

Vitamin D deficiency in critically ill children

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Abstract:

Background: In critical illness, there also is evidence of rapid falls in circulating 25(OH)D concentrations. So, we aim to assess the prevalence of VDD in a pediatric ICU (PICU) patients and to determine whether there is any relationship between VDD and illness severity and mortality.

Patients and methods: this is a case control study that included 40 children :20 patient admitted to pediatric intensive care unit in Qena university at time of the study (from January 2018 till December 2018) compared to 20 apparently healthy well-matched children regarding age and sex to be compared as controls. All patients subjected to: Full history, detailed physical examination, diagnostic modalities as: laboratory investigation and severity of illness was assessed with the pediatric risk of mortality III

Result: Our study included 40 child with the age of patients ranged from 5 months to 12 years with mean \pm SD 3.7 \pm 3 year. Male patients represented 70%. In our study, the prevalence of vitamin D deficiency among critically ill children was 70 % we did not find significant correlation between 25(OH) vitamin D and pediatric risk of mortality III (PRISM III)

Conclusion: Vitamin D Deficiency (VDD) prevalence was reported in 70% of the critically ill patients, and it was observed to be related to multiple organ dysfunctions and rapid clinical deterioration.

Keywords: vitamin D deficiency, pediatric critical illness.

Introduction

Vitamin D plays an important role in metabolism and homeostasis in the general population, nowadays there is a growing interest in its potential association with critical illness (Norman et al, 2008).

In critical illness, there is acute drop of Vitamin D serum concentrations owing to increased tissue demands and impaired compensatory mechanisms by inflammatory process and organ destruction that may prolong the pathophysiology of critical illness (McNally et al, 2012).

Although several studies from different pediatric ICUs (PICUs) around the world

have been published revealing an increased prevalence of Vitamin D deficiency (VDD) in range of 30-71%, (Ponnarmeni et al., 2016).

The question if vitamin D deficiency (VDD) is involved in multiple organ dysfunction and mortality is not answered yet. Our study investigated the hypothesis that VDD might be related to higher severity scores and risk of mortality. The primary objective of this study was to estimate the prevalence of VDD in a group of critically ill children, and the secondary objective was to correlate vitamin D status with pediatric risk of mortality III (PRISM III) score.

Patients and methods

Our study included 40 children :20 patient admitted to pediatric intensive care unit in Qena university hospital at the time of the study from January 2018 till December 2018, compared to 20 apparently healthy well-matched children regarding age and sex as a control group

Inclusion criteria

Our study included all patient received treatment in pediatric intensive care unit of Qena University Hospitals in time of the study.

Exclusion criteria

We excluded patients who received vitamin D therapy during the last 6 months or refusing to participate in the study and cardiac surgical patients

Study tools:

After obtaining informed consent, all of the patients had been subjected to the following:

1-Full history was obtained from Parents about intake of vitamin D-containing drugs stressing on the onset and duration of the disease, manifestations suggesting disturbances in calcium metabolism, for example, bone pains, cramps of the hand or feet, fractures.

2-Detailed physical examination, Blood pressure measurement, patient height, weight and BMI were recorded. Severity of illness was assessed within the first 24 h of PICU admission with the PRISM III score using 16 variables

3- Laboratory investigation

-Vitamin D samples were collected within the first 24 h of admission to the PICU, measurements of Vitamin D was performed using commercially available sandwich enzyme-linked immunosorbent assay (ELISA) kits, supplied by Chongqing Biopsies Co., Ltd (Chongqing, People's Republic of China) with the catalog numbers: BYEK1472, using microplate ELISA

reader (EMR -500, USA).(Hassan et al 2018)(Kim et al 2013).

The serum 25-OHD level of:

- ≥ 30 ng/ml was considered optimal,
- ≤ 20 ng/ml was considered to have vitamin D deficiency,
- Vitamin D insufficiency was diagnosed at serum levels from 21 to 29 ng/ml. (Holick et al.,2011)

- Phosphorous, ionized calcium, and alkaline phosphatase
- C reactive protein
- Blood culture
- Arterial blood gases

Statistical analysis:

All patients had been analyzed using Statistical package for Social Sciences (SPSSV26).

