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"Association of Vitamin D Level and Pediatric Risk of Mortality III Score In Critically Ill Children "

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ABSTRACT:

Background: Twenty-five hydroxy vitamin D is an essential nutrient that is made up of a combination of fat-soluble secosteroids and has a key role in the endocrine system additionally there is evidence that low vitamin d level is associated with increased fatality rate. **Aim:** Our research aimed to investigate the association amongst critically ill Children`s vitamin 25(OH)D levels and their illness severity measured by PRISM III scores. **Patients and methods:** This case-control research was performed on 30 children with critical illness admitted to the ICU of Pediatric of El-Salam Port-Said General Hospital in addition to 30 healthy children as the control group. **Results:** In the patients group (n=30), the PRISM III ranged from 5 to 24, with a median of 9.00, a 95% of the CI of the median of 7.00-15.00, and 25th Percentile –75th Percentile of 6.00-15.00. It was noted no statistically significant variance in PRISM III Score amongst the individuals with different diagnosis (p=0.053). The PRISM III Score was significantly greater in the deceased individuals relative to the discharged individuals (p=0.005),a statistically significant association is noted amongst PRISM III and Serum 25(OH)D (ng/ml) (p<0.001).

Conclusion:.low serum 25(OH)D was correlated with higher PRISM III score.

Keywords: 25(OH)D level; PRISM III,CV-SOFA

Introduction:

Twenty-five hydroxy vitamin D is an essential nutrient that is made up of a combination of fat-soluble secosteroids and plays a key role in the endocrine system. It is crucial for good health, particularly in infants and children, who are depending on it for proper bone development and growth. It is an essential mediator in extra-skeletal metabolic processes, immune and cardiovascular systems in addition to its vital function in bone metabolism and calcium homeostasis, almost all of our tissues and cells contain receptors for vitamin D and many of these receptors are capable of converting the primary non-active form of vitamin D to the active form [1, 2].

The PRISM score is utilized widely, biologically grounded sickness severity measure that integrates seventeen commonly measured physiological variables and their corresponding ranges. PRSM scores are used to determine the severity of illnesses in children. The PRISM score is a quantifiable depiction of physiological status of the individual. It makes use of specified variables and ranges to make use of categorical factors in order to provide an accurate evaluation of the vulnerability to death [3].

Numerous studies conducted in PICUs all over the world have indicated a significant prevalence of VDD that ranges from thirty percent to seventy-one percent [4].

There is also a known relation amongst the severity of the sickness, as shown by the PRISM-III score at the time of admission, an increased requirement for inotropes, the necessity of mechanical support, the length of time it is required, prolonged hospitalization and higher fatality rates and 25(OH)D levels [5-9].

Patients and methods

This case-control research was performed on 30 children with admitted to the Intensive Care Unit of Pediatric of El-Salam Port-Said General Hospital ,in addition to 30 healthy children as the control group.

Patients group

Inclusion Criteria: Children with illnesses requiring PICU stay for more than forty-eight hrs,those with ages from 2 months to 14 years old and both males and females.

Exclusion Criteria: Children admitted for monitoring after surgical operations. patients who had chronic diseases (endocrinal diseases, renal disease, chest diseases, cardiovascular diseases, DM). patients who have been treated with vitamin D therapy during the past half twelve months. Parents otherwise surrogates provide written informed consent.

Control group

They were healthy volunteers matching the age group and gender.

Inclusion criteria of the control group: Those with ages from two months to 14 years old,both males and females and caregivers of participating children provided informed permission.

Exclusion criteria of the control group: children who had chronic diseases (endocrinal diseases, renal disease, chest diseases, Cardiovascular diseases, DM) and individuals who got vitamin D therapy throughout the last six months.

Methods

All studied patients were subjected to: History: (personal history, present, past and nutritional history: details of the child's vitamin D intake, including vitamin D, formulas containing it, or any other vitamin D supplements), detailed physical examination and

Laboratory investigation: Samples of vitamin D were collected as early as possible upon PICU admission before the patient received treatment or parenteral nutrition. Each sample of two ml venous blood was collected by standard technique in a plain tube and then centrifuged to obtain 100 µL serum for assay of serum 25(OH)D by VIDAS 25 OH Vitamin D TOTAL assay kit which is based on an enzyme immunoassay competition method with a final fluorescent detection (ELFA) by VIDAS instrument where all the assay steps are done automatically by the instrument and completed within approximately 40 minutes.

Mortality: was assessed within the first twenty-four hours hrs. by PRISM-III score in which physiological factors were assessed solely throughout the 1st four hrs of the pediatric ICU, while varied laboratory conditions were measured throughout the time period beginning two hours prior admission to the PICU & continuing during the first four hours of treatment. GCS and pupillary reflexes scores are used for neurological score calculation, and the non-neurological score is calculated from the remainder.

CV-SOFA: the highest possible levels of vasopressors given throughout the stay in PICU in the following score manner was used to assess cardiovascular organ failure for illness severity assessment.

0–1: absence of vasopressors. 2: Dopamine levels below five µg/kg/min .

3: Dopamine ranging from five to fifteen μg/kg/min, or norepinephrine or epinephrine below 0.1 μg/kg/min and 4: Dopamine >15 μg/kg /min otherwise Norepinephrine/Epinephrine >0.1 μg/kg/min.

Statistical methodology:

The data were gathered & inputted into the computer utilizing the SPSS software, version 25, for the purpose of conducting statistical analysis. The data were inputted as either numerical or categorical, depending on the nature of the data.

