Original Article

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Vitamin D Deficiency in Children - Are we over Diagnosing and Over Treating?

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Abstract

Objective: To assess the 25 (OH) vitamin D level in children of Central Kerala, aged 1 to 5 years and to find its correlation with clinical manifestations of vitamin D deficiency. *Methods:* Children aged 1 to 5 years, attending the immunization clinic, OPD and well baby clinic in the department of Pediatrics, Government Medical College, Thrissur, Kerala. Children were examined for clinical features of rickets. Serum 25(OH) D and PTH levels were assessed. *Results:* Among the 108 children included in the study group, none had clinical features of rickets. Male to female ratio was 56:52. The mean Vit D level detected was 18.51ng/ml (3.7-68.0ng/dl). Majority of them (54.6%) had levels between 10-20 ng/ml. The mean PTH was 31.3pg/ml (6.5-53.6pg/ml). Ca, P and ALP level had average values of 8.77mg/dl, 6.17mg/dl and 202.7 IU respectively. *Conclusions:* The mean level of 25OH D in Indian children is 'low' when compared to the western literature, though none of them had rickets or biochemical evidence of secondary hyperparathyroidism. More data in children are needed to determine the 'cut off ' level of 25 hydroxy D in children below which appropriate vitamin D supplements can be prescribed.

Keywords: Vitamin D; Deficiency; 25 Hydroxy D Level.

Introduction

Vitamin D deficiency and its potential health implications are widely studied nowadays. The serum level of 25-hydroxyvitamin D (25OHD) is currently used as the marker of the vitamin D status of an individual in the present era, owing to its longer half life of about three weeks [1]. However, the level of vitamin D to define its deficiency is still unknown, particularly in children, where studies are limited.

Different studies have used different 'cut off's for definitions of Vit D deficiency, including less than 15 ng/ml and less than 20 ng/ml [2]. Levels above 30 ng/ml are considered to be normal and associated with the best outcomes in adults and hence the same level is regarded as normal in children [2].

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Literature search reveals few studies regarding vitamin D levels in Indian children, residing in coastal areas, where they are exposed to adequate sunlight and diet rich in sea food. The objective of our study is to assess the 25 (OH) vitamin D level in children of Central Kerala, in the preschool age and to find its correlation with clinical manifestations of vitamin D deficiency.

Method of Study

This cross sectional study was conducted in a tertiary care hospital in Central Kerala from June 2016 to June 2017. This study was approved by Institutional Ethics Committee. Children aged 1 to 5 years, attending the immunization clinic, OPD and well baby clinic run by Department of Pediatrics were randomly enrolled into the study after obtaining informed consent from parents or caretakers. Children with chronic illness, those who are on Calcium and Vit D supplements and whose parents who have not given consent were excluded from the study. Along with documenting the baseline demographic details, all the participants were subjected to detailed clinical history taking and complete physical examination. Children were examined for clinical features of rickets. Serum levels of 25OH Vit D was tested in all children using

Chemiluminescent Micro particle immunoassay-(CMIA Abbott). PTH level was assessed by Electro Chemiluminescent Immunoassay-(ECLIA Roche). Serum calcium, phosphorous and ALP were also measured simultaneously. If features of rickets were found, X-ray of the extremities and other laboratory investigations including liver and renal function tests were done and an abdominal ultrasound were performed whenever indicated.

Statistical analysis was performed by SPSS. We categorized serum 25 (OH) D levels as <10, 10-20, 20-30, and >60 ng/dl. Primary descriptive analysis is done with 95% confidence intervals (CIs).

Results

Among the 108 children included in the study group, there were 56 boys and 52 girls. Mean age was 3.8 years. Male to female ratio was 1.07:1. None of the children had clinical features of rickets. The mean Vit D level detected was 18.51ng/ml (3.7-68.0 ng/ml). 76% children had a vit D level of <30ng/ml (Fig. 1). Majority of them (54.63%) had levels between 10-20 ng/ml. Seventeen children (15.7%) had a vit D level reported less than 10ng/ml. None of these children had hypocalcemia. Two of them had high PTH levels (PTH>55pg/dl), but clinically asymptomatic. High level of VitD (68ng/ml) was reported in one case. The mean PTH was 31.3pg/ml(6.5-63.6pg/ml). Ca, P and ALP level had mean values of 8.77mg/dl, 6.17mg/dl and 202.7 IU respectively (Table 1).

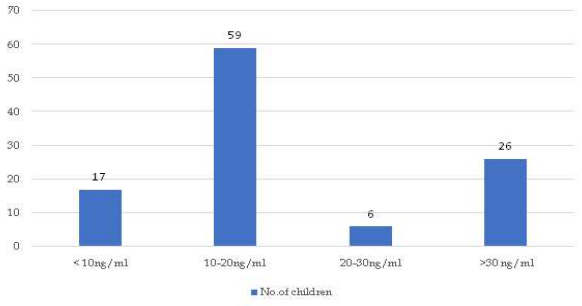

Fig. 1: Graph showing serum 25OH D levels

Discussion

Vitamin D is a secosteroid which naturally occurs in two forms – vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) [2]. Since not many foods contain vitamin D precursors, sunlight exposure is the primary determinant of vitamin D status in humans [2].