Results

Table 1: Demographic data of critically ill patients and control

Variable		Patients (20 cases)	Control (20 cases)	P value
Age (years)		3.7 \pm 3	3.8 \pm 3.5	0.9
Sex	Males	14(75%)	16(80%)	0.5
	Females	6(30%)	4(20%)	
Residence	Rural	9(45%)	12(60%)	0.3
	Urban	11(55%)	8 (40%)	
Weight (kg)		14.5 \pm 8.4	13.8 \pm 8.7	0.8
BMI		14.4 \pm 4.5	15.1 \pm 2.3	0.8
PRISM score 3		16.9 \pm 7		
MV	YES	4 (20%)		
	NO	16 (80%)		
VIT D state	Optimum	4 (20%)		
	Insufficient	2 (10%)		
	Deficient	14 (70%)		

(PRISM 11=pediatric risk of mortality, MV=mechanical ventilation)

The table shows

- Mean age is 3.7 ± 3 year.
- Male patients represented 70%.
- Residence of most patient was urban (11 cases, 55%)
- BMI of patient ranged with a mean is 16.9 ± 7 .
- 20% of patient were connected to mechanical ventilation
- PRISM score ranged with a mean is 16.9 ± 7

phosphate and CRP have highly significant difference between patient group and control group .

- Also shows that PTH, ionized Ca, PH, CO₂, and HCO₃ have no significant difference between the two groups

Figure(1): showing relation PRISM11 and vitamin D level

This figure shows: The mean of pediatric risk of mortality score 111 higher in patient of vitamin D deficiency

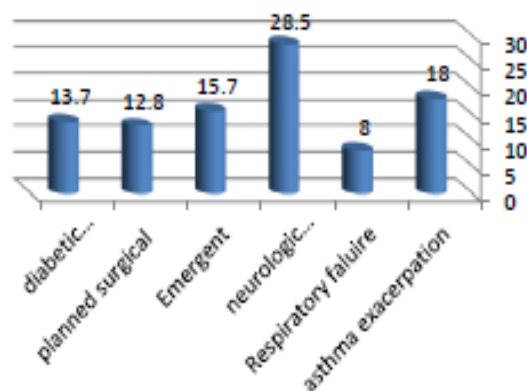


Figure 2: vitamin D level associated with PICU admission

This figure shows: a mean of vitamin D level was the lowest in patients with respiratory failure, surgical problems and diabetic ketoacidosis

Table (3): Relation between vitamin D deficiency status and markers of illness severity and intensive care unit outcome.

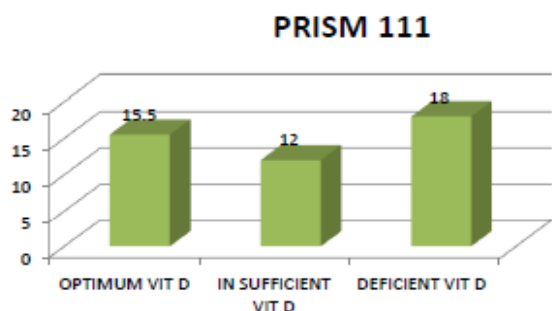
Variable		N	%	25 (OH)D	P value
Mortality	Died	4	20%	13.3±14.4	0.4
	Improved	16	80%	20.6 ± 15.3	
Mechanical ventilation	Yes	4	20%	13.3±14.4	0.4
	No	16	80%	20.6±15.3	
Vasopressor use	Yes	7	35%	13.7±11.7	0.2
	No	13	65%	22.1 ± 16.2	

Table 2 : Mean ± SD of laboratory data of patients and control.

Variable		Patients (20 cases)	Control (20 cases)	P value
25OH VIT D level (ng/ml)		19.2± 15.1	35.9 ± 6.7	0.03
PTH (ng/l)		40.8±16.5	26.7±10.5	0.09
ionized ca (mmol/l)		1.1±.1	1.2±.05	0.8
Phosphate (mmol/l)		3.8±.3	4.9±.8	0.000
PH		7.3±.1	7.4±.05	0.1
CO ₂ (mm Hg)		28.4±14	20.6±1.7	0.1
HCO ₃ (mEq/L)		14.8±6.7	20.6 ± 1.7	0.07
CRP (mg/l)		24.2±19.6	4.6±.5	0.04
Blood culture	No growth	14		
	Growth	6		

This table shows:

- laboratory results of the studied group compared to control group , shows that 25 OH vitamin D ,



Infection	Yes	6	30%	17.1±10.5	0.6
	No	14	70%	21±16.7	
Vitamin D	Deficient	14	70%	10.9±4.9	0.03
	Optimum	4	20%	45.1 ± 10	
	Insufficient	2	10%	24.9 ± 1.3	

This table shows:

- mean of vitamin D is less in died patient compared to improved patient.
- It is less in patients connected to mechanical ventilation compared to those who were not connected to mechanical ventilation
- Also, it is less in patients with proved infection and those who used vasopressor.

