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Investigation of serum 25 hydroxy vitamin D level in critically ill children and its relation with demographic and clinical risk factors.

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Abstract

Background: Vitamin D is a pleiotropic hormone important for the proper functioning of multiple organ systems. It has been hypothesized that vitamin D deficiency could contribute to mortality, disorders, or worsen outcomes in critical illness. The aim of this study was to investigate the relation of vitamin D deficiency with potential demographic and clinical factors.
Methods: Eighty two children hospitalized in ICU section of Children's Medical Center were contributed into this study and serum level of vitamin D was extracted from patients' file.
Results: The level of vitamin D significantly decreased from 37.9532 to 23.8771 ng/mL. Logistic regression analysis, also, confirmed the relation between age and vitamin D serum level. This change probably was because of higher growth rate among children older than 2 years. So, vitamin D should be added to the older children's nourishment.

Keywords Vitamin D, Intensive care unit, Risk factors, Age.

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Introduction

Vitamin D is a fat soluble vitamin which its main production sources are skin by UV-B light conversion of 7-dehydrocholesterol, or ingested in the diet from fatty fish, cod-liver oil, eggs, fortified milk products, or dietary supplements [1]. Vitamin D classically plays an important role in calcium, phosphorus, and glucose metabolism as well as bone formation and mineralization. Also, before the development of antibiotics, vitamin D was being used against infection. Already, vitamin D was generally used to treat tuberculosis, as well as other severe infections [2].

Low levels of vitamin D have been commonly observed in adult and pediatric populations [3]. Presently, overall mortality [4], and disorders like prevention of infections innate immunity [5], hypertriglyceridemia, type 1 and 2 diabetes mellitus [6], hypertension [7], neoplasms [8], and autoimmune disorders [9] have been considered to be consequences of vitamin D deficiency. Moreover, in children, low level of vitamin D has been found in relation with lower response to corticoids, bronchiolitis episodes and severe asthma [10]. Vitamin D deficiency rickets in early infancy is prevalent in infants of mothers who have poor vitamin D stores [11]. The vitamin D status of breastfed newborns depends mainly on the vitamin D stores acquired during intrauterine life [12], because It is well known that the human milk content of vitamin D is very low [13].

Recently, higher illness severity upon admission in adult intensive care units (ICU) patients along with mortality, and worse outcomes has been associated with vitamin D deficiency [14-16]. Even in children admitted to paediatric ICUs (PICUs), lower vitamin D status was found common and associated with greater severity of critical illness [17-19]. Moreover, although role vitamin D status in acute stress and critical illness, such as immunity, endothelial and mucosal functions, and glucose and calcium metabolism [20], are obvious, its pleiotropic effects in acute illness are not proven. During critical illness, a lot of confounding factors, such as interstitial extravasation, pH, season of the year, decreased synthesis of binding proteins, renal wasting of 25 (OH) vitamin D, underlying disease, age, and dietary supplementation influence vitamin D status [21].

Low vitamin D levels favour atherosclerosis enabling vascular inflammation, endothelial dysfunction, formation of foam cells, and proliferation of smooth muscle cells. The antihypertensive properties of vitamin D include suppression of the renin-angiotensin-aldosterone system, renoprotective effects, direct effects on endothelial cells and calcium metabolism, inhibition of growth of vascular smooth muscle

cells, prevention of secondary hyperparathyroidism, and beneficial effects on cardiovascular risk factors [22-24].

Since the vitamin D deficiency may play a key role in outcome of critically ill patients, the aim of this study is to investigate the prevalence of vitamin D deficiency in patients hospitalized in ICU section of Children's Medical Center, and assess the impact of demographical and clinical factors on the serum level of vitamin D.

Patients and Methods

Patients

This study was performed in a cross-sectional way and on 82 children who were hospitalized in ICU section of Children's Medical Center, Tehran University of Medical Sciences, in 2015.

Performance

During a period of 6 months, information of 82 patients was recorded on designed forms. This task was done by nurses, presented during transfusion, and acquired data were accumulated at the end of each month. Of course, before the start of the project an adequate description about the forms and objectives of the study were given to nurses. In addition, during the study on the presenters accidentally been presented in ICU in same days and monitored how they fill out the forms. Information forms contained three main sections: 1. Demographic record (name, gender, age); 2. Growth and development record (height, weight, BMI); 3. Effective factors on vitamin D serum level (mothers' education, mother's age, order of birth, cause of hospitalization, type of disease, duration of hospitalization). Serum level of vitamin D was acquired from patients' files.