Vitamin D undergoes hydroxylation in the liver to 25-hydroxyvitamin D (25 [OH] D), the precursor hormone which is tested to evaluate for vitamin D status and later in the kidney, catalyzed by the 1-α hydroxylase enzyme, to the biologically active 1,25 dihydroxyvitamin D (1, 25 [OH] 2D). The action of 1-α hydroxylation at target tissues other than kidney is thought to be responsible for the non calcemic actions of vitamin D [3].

Vitamin D deficiency was initially considered rare in India, since the studies were based on serum calcium and alkaline phosphatase in our population [4]. Assessment of vitamin D had its rise after the year 2000 and thereafter significant as well as subclinical hypovitaminosis D became quite prevalent.

However, the cut off levels of 25hydroxy VitD are not well described in children. The AAP defines vitamin D insufficiency as 25-OH-D concentrations <20 ng/mL in the pediatric population [5]. The Endocrine Society as well as the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines classify insufficiency as calcidiol concentrations < 30 ng/mL. While the Endocrine Society defines deficiency as < 20 ng/mL, KDOQI defines it as < 15 ng/ml [6,7]. These definitions, as discussed, are based on classification system used in adults [5].

This study is done to assess the vitamin D level in Indian children, especially Central Kerala, where they are adequately exposed to sunlight and have reasonably good health index. In Kerala, we have a good antenatal care system and they assure better maternal nutritional status [8]. Majority of the people are non vegetarians, where sea food is a major part of their diet.

In our study, the mean value of VitD measured was well below the accepted normal levels. However our children had neither clinical features

Table 1: The mean values of laboratory investigations

	Calcium (mg/dl)	Phosphorus (mg/dl)	ALP (IU)	Vit D (ng/ml)	PTH (pg/ml)
Mean	8.77	6.17	202.7 IU	18.51	31.3
Min	8.3	2.8	100	3.7	6.5
Max	10.9	7.8	317	68.0	63.6
Lab value – normal	8.5-10.5	3.8-7.6	40-390		15-65

of rickets nor they had other laboratory evidence suggestive of Vit D deficiency. In a vitamin D deficient patient, the intestinal absorption of calcium and phosphorus is decreased. The parathyroid gland recognizes this low serum calcium and releases PTH. PTH, in turn, increases the calcium reabsorption in the kidneys and the excretion of phosphorus which subsequently leads to decrease in bone mineralization. Over a period of time, osteomalacia and rickets may develop [9].

Atapattu et al. had reported that majority of children in their study with abnormal bone metabolites had 25 (OH) D levels < 34 nmol/l and PTH levels > 50 ng/l(10). In our study, mean PTH detected was 31.3pg/ml. Only two children had PTH level more than 55pg/ml and they were clinically asymptomatic. Serum calcium, phosphorous and ALP level were normal in all the children enrolled in the study.

The present era witnesses many diseases being etiologically attributed to vitamin D deficiency. Hence, over prescribing Vitamin D especially in pediatric age group is quite common. Vitamin D is infact, toxic in large doses and there are sporadic reports of vitamin D toxicity in literature. Pandita et al reported a case series of fifteen patients with symptomatic hypercalcemia and toxicity occurred due to excessive administration of vitamin D by oral and parenteral route [3].

Despite the concerns for over diagnosis and overtreatment of vitamin D deficiency, the frequency of testing for vitamin D deficiency using 25 hydroxy Vit D assay is on the rise. Many studies from western countries have reported increased testing of Vit D levels leading to consequences like quality of care, unnecessary cost, and potential over diagnosis. UK had seen a six fold increase in these tests between 2007 and 2010 [11]. In Canada, testing increased 25-fold from 2004 to 2010. The cost of testing in Australia increases on average 59% each year [11]. In India, scenario is not different. Also, literature reveals that this large increase in vitamin D testing did not pave way to improved vitamin D status in the population and subsequent health outcomes, as shown by the flat trend in bone density measurements [12].

There is a definite need for rational prescribing of vitamin D supplements in Indian population. Vit D ssupplementation is indicated only in specific children, at risk of developing Vitamin D deficiency.

Bolland and his colleagues had conducted a systematic analysis and concluded that there is no clear evidence for benefits of vitamin D supplementation [13]. Clinicians, rather than focussing on detecting or treating individuals with vitamin D insufficiency, should consider treating those at high risk of vitamin D deficiency and those with specific clinical indications. Treatment for these individuals does not require vitamin D measurements. The study recommended that further adequately powered, randomised controlled trials of vitamin D supplementation to demonstrate safe improvements in health are much needed. Moreover, Vitamin D measurement is often inaccurate and imprecise, and majority of tests performed currently fail to reveal vitamin D deficiency [14].