Discussion

Our study included 40 children :20 patient admitted to pediatric intensive care unit in Qena university hospital at the time of the study compared to 20 healthy well-matched children regarding age and sex as a control group age of them ranged from 5 months to 12 years with mean 3.7 ± 3 yr .

Badawi et al 2017 studied 88 children from 1 month to 12 years of age, a median of 36 months.

Male patients in our current study represented 70%. This is similar to **Badawi et al 2017** who found that 57% were males.

In our study neurologic disorders were the most common diagnosis in 35%. Respiratory disorders 30% (15% respiratory failure and 15% for status asthmaticus), diabetic ketoacidosis in 15%, elective postoperative illness in 10%. This is in contrast to **Badawi et al 2017** where Respiratory disorders were the most common diagnosis in 45% (43% pneumonia and 2% for status asthmaticus), neurological disorders in 22.7% heart failure in 10.5%, diabetic ketoacidosis in 6.8%, elective postoperative illness in 4.5%,

Admission diagnoses among the studied children included a variety of medical

critical conditions, whereas postoperative patients comprised only 10% with exclusion of cardiac surgical patients, unlike **McNally et al 2012** and **Ripple et al 2012**; both had a large category of postoperative cardiac and surgical diagnoses. **Madden et al 2012**. excluded cardiac surgical cases because of the effect of cardiac bypass on vitamin D levels.

In our study ventilated patients represented 20% of the admissions. We found no relation between vitamin D and need for mechanical ventilation. In contrast to **Ebenezer et al 2014** where 51% of patients were ventilated and found that Children who were ventilated during their PICU stay had a significantly lower median serum 25(OH) D level than those who were not ventilated.

In our study proved infection by blood culture was present in 30% of cases, similar to **Ebenezer et al 2014** in which microbiological confirmation was present in 37 % of them, neither our study nor **Ebenezer et al 2014** could demonstrate an association between vitamin D status and infection in these groups of critically ill children.

In our study mortality rate was 20% , the high mortality of 20% has many contributing factors such as delayed PICU admission due lack of beds, poor access to appropriate care and high percentage of multiple organ failure.

Gemke and Bonsel (1995) in a multicenter study showed a mean 7.1% mortality (range=1–10%) in PICU patients; one of the reasons for this variable mortality was related to the different severity of disorders. **El-Nawawy, 2003** showed 38% PICU mortality, but in India (**Thukra et al, 2006**) this was 35% and in Argentina (**Eulmesekian et al, 2007**) it was lower (2.6%) .

In our study, the prevalence of vitamin D deficiency among critically ill children

was 70 %. Another 10% of children had vitamin D insufficiency. This is higher than the reported prevalence of 29.5 % from Brazil (**Rey et al, 2014**) and 34.5 and 40.1 %, among critically ill Australian and Canadian children respectively and similar to the prevalence of 69 % reported by Madden et al. from North America (**Madden et al, 2012**)

In our study, we did not find significant correlation between 25(OH) vitamin D and pediatric risk of mortality III (PRISM III) , need for mechanical ventilation and inotropes these results similar to Reye, Ripple and Ponnarmani which could not find an association between (PRISM III) and vitamin D levels.

In contrast to **Madden et al, 2012** and **McNally et al, 2012** in which 25 (OH) D levels was inversely associated with PRISM III score on admission among PICU patients.

Also in contrast to **Braun et al, 2011** who showed a significant association between low serum 25(OH) D concentrations and an increase in blood culture positivity .we could not find such relation in our study.

In our study, the recorded values of vitamin D showed lower levels among patients with diabetic ketoacidosis, respiratory failure, but this was just an observation that was not feasible for statistical analysis because of the small sample size of the subgroups.

The role of vitamin D in the pathogenesis of diabetes is well known but whether the marked deficiency had a role in diabetic ketoacidosis precipitation or whether this is a sequence of the critical illness still needs to be investigated. (**Mutlu et al, 2011**).

Further research in category specific critical illness would be helpful to explore the possible relation between VDD and deterioration of chronic illnesses such as cardiomyopathy, Asthma and DKA.

Conclusions:

Vitamin D Deficiency (VDD) prevalence was reported in 70% of the critically ill patients, and it was observed to be related to multiple organ dysfunctions and rapid clinical deterioration.

Study Limitations

Mainly are the relatively small number of patients and being a single center study so that some subgroup comparisons may have lacked power to detect significant differences for selected variables, Further research in the category specific critical illness especially on larger number of patients and on other patients' categories are recommended and would be helpful to explore the possible relation between VDD and deterioration of chronic illnesses

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