Section: Pediatrics & Adolescent Medicine

Original Research Article

VITAMIN D STATUS AT ADMISSION IN CHILDREN ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT AT A TERTIARY CARE CENTER IN EASTERN NEPAL

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Received : 06/10/2022
Received in revised form : 15/11/2022
Accepted : 13/02/2023

Keywords:
Children, Vitamin D deficiency, Sepsis.

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DOI: 10.47009/jamp.2023.5.2.63

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 304-308

Abstract

Background: The primary aim of this study was to identify the burden of vitamin D deficiency (VDD) in children with critical illness admitted to pediatric intensive care unit (PICU). **Materials and Methods:** A total of 105 children aged 1–15 years were prospectively enrolled from PICU in the pediatrics department of a tertiary care center over 1 year period. Plasma 25-hydroxy vitamin D [25(OH)D] levels were measured by chemiluminescence immunoassay technique (CLIA) (MAGLUMI 25-OH Vitamin D; CLIA) within 24 hours of admission. Vitamin D concentrations of <20 ng/mL (50 nmol/L) were considered as deficient. **Result:** Of the 105 children enrolled, the majority 74 (70.48%) had vitamin D deficiency which was most prevalent in the age group 1 to 5 years accounting 77% in the age group. Vitamin D deficiency was maximum (80%) in underweight children. In the VDD group, 81.5% had severe sepsis, whereas only 18.5% had severe sepsis in vitamin D sufficient group with significant statistical association with sepsis severity and vitamin D deficiency. **Conclusion:** A high burden of VDD is present in children admitted to the pediatric intensive care unit.

INTRODUCTION

Vitamin D deficiency (VDD) is exceedingly predominant in children leading to dysregulation of the immune system and inflammation.[1,2] Vitamin D concentrations of >20 ng/mL (50 nmol/L) are considered as sufficient and below 50 nmol/L (<20 ng/mL) is considered as deficient. The availability of vitamin D in most foodstuffs is constrained, and mostly endogenous vitamin D is synthesized by exposure to bright sunlight.[3,4] However, sun exposure, skin pigmentation, and fat retention can markedly alter vitamin D levels. Higher levels of melanin frequently lead to darker skin pigmentation, which decreases vitamin D synthesis. Madden K et al. noted that race and age were related to VDD in critically ill children. Moreover, the genotype and concentration of vitamin D binding protein (DBP) can influence the half-life of 25(OH)D.[5,6]

Recent studies in children have demonstrated that there are grounds for vitamin D supplementation in septic children with VDD which could be a potential novel strategy in decreasing death by reducing the severity of illness and duration of hospital stay.[5,7,8] Data on the prevalence of VDD in septic children in Nepal are very few. Moreover, none of the studies have assessed vitamin D status in children with sepsis as a homogenous population.

The primary aim of this study was to identify the burden of vitamin D deficiency (VDD) in children admitted to the intensive care unit in the department of pediatrics and adolescent medicine at BP Koirala Institute of Health Sciences, Dharan, Nepal.

MATERIALS AND METHODS

A cross-sectional prospective, observational study was done in the department of pediatrics and adolescent medicine BPKIHS, Dharan from January 2017 to December 2017 in children (1-15 years) admitted with the diagnosis of sepsis in pediatric wards and pediatric intensive care unit/ PICU. Census sampling was used and admitted children (aged 1–15 years) with the diagnosis of sepsis were eligible for inclusion in the study. Parents of those children who refused to give consent, or were immune compromised or with chronic renal disease, or liver disease, or conditions associated with gastrointestinal malabsorption, or who have received Vitamin D within 3 months before hospital admission were excluded.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Baseline demographic data such as age, gender, height/ length, weight, Body mass index (BMI) (as defined and classified by world health organization /WHO) were recorded for each patient at the time of enrollment for the study.[9] The severity of illness was measured using the sequential organ failure assessment (SOFA) score in the first 24 hours of admission to the PICU or pediatric wards.[10]

