ORIGINAL ARTICLE

Prevalence of Vitamin D Deficiency in Critically Ill Children and its Impact on Morbidity

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Abstract:

Background: Vitamin D Deficiency (VDD) is said to be a risk factor for critical illness as well as enhanced morbidity and mortality from critical illness. As there is lack of data from the paediatric population and absence of interventional studies showing improved outcome by giving vitamin D in critically ill, it is still unclear if VDD is a marker of severity of illness. *Aim and Objectives*: To assess the prevalence of VDD in our Paediatric Intensive Care Unit (PICU) and to see it's correlation with morbidity. *Material and Methods:* This was a prospective observational study carried out from 1stNovember 2019-31stMarch 2020 in a 16 bedded PICU with level 3 care. All children admitted to PICU aged one month to 17 years were eligible for inclusion. Children discharged or who died within 24 hours of PICU stay, children who had received 60,000 IU or more of vitamin D in last 3 months, children with chronic renal disease and children whose parents did not give consent were excluded. Blood sample for vitamin D estimation was collected within 24 hours of admission. VDD was taken as cut off value of serum 25 hydroxy vitamin D <20 ng/ml. Data were analysed using SPSS version 16. *Results:* There were 63 children included in study. Prevalence of VDD (serum 25 (OH) vitamin D <20 ng/mL) was 44%. Duration of PICU stay was significantly more in the VDD group with a difference in mean of PICU stay of 3.48 days. Mechanical ventilation and inotrope requirement was also significantly high in VDD group with p-value of 0.000 and 0.02 respectively. *Conclusions:* In this study the prevalence of VDD in critically ill children is 44% which is similar to that in the general Indian population. Our study also showed that the morbidity in the form of length of stay, need for mechanical ventilation and inotropes were significantly increased in the VDD group.

Keywords: Duration of Stay, Mechanical Ventilation, Vitamin D Deficiency

Introduction:

Vitamin D Deficiency (VDD) is traditionally associated with rickets and osteomalacia [1-2]. VDD affects around one billion population all over world [3]. Many adults and children have subclinical deficiency that may make them more vulnerable to cardiac, respiratory, neurologic and immunologic pathologies [4-6]. As these are essential organ systems, VDD is supposed to be a risk factor for critical illness as well as enhanced morbidity and mortality from critical illness [7], although it is a matter for debate. In some studies, VDD has been associated with severity of illness at admission, more requirements of inotropes and mechanical ventilation, more ICU stay and even mortality [8-13] but in others no such association was seen [14-15]. As there is lack of data from the paediatric population and absence of interventional studies showing improved outcome by administering vitamin D to critically ill children, it is still unclear if VDD is a marker of severity of illness or

just a bystander. The study was aimed to assess the prevalence of VDD in our Paediatric Intensive Care Unit (PICU) and to see it's correlation with morbidity.

Material and Methods:

This was a prospective observational study carried out from 1st November 2019- 31st March 2020 in a 16 bedded PICU with level 3 care.

Inclusion criteria

1. All children admitted to PICU aged one month to 17 years.

Exclusion criteria

1. Children discharged or died within 24 hours of PICU stay.
2. Children who had received mega dose i.e. 60,000 IU or more of vitamin D in the 3 months prior to admission.
3. Known case of chronic renal disease.
4. Children whose parents were not willing to give consent.

Eligible patients were included in the study after getting written informed consent from parents. Approval of Institutional Ethics Committee was taken.

Demographic data, history including drug intake, anthropometry, and examination findings, primary diagnosis, Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score, need for mechanical ventilation, inotropic support, outcome, and duration of stay were recorded. Blood sample for vitamin D estimation was collected within 24 hours of admission. VDD was taken as cut off value of serum 25 hydroxy vitamin D (25(OH) D) <20 ng/ml [16]. Data were analysed using SPSS version 16. $p<0.05$ was taken as statistically significant. To determine correlation of VDD with demographic and clinical outcomes, Student t-test/Wilcoxon rank-sum test and Chi-square test were used for continuous and categorical variables.

Results:

A total 131 children were admitted to PICU during study period. Out of them 65 were excluded (Fig. 1). Baseline data are shown in Table 1.