Ethical consideration

The study was carried out in accordance with the Declaration of Helsinki, and the ethics committee of the Tehran University of Medical Sciences approved the protocols of the study. The patients' records were kept confidential. Patients' consent were provided for blood sampling and vitamin D serum level was assessed from patients' files, so no invasive method or extra blood sampling was done.

Data analysis

Qualitative and quantitative data were analyzed and reported as frequency (%) and mean ± standard deviation, respectively. P value<0.05 was considered significant. Univariate and bivariate analysis were performed to determine effective factors of vitamin D serum level and extracting regression model, respectively. All data were analyzed with IBM SPSS Statistics for Windows, version 21.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Demographic and clinical characteristics of 82 patients, contributed in this study, are shown in Table 1. The main reason for admission was sepsis, and 64.6% of patients showed vitamin D serum levels under 30 ng/mL. The differences based on indices of patients' age and mothers' age was lower than other indices.

Table 1. *Patients' Demographic and development record, and effective factors of vitamin D serum level *.*

Variable	Value
Age, month	
<24	47 (57.3)
>25	35 (42.7)
BMI	
<18	53 (64.6)
>18.1	29 (35.4)
Hospitalization period, day	
<10	29 (35.4)
>10	53 (64.6)
Mothers' education	
<diploma	51 (62.2)
>diploma	31 (37.8)
Mothers' age, yrs	
<30	37 (45.1)
>30	45 (54.9)
Birth order	
Two first	54 (65.9)
Third and more	28 (34.1)
Cause of admission	
Urinary infection	4 (4.9)
Trauma	3 (3.7)
TEF	3 (3.7)
Sepsis	15 (18.3)
Seizure	13 (15.9)
Respiratory infection	13 (15.8)
Metabolic	5 (6.1)
Immunologic	5 (6.1)
DKA	4 (4.9)
Diarrhea	5 (6.1)
Cardiac	3 (3.7)
Brain tumor	4 (4.9)

Brain infection	1 (1.2)
ALL	4 (4.9)
Vitamin D serum level, ng/mL	
>30	29 (35.4)
<30	53 (64.6)

*Data are presented as frequency (%)

Subjects are mostly hospitalized due to sepsis (18.3%), seizure (15.9%), and respiratory infections (15.8%). Table 2 shows the reason of hospitalization of patients.

Table 2. The reason of hospitalization of patients.

	Urinary infection	trauma	TEF	sepsis	Seizure	Respiratory infection	metabolic	Immunologic	DKA	Diarrhea	cardiac	Brain tumor	Brain infection	All
Frequency	4	3	3	15	13	13	5	5	4	5	3	4	1	4
Percent	4.9	3.7	3.7	18.3	15.9	15.8	6.1	6.1	4.9	6.1	3.7	4.9	1.2	4.9

The serum level of vitamin D in relation with demographic and clinical factors is shown in Table 2. Vitamin D serum level decreased from 37.9532 to 23.8771 ng/mL in children older than 2 years and this change was significant (P=0.003), although no difference was seen between vitamin D levels in children with mothers less than 30 years old and more than 30 years old (P=0.968). There was no significant difference in level of vitamin D between Male and Females (P=0.733). There was no significant difference between the levels of Vitamin D in patients with BMI more than 18 and less than 18 (P=0.465). In addition, no relation was found between the level of education of mothers and the levels of vitamin D (P=0.968). Also, there was no relation between the vitamin D level and the Hospitalization period and Birth order (P=0.116 and P=0.593). Except gender and mothers' education, in relation with other factors, differences in vitamin D serum level are considerable; however, these differences are not significant.