Serum vitamin D (25-hydroxycalciferol; (25-OH-D) level was estimated soon after the admission of the patient in the biochemistry lab of the institute by chemiluminescent-immunoassay technique (MAGLUMI 25-OH Vitamin D; CLIA). Serum sample for 25(OH) D measurement was obtained as close as possible to admission usually within 24 hours. By running internal controls with every batch of the test; the reliability of the vitamin D assay was assured. Vitamin D concentrations of >20 ng/mL (50 nmol/L) were considered as sufficient, <20 ng/mL (50 nmol/L) as deficient as categorized by the American Academy of Pediatrics classification system 2008.[11]

Sample size was calculated by considering 95% CI and 80% power. According to the study by Satheesh et al[23], the prevalence of vitamin D deficiency among septic patient was 51%, where P = 51%, Q = 49%, Permissible error L = 20% of P i.e. 10.2%. So, n = ($z^2$1-α/2 p q) / L^2 which is (1.96)2*51*49/ (10.2)2 =93. Adding 10% for non-response, n = 102. Hence, sample size was estimated to be 102.

Collected data were entered in Microsoft excel 2007 and converted into Statistical Package for Social Sciences 16 for Statistical analysis. For descriptive statistics percentage, mean, median, Standard deviation (SD), interquartile range (IQR) was calculated along with graphical and tabular presentation was made. For inferential statistics Chi-square was applied to find out the significant differences between the groups at 95% confidence interval (CI) where p≤0.05.

Ethical clearance was obtained from the Institutional Review Committee (IRC) of BPKIHS prior to the initiation of the study (IRC/0868/016). Informed written consent was obtained from each of the parents before enrollment in the study.

RESULTS

Of the 265 children admitted with sepsis in the department of pediatrics and adolescent medicine; 180 were eligible for the study and only 105 participated in this study. The results of this study are as follow:

In this study, 45 children were below 5 years of age, 31 children were in the age group 5-10 years and 29 children were in the 10 -15 years age group accounting 42.85%, 29.52% and 27.63% respectively of the total study subjects.

In all the 3 age groups, majority had normal BMI where as 20%, 22.6% and 13.8% were undernourished in children under 5,5-10 and 10-15 years age group [Table 1].

Of the 105 children enrolled, only 31 (29.5%) had vitamin D level in normal range with mean vitamin D level being 27.5± 5.51 ng/ml. In the 74 subjects (70.48%), vitamin D was in deficient range with mean value 15.35± 1.74 ng/ml. Median level of vitamin D in deficient children (74) was 15.3(IQR:13.17- 18.12) ng /ml whereas, median level of vitamin D in sufficient population (31) was 25.5(IQR: 21.9- 32.10) ng /ml [Table 2].

The mean vitamin D level in the age group 1 to 5 years was 15.81±2.51 ng/ml and that in age group 5 to 10 years was 15.40±2.23 ng/ml and that in 10 to 15 years was 18.53±3.14 ng/ml [Table 3].

Vitamin D was deficient (≤20ng/dl) in 77% of children in 1-5 years of age group, whereas 65% of children had Vitamin D deficiency in 5-10 years and 66% in 10-15 years age group.By gender, 76% of males had vitamin D deficiency whereas only 63% of females were deficient in vitamin D. As per BMI, in normal weight category group (5th -85th percentile) nearly 65% had vitamin D deficiency, whereas in underweight category (<5th percentile BMI) 80% had vitamin D deficiency. In overweight category around 76% of them had vitamin D deficiency. In children with less severe sepsis (SOFA score <2) nearly 59% had vitamin D deficiency, whereas in the severe sepsis group (SOFA score ≥2) 81.5% had vitamin D deficiency.

In this study, respiratory system disorder as a primary cause of sepsis was found in 43% followed by GI system (41%). CNS and genitourinary system involvement were found in 9% and 7% respectively. Those children with disorder in CNS as a primary cause of sepsis, 89% had vitamin D deficiency, whereas vitamin D was deficient in 75% of children with respiratory disorder, 67% had genitourinary disorder and 65% had GI disorder [Table 4].