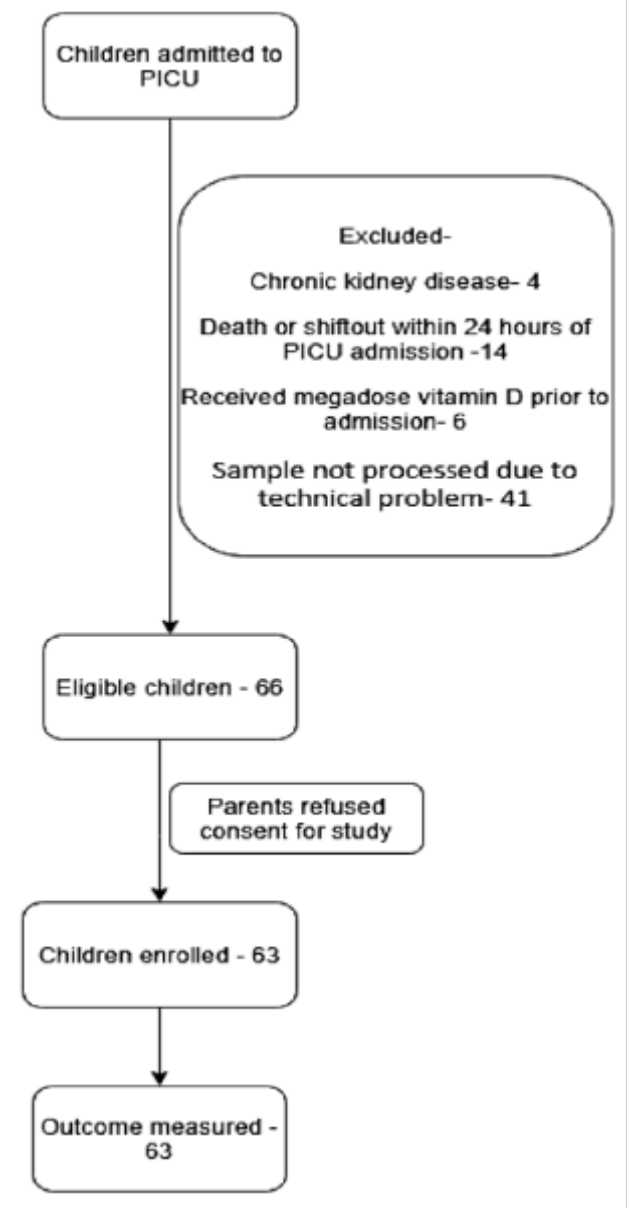

Fig. 1: Flow Chart

Table 1: Baseline Data of Children Enrolled in the Study (n=63)

Variable	Outcome
Age in years – mean (SD)	4.78 (4.62)
Male - Number (%)	32 (50.8)
Diagnosis - Number (%) **Respiratory system** **Cardiovascular system** **Central nervous system** **Gastrointestinal system** **Hepatobiliary system** **Others**	24 (38.1) 06 (09.5) 12 (19.1) 05 (07.9) 04 (06.4) 12 (19.0)
Nutritional status - Number (%) **Normal** **Malnutrition** **Obesity**	28 (44.4) 31 (49.2) 04 (06.4)
Duration of PICU stay in days - mean (SD)	8.49 (4.44)
PELOD-2 score within 24 hours of admission - mean (SD)	6.07 (3.61)
Vitamin D level in ng/ml mean (SD)]	23.84 (12.93)

SD- standard deviation, PICU- paediatric intensive care unit,
PELOD-2- Pediatric logistic organ dysfunction-2

Twenty eight (44.4 %) children required ventilator support, and mortality in the study population was 14.3%. The comparison of the clinical variables between the vitamin D deficient and sufficient groups is shown in Table 2. The study showed a 44.4% prevalence of VDD. Four out of 63 children had vitamin D levels <10 ng/ml. None of them had hypervitaminosis D i.e. vitamin F level >100 ng/ml. Both vitamin D deficient and sufficient groups did not differ in sex and weight distribution. Association between VDD and length of PICU stay is shown in Fig. 2.

Table 2: Comparison of Demographic and Clinical Variables between Vitamin D Deficient and Sufficient Groups

Variables	Vitamin D deficient group (n=28)	Vitamin D sufficient group (n=35)	*P* value
Mean value of vitamin D (ng/ml)	13.33	32.25	0.000
Mean age (years)	4.81	4.75	0.95
Male	12	20	0.26
Mean weight (kg)	15.55	14.06	0.639
Malnutrition	15	16	0.276
Obesity	3	1	0.27
Mean PICU stay (days)	10.42	6.94	0.001
PELOD 2 score	7.1	5.25	0.04
Mechanical ventilation (n)	20	8	0.000
Inotrope (n)	17	11	0.02