Moreover, there is a need for educating the practitioners as well as public about sun exposure for vitamin D synthesis and dietary intake of vitamin D rich foods rather than promoting high market sales of calcium supplements ; which could predispose to toxicity.

Studies have shown that children, especially infants, require less sun exposure than adults to produce adequate vitamin D concentrations. This is due to their greater surface area to volume ratio and increased ability to produce vitamin D [15]. Studies have shown that at least 30 minutes of sun exposure per week for 16-18 weeks over 40% exposed body surface of an infant will be sufficient to maintain body 25 (OH) Vit D levels above 20 ng/ml [16]. Asian children, because of dark skin colour, require three times the recommended amount of sun light exposure to maintain these levels. Excessive exposure to sunlight does not lead to vitamin D toxicity [17]. Playing or adequate physical activity in the sun will also help in preventing obesity, which is a common comorbid condition seen in Vit D Deficiency.

This study was done to evaluate the role of Vit D assay in asymptomatic children and the need to treat them unless they are at risk of developing Vit D deficiency. A major limitation of the study is its small sample size. Also, this study has not addressed tononspecific musculoskeletal symptoms or other clinical features attributable to Vit D deficiency, other than clinical rickets. Further research is needed concerning the laboratory assessment of Vitamin D and Vitamin D therapy in pediatric age group in our subcontinent.

Conclusion

The mean level of 25 (OH) D in asymptomatic Indian children is 'low' when compared to the western literature. Low 25 (OH) D level alone should not taken as "deficiency'. More data in children are needed to determine the 'cut off

'level of 25 hydroxy D in children below which appropriate vitamin D supplements can be prescribed. Adequate sun exposure and dietary modification will be enough to maintain adequate levels of vitamin D levels in body. Measures should be taken to create general awareness among the masses, regarding irrational intake and toxicity due to Vit D supplements.

References

1. FraserDR.VitaminD.Lancet.1995;345(8942):104-107.
2. Melamed ML, Kumar J. Low levels of 25-hydroxy vitamin D in the pediatric populations: prevalence and clinical outcomes. Ped Health 2010;4:89–97.
3. Pandita et al, "Excess gooD can be Dangerous". A case series of iatrogenic symptomatic hypercalcemia due to hypervitaminosisDClin Cases Miner Bone Metab. 2012 May-Aug;9(2):118–20.
4. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25hydroxyvitamin D concentrations in healthy subjects in Delhi. Am J ClinNutr 2000;72:472-5.
5. LeeJ Y et al. A Review on Vitamin D Deficiency Treatment in Pediatric Patients; Pediatr Pharmacol Ther. 2013 Oct-Dec; 18(4):277–91.
6. National Kidney Foundation, Inc. Guideline 8. Prevention and treatment of vitamin D insufficiency and vitamin D deficiency in CKD patients. KDOQI clinical practic guidelines for bone metabolism and disease in children with chronic kidney disease. 2005 http://www.kidney.org/professionals/kdoqi/guidelines_pedbone/guide8.htm.
7. Holick MF, Binkley NC, Bischoff-Ferrari HA et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911–30.
8. Jose JA, Sarkar S, Kumar SG, Kar SS. Utilization of maternal health-care services by tribal women in Kerala. Journal of Natural Science, Biology, and Medicine. 2014;5(1):144-147. doi:10.4103/0976-9668.127314.
9. Misra M, Pacaud D, Petryk A et al. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008;122(2):398–417.
10. Atapattu N, Relationship between serum 25hydroxy Vit D and Parathormone in the search for a biochemical definition of Vitamin D deficiency in children, Pediatric Research, 2013;74:552-56.
11. K Bilinski. The rise and rise of Vitamin D testing. BMJ 2012;345:e4743.
12. M Razzaghy Azar. Assessment of Vitamin D status in healthy children and adolescence living in Tehran and its relation to iPTH, gender, weight and height. Ann Hum Biol. 2010 Sep-Oct;37(5):692-701. doi: 10.3109/03014460903527348.
13. Bolland MJ, Grey A, Gamble GD, Reid IR. The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis. Lancet Diabetes Endocrinol. 2014;2(4):307-20.
14. Bolland MJ, Grey A, DavidsonJS, Cundy, ReidIR. Should measurement of vitamin D and treatment of vitamin D insufficiency be routine in New Zealand?NZ Med J. 2012;125(1349):83–91.
15. Munns C, Zacharin MR, Rodda CP et al. Prevention and treatment of infant and childhood vitamin D deficiency in Australia and New Zealand: a consensus statement. Med J Aust. 2006;185(5):268–272.
16. Meena P et al. Sunlight Exposure and Vitamin D Status in Breastfed Infants ; Indian Pediatr 2017;54: 105-11.
17. Balasubramanian, S., Dhanalakshmi, K., & Amperayani, S. Vitamin D Deficiency in Childhood – A Review of Current Guidelines on Diagnosis and Management; Indian Pediatr 2013;50: 669-75.