Table 1: Demographic profile of the septic children N= 105

Age group 1 to 5 years		**n1= 45 (42.85%)**	
		Frequency	**Percent (%)**
Sex	Male	23	51.1
	Female	22	48.9
BMI (percentile)	5th – 85th	29	64.4
	<5th	9	20.0
	85th -95th	2	4.4
	>95th	5	11.1
Age group 5 to 10 years		n2= 31 (29.52%)	
Sex	Male	17	54.8
	Female	14	45.2

ISSN (O): 2687-5365; ISSN (P): 2753-6556

BMI (percentile)	5th – 85th	16	51.6
	<5th	7	22.6
	85th -95th	3	9.7
	>95th	5	16.1
Age group 10 to 15 years	n3= 29 (27.63%)		
Sex	Male	19	65.5
	Female	10	34.5
BMI (percentile)	5th – 85th	19	65.5
	<5th %	4	13.8
	85th -95th	2	6.9
	>95th	4	13.8

BMI: body mass index, n1= 45, n2= 31, n3= 29, N= n1+n2+n3 = 105

Table 2: Vitamin D level at admission (ng/ml)

Vitamin D level (ng /ml)	Frequency /Percent (%)	Mean value ±SD	Median (IQR)
Sufficient (21- 100)	31/29.52	27.5± 5.51	25.5 (IQR: 21.9- 32.10)
Deficient (<20)	74/ 70.48	15.35± 1.74	15.3 (IQR:13.17- 18.12)

SD: Standard Deviation; IQR: interquartile range

Table 3: Vitamin D level in age category with mean and SD value N=105

Age (years)	Frequency (%)	Mean (ng/ml) ± SD
1-5	45 (42.85)	15.81±2.51
5-10	31 (29.52)	15.40±2.23
10 – 15	29 (27.63)	18.53±3.14

SD: Standard Deviation

Table 4: Vitamin D level in accordance to age group, gender, BMI, sepsis severity and System involved N= 105

Vitamin D level (ng /ml)		Deficient (<20)	Normal (21- 100)
Age (years)	1-5	35 (77.8%)	10 (22.2%)
	5-10	20 (64.5%)	11 (35.5%)
	10-15	19 (65.6%)	10 (34.4%)
Gender	Male	45 (76.3%)	14 (23.7%)
	Female	29 (63.0%)	17 (37.0%)
BMI (percentile)	5th- 85th	42 (65.6%)	22 (34.4%)
	<5th	16 (80.0%)	4 (20.0%)
	>85th	16 (76.2%)	5 (23.8%)
SOFA Score	<2	30 (58.8%)	21 (41.2%)
	≥2	44 (81.5%)	10 (18.5%)
System Involved	Respiratory	34 (75.6%)	11 (24.4%)
	CNS	8 (88.9%)	1 (11.1%)
	GI	28 (65.1%)	15 (34.9%)
	GU	4 (66.7%)	2 (33.3%)

BMI: body mass index, SOFA: sequential organ failure assessment, CNS central nervous system, GI: gastro-intestinal system GU: genitourinary system

DISCUSSION

There is a paucity of literature regarding the burden of vitamin D deficiency on pediatric sepsis especially from Nepal and its association with sepsis severity. Understanding of which would aid in the management and improve the outcome of the pediatrics sepsis.