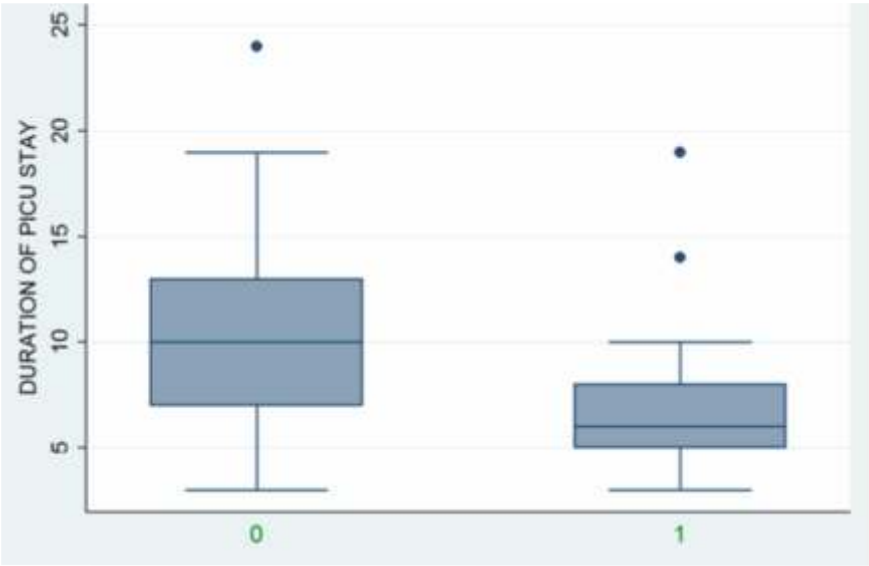

Fig. 2: Association between VDD and Length of ICU Stay

0- Vitamin D deficient group, 1- Vitamin D sufficient group

Discussion:

VDD is defined as a value of 25(OH) D of <20 ng/mL or <50 nmol/L [16, 22]. There was a prevalence of 44% of VDD in children admitted to our PICU. In one of Indian studies, prevalence of VDD in critically ill children was 40% [11] and in another Indian study in children with sepsis it was about 50% [17]. Our prevalence is similar to both these studies. Prevalence is also similar to a study by Madden *et al.* who reported 40% VDD prevalence in critically ill children [8]. Factors like timing and duration of sun exposure, area of skin exposed, amount of skin pigmentation, dietary intake and genetic factors, are sought as plausible explanations for the high VDD prevalence in the tropics [18-19]. Though high prevalence of VDD in critically ill population has been reported previously multiple times, the impact of it on outcome is still not clear.

The length of PICU stay in our study was more in the VDD group with a mean difference between the two groups of 3.48 days. This was statistically significant. This result is similar to the study by Shankar *et al.* [20]. The population studied was also similar in their study. In our study the requirement of mechanical ventilation was significantly higher in the VDD group, though we did not compare the duration of mechanical ventilation in the 2 groups. Shankar *et al.* [20] did not find any such association. Significantly increased frequency of mechanical ventilation was seen in the VDD group in a meta-analysis by Mcnally *et al*. [21] done in 14 studies. Inotrope was used in 28 children out of 63 in our study population. Inotrope use was more prevalent in the VDD group. Duration and inotrope score were not studied in every patient and hence it was not included in the final statistics. Shankar *et al.* [20] have also shown increased inotrope use in the VDD group. It was noted that the PELOD-2 score calculated in the first 24 hours of PICU stay was significantly high in the VDD group. This may suggest that children having VDD tend to have severe presentation of disease. However, this score was not compared in system wise illness and may have caused bias. This finding has not been seen by previous researchers like Shankar *et al.* [20]. VDD may increase morbidity and mortality by pleiotropic effects on respiratory, cardiac, and immunity systems [4-6]. VDD may trigger or aggravate multi-organ dysfunction in critically ill patients and may increase morbidity and mortality [7-9].

At present there is no evidence of improvement in outcome of critically ill paediatric patients with vitamin D supplementation. Hence vitamin D should be supplemented only if there is clinical or radiological evidence of VDD, rather than just considering serum value in isolation [23]. A randomized placebo controlled trial done in the adult ICU on vitamin D supplementation to deficient population admitted to ICU showed no significant difference in length of ICU stay, hospital mortality or six month mortality [24]. Currently, there is no recommendation to supplement vitamin D routinely to deficient population needing ICU care. Therefore, there is a need for an intervention trial in paediatric patients to see if it changes the outcome in the VDD population. The strengths of our study were well defined eligibility criteria, prospective study and variety of cases. Limitation was the relatively small sample size.

Conclusion:

In this study the prevalence of VDD in critically ill children was 44% which is similar to that in the general Indian population. Our study also showed that the morbidity in the form of length of stay, need for mechanical ventilation and inotropes were significantly increased in the VDD group.

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