Table 3. *Serum level of vitamin D in relation with different factors.*

Variable	N	Vitamin D serum level, ng/mL *	Chi-square	P Value
Gender			0.116	0.733
Male	46	33.38 ± 30.79		
Female	36	30.1 ± 29.52		
Age, yr			8.871	0.003
<2	47	37.9532 ± 30.72059		
>2	35	23.8771 ± 27.66524		
BMI			1.533	0.465
<18	53	36.3943 ± 35.21924		
>18	29	23.6643 ± 14.81319		
Mothers' education			0.941	0.332
<diploma	51	31.1373 ± 29.90500		
>diploma	31	33.2742 ± 30.87957		
Mothers' age, yr			0.002	0.968
<30	37	27.7243 ± 22.92058		
>30	45	35.4156 ± 34.80337		
Hospitalization period, day			2.475	0.116
<10	29	23.3655 ± 15.39237		
>10	53	36.6396 ± 34.93767		
Birth order			0.286	0.593
Two first	54	28.6185 ± 26.78397		

Third and more	28	38.3607 ± 35.29699
*Data presented as mean ± SD		

As presented in Table 4, logistic regression analysis confirmed the relation between age and vitamin D serum level of patients hospitalized in ICU.

Table 4. *Logistic regression analysis between age and vitamin D serum level.*

	Df	P Value	OR
Age	1	0.004	0.216
Constant	1	0.000	4.833

Discussion

The prevalence of vitamin D deficiency, based on different geographical regions, has been reported to be 18% in European cities (Oviedo's and Mansbach's population) [25] to higher ratios, ranged from 29% to 68%, in North American and Australian adolescents [26,27]. The prevalence of vitamin D deficiency in the sample of this study is 65.6 % that is closely similar to western countries. Although previously low level of vitamin D was found in prolonged critically ill patients in the study conducted by Cecchi et al. influence of vitamin D deficiency in the acute phase of sepsis on final outcome did not confirmed [2,28]. Also, even significant lower level of vitamin D was not found to be related with mortality in trauma and septic patients [2]. In addition, recently has been shown that hemodilution after fluid resuscitation significantly lowers serum vitamin D levels [29].

It has been shown that the incidence of vitamin D deficiency increased with age in both group of healthy and PICU children. PICU patients had double incidence of hypovitaminosis D in all three age groups (<1 year, 1-5 year, >5 year), but the differences were clearly statistically significant in the older age group, and were almost significant in the medium age group [30]. Moreover, lower level of vitamin D after age correction suggested that the pivotal role of vitamin D in sepsis pathophysiology, and consequently in outcome [2]. These declared relations between age and vitamin D serum level was in consistence with our data. Results of the present study showed that in patients older than 2 years the level of vitamin D was significantly lower than those younger than 2 years. Also, multivariate logistic regression model verified the significant correlation between age and vitamin D level (P=0.004). Such difference might be because of the higher rate of growth among children older than 2 years which demand higher vitamin D for their metabolisms.

Vitamin D deficiency has not recognized to be associated with higher anticipation of mortality risk scores and length of hospitalization. In studies performed on Australian and Spain children, length of PICU stay did not show differences between groups with low and normal vitamin D serum level that these results are in agreement with the observed data in present study [17,30]. However, it was observed that the increase in the length of stay trigger to the increase in vitamin D serum level (from 23.36 to 36.61 ng/mL), this growth in the amount of vitamin D was not significant (P value=0.116). This alteration might be attributed to the more receive of complementary pills which contains a ration of different vitamins.

Mothers' education and age can be effective factor on children nourishment, and consequently serum vitamin level. It has been observed that in the treatment of childhood rickets associated knee deformities, which is in relation with vitamin D deficiency, was significantly affected by mothers' education, age, and previous birth [31]. Also, the low educational level has been considered as a risk factor for low maternal serum vitamin D level [32]. The results of our study showed that there was no significant relation between mothers' education and vitamin D serum level. On the other hand, with increase of mother's age, the serum level of vitamin D increased; however, this increase was not significant (P=0.968). In the case of birth order, also, such difference in vitamin serum level is observable regarding the higher birth number, but there is no significant relation. These results suggest that mothers' age and birth orders, in larger samples, can be effective on the serum level of vitamin D maybe because of their more experience and more attentions to the nourishment of their children.

In conclusion, the present study showed that the prevalence of serum vitamin D deficiency among pediatric intensive care unit patients is similar to western countries, along with similar age and BMI distribution. Also, significant relation was observed between age and serum level of vitamin D, which was confirmed with logistic regression analysis, and indicate to higher attention to nourishment of older children. It seems that more prospective studies, with larger samples, are necessary to find effective factors on vitamin D serum level and side effects of vitamin D deficiency.

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