In this study, 42.85% and 29.52% of children were in the age group 1- 5 years and 5-10 years among them 20% and 22.6% were undernourished respectively. Only 29.5% had vitamin D levels in the normal range. The median level of vitamin D in deficient children was 15.3 ng /ml whereas, in the sufficient group, it was 25.5 ng /ml which is also in the lower range of normal value. In Delhi, over 80 % of young children (9–30 months of age) from two slum areas had serum 25(OH) D values <14 ng/ml; this deficit noted is much higher than this study.[12] In other studies; prevalence of vitamin D deficiency in Indian children was found to be 40.3 %.[13,14] The reported prevalence of vitamin D deficiency in Brazil was 29.5%, in Australia was 34.5 %, in Canada 40.1 %, was and in North America was 69 %.[15,16] This shows that, the burden of Vitamin D deficiency is very high in our setting as compared to developed counties but is comparable to that of Indian children.

The mean vitamin D level in the age group of 1 to 5 years and 5 to 10 years was nearly equal (15.81 and 15.40 ng/ml) whereas in 10 to 15 years, was slightly higher (18.53 ng/ml) suggesting that it was not in the sufficient level in all the age group. The highest Vitamin D deficiency was noted in the under 5 children (77%) whereas in the age group 5-10 and 10-15 years was 65 and 66% respectively. Hypovitaminosis D (serum 25(OH) D <20 ng/ml) among Delhi school children (10–18 y of age), was seen in 92.6 % of the low socioeconomic group and 84.9 % of the upper socio-economic group with over a third of them having 25(OH) D values <9

ISSN (O): 2687-5365; ISSN (P): 2753-6556

ng/ml.[17] Despite normal assumptions, males (76%) had higher deficiency than girls (63%) in this study.

In this study, vitamin D deficiency was more in overweight children (76%) as compared to those with normal BMI (65%) whereas, it was highest in the children with underweight (80%). More children (81.5%) in the severe sepsis group (SOFA score ≥2) had vitamin D deficiency than those (59%) in the less severe group (SOFA score <2) which was statistically significant. In contrary to this study, a few studies have found no such association between VDD and severity of illness whereas some others have found an inverse correlation.[18-21]

Involvement of respiratory and GI system as a primary cause of sepsis was found in 43 and 41% of children whereas, vitamin D deficiency was noted in 89, 75, and 67% of children with CNS, respiratory, and genitourinary system involvement respectively as a primary cause of sepsis.

Of the 74 children with the vitamin D deficiency, 81.5% had severe sepsis, whereas only 18.5% had severe sepsis in vitamin D sufficient group depicting significant statistical association with sepsis severity and vitamin D deficiency. In the meta-analysis done by Xiao D et al., it was noted that the association between vitamin D deficiency and sepsis was significant, with an odds ratio (OR) = 1.13 (95% CI, 1.18 to 1.50, $p < 0.05$).[22] Contrary to this in the study by Satheesh Ponnarmeni in Chandigarh, India, it was found that the prevalence of VDD in critically ill children with sepsis was high (50.8%) but it was not associated with greater severity of illness or other clinical outcomes.[23]

The prevalence of VDD by different studies have noted wide variations which might be due to the differences in the studied populations, sunlight exposure, weather, dietary intake, vitamin D supplementation, genotype variation in the proteins involved in vitamin D transportation, functioning, and metabolism, different methods of measuring 25(OH)D and different cut-off values.[24,25] In critically ill patients, the low concentration of 25(OH) D may be because of altered metabolism, transcapillary leak, fluid administration.[26-28]

CONCLUSION

In conclusion, this study revealed that there is a high burden of vitamin D deficiency (70.5%) in all the age groups. Vitamin D deficiency was maximum (80%) in underweight children though overweight had (76%) more burden than the normal weight children (65%).

Strengths and Limitations

Strength of this study include recruitment of every patient over one year period admitted to the pediatric wards and PICU fulfilling the inclusion criteria and giving consent for the study so that every subspecialty participated in the study. To minimize the influence of factors contributing to the decline of serum levels of vitamin D following admission; a prompt collection of blood samples soon after admission (within 24 h of admission) was ensured. The limitation of this study is the sample size which was enrolled from a single center that may not be generalized.

Recommendations

Further studies in Nepal on a larger number of septic children exploring the association of vitamin D with sepsis severity warrant urgent study.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556