by Harinarayan *et al*. [10]. Although 25% of the children had adequate calcium intake for given age and sex, yet among them, only 18% had sufficient 25(OH)D levels.

The majority of Vitamin D (up to 90%) in body is acquired with the action of sunlight on the skin, wherein conversion of 7-dehydrocholesterol to Vitamin D_3 takes place [22]. Adequate sunlight exposure was seen in 17.8% of children. However, only 18.7% of them had sufficient Vitamin D levels which are similar to the study done by Harinarayan *et al.* in adults, where they found that longer sunshine exposure results in better 25(OH)D status among subjects residing in rural areas as compared to urban counterparts, yet almost two-third of the rural subjects remained VDD with values <20 ng/ ml [23].

The biochemical parameters S. calcium and phosphorous revealed a significant correlation with Vitamin D status as was reported by Nisbet *et al*. and Preece *et al*. [24,25]. In the present study, calcium level was significantly low in children with VDD. This was similar to the results obtained by Harinarayan and Akhila [26]. Similarly, ALP level was significantly higher in VDD children as compared to those with Vitamin D insufficiency or sufficiency. These results were in accordance with the results observed by Wacker and Holick and Harinarayan *et al*. [22,23].

Rickets is caused by deficiency in mineralization of bones at the growth plates [27]. Vitamin D acts a prohormone for normal absorption of calcium from gut and its deficiency is the most common cause of rickets. Radiological features of rickets are considered as hallmark of VDD. In our cases, only 40.5% of the children who had VDD showed radiological features of rickets. Similarly, among the children in insufficient Vitamin D group, only 14.3% showed evidence of rickets on X-rays. This is similar to the findings by the National Institute of Nutrition in 2009, and thus, VDD cannot be considered as a diagnostic hallmark [21].

Table 3: Comparison in mean values of lab parameters based on levels of Serum Vitamin D

Lab parameters	Vitamin D status	Statistics for the lab parameters				One-way ANOVA	
		Mean	SD	Median	IQR	F-value	p-value
Sr. Calcium (mg/dl)	Deficient	8.34	1.25	8.5	1.9	13.201	0.00136
	Insufficient	8.95	0.82	9	1.1		
	Sufficient	9.43	0.85	9.45	1.2		
Sr. Phosphorus (mg/dl)	Deficient	5.31	1.32	5	1.3	3.184	0.204
	Insufficient	5.37	1.15	5.4	1.6		
	Sufficient	5.77	0.94	5.75	1.05		
Sr. ALP (IU/L)	Deficient	1003.22	1210.37	607	774.5	13.621	0.0011
	Insufficient	439.03	219.75	401	241		
	Sufficient	721.22	792.34	494	332		
Sr. PTH (IU/ml)	Deficient	143.83	36.14	146.65	67.33	54.322	0.00126
	Insufficient	17.25	6.86	17.25	9.7		
	Sufficient	419	0	419	0		

Table 4: Radiological features of rickets and Vitamin D status

Vitamin D status	Radiological features of rickets		Total
	Yes, n (%)	No, n (%)	
Deficient	15 (40.5)	22 (59.2)	37
Insufficient	5 (14.3)	30 (85.7)	35
Sufficient	2 (11.1)	16 (88.9)	18
Total	22 (24.4)	68 (75.6)	90
Chi-square tests	df	p-value	Association
Pearson's Chi-square	2	0.012	Significant

Our study had a few limitations. Vitamin D estimation was conducted in children admitted for AFI and no control subjects were included. The nutritional pattern in the children was very varied since the age of the children ranged from 1 month to 12 years. This could be a confounding factor for Vitamin D levels.

CONCLUSION

Efforts need to be made to improve the Vitamin D status, such as increasing outdoor activities for more exposure to sunlight. It is recommended to add Vitamin D supplements in the nutritional guidelines for the sick children.

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