The data were characterized utilizing the minimum, maximum, mean, standard deviation, & median. The tests employed included the Mann-Whitney U test, frequency, percentage analysis, the Kruskal-Wallis test, & non-parametric Kendall's tau correlation (τ). The study participants were subjected to regression analysis to predict the risk factors associated with all-cause death. A significance level of 95% was used, with an alpha level set at 5%. The statistical significance was assessed using a p-value < 0.05.

Results

No statistically significant variance was noted amongst control and patient groups regarding age, gender, weight, weight Z Score, height, height Z score, BMI and BMI Z score respectively (p=0.175), (p=0.796), (p=0.157), (p=0.195), (p=0.529), (p=0.055), (p=0.056) and (p=0.318) **Table (1)**.

In the patients group (n=30), the serum 25(OH)D ranged from 8.10 to 45.00 ng/ml, with a median of 18.10 ng/ml, a 95% of CI of the median of 15.50-24.00 ng/ml, and 25th Percentile –75th Percentile of 15.40-26.00 ng/ ml.

In the control group (n=30), the serum 25(OH)D ranged from 7.26 to 50.23 ng/ml, with a median of 25.33 ng/ml, a 95% of CI of the median of 21.87-34.58 ng/ml, and 25th Percentile –75th Percentile of 21.42-38.02 ng/ ml.

It was noted a statistically significant lower serum 25(OH)D level in the patient group in comparison to control one **Table (2)**.

In the patients group (n=30), the PRISM III ranged from 5 to 24, with a median of 9.00, a 95% of the CI of the median of 7.00-15.00, and 25th Percentile –75th Percentile of 6.00-15.00 **Table (3)**.

It was noted no statistically significant variance in PRISM III Score amongst the individuals with different diagnosis (p=.053). This may be due to the low sample size in three of the diagnosis groups (n=1) **Table (4)**.

The PRISM III Score was significantly greater in the deceased individuals when compared to the discharged individuals (p=.005) **Table (5)**.

There is a statistically significant relationship amongst PRISM III & Serum 25(OH)D (ng/ml) (p<0.001).

There is a statistically significant correlation amongst PRISM III &CV-SOFA (p=0.019) **Table (6)**.

Table 1: Basic characteristics of the two studied groups.

Basic characteristics	Group		Test of significance p value
	Patients (n=30)	Control (n=30)	
Age (years) - Mean±SD	1.85±0.84	2.43±1.41	$Z_{(MW)}$=1.356 p=.175 NS
Male - n - % within Group Female - n - % within Group	 15 50.00% 15 50.00%	 14 46.67% 16 53.33%	$\chi^2_{(df=1)}$=0.067 p=.796 NS
Weight (kg) - Mean±SD.	12.33±3.81	13.29±3.63	$Z_{(MW)}$=1.416 p=.157 NS
Weight Z score - Min – Max - Median	-1.38 -1.64 0.30	-0.25-3.00 0.46	$Z_{(MW)}$=1.295 p=.195 NS
Length or Height (m) - Mean±SD	0.88±0.15	0.90±0.13	$Z_{(MW)}$=0.629 p=.529 NS
Length Z score - Min – Max - Median	–2.70 – 3.40 0.0	–1.55 – 3.60 0.57	$Z_{(MW)}$=1.923 p=.055 NS
BMI (kg/m^2) - Mean±SD	17.06±2.01	16.20±1.15	$Z_{(MW)}$=1.915 p=.056 NS
BMI Z score - Min – Max - Median	–2.75 – 1.85 0.02	–1.75 – 0.60 –0.15	$Z_{(MW)}$=.998 p=.318 NS

n: Number of patients Min-Max: Minimum – Maximum
SEM: Standard error of the mean CI: Confidence interval
χ^2= Pearson Chi-Square df=degree of freedom
NS: Statistically not significant (p≥ .05)

Table 2: Serum 25(OH)D (ng/ml) in the two studied groups.

Serum 25(OH)D (ng/ml)	Group		Test of significance p value
	Patients (n=30)	Control (n=30)	
- Min – Max - Mean±SD. - Median	8.10-45.00 20.85±9.87 18.10	7.26-50.23 28.66±11.94 25.33	$Z_{(MW)}$=2.691 p=0.007*

Min-Max: Minimum – Maximum
CI: Confidence interval

Table 3: PRISM III in the Patient groups.

PRISM III	Patients (n=30)
- Min – Max - Mean ± SD. - Median	5.00-24.00 10.73 ± 5.35 9.00

Table 4: PRISM III in the Patient groups according to diagnosis.

PRISM III	Diagnosis						Test of significance p-value
	Pneumonia + Septic Shock	Myocarditis and Heart Failure	Pneumonia	Convulsions	Bronchopneumonia	Status epilepticus	
- n	1	1	21	1	3	3	$H_{(df=5)}$=10.899 p=0.053 NS
- Min – Max	24.00-24.00	23.00-23.00	5.00-18.00	9.00-9.00	6.00-8.00	5.00-7.00	
- Mean±SD.	24.00	23.00	10.90±4.29	9.00	6.67±1.15	5.67±1.1	
- Median	24.00	23.00	11.00	9.00	6.00	5.00	

H=Kruskal-Wallis H

Table 5: PRISM III in patients by outcome.

PRISM III	Patient (n=30)		Test of significance p-value
	Discharged (n=28)	Deceased (n=2)	
- Min – Max	5.00-18.00	23.00-24.00	$Z_{(MW)}$=2.341 p=0.005*
- Mean±SD.	9.82±4.22	23.50±0.71	
- Median	9.00	23.50	

Table 6: Correlation between PRISM III and Serum 25(OH)D (ng/ml).

	PRISM III
Serum 25(OH)D (ng/ml)	Kendall's tau-b = -0.926 p<0.001*
Cv-SOFA	Kendall's tau-b = 0.372 p=0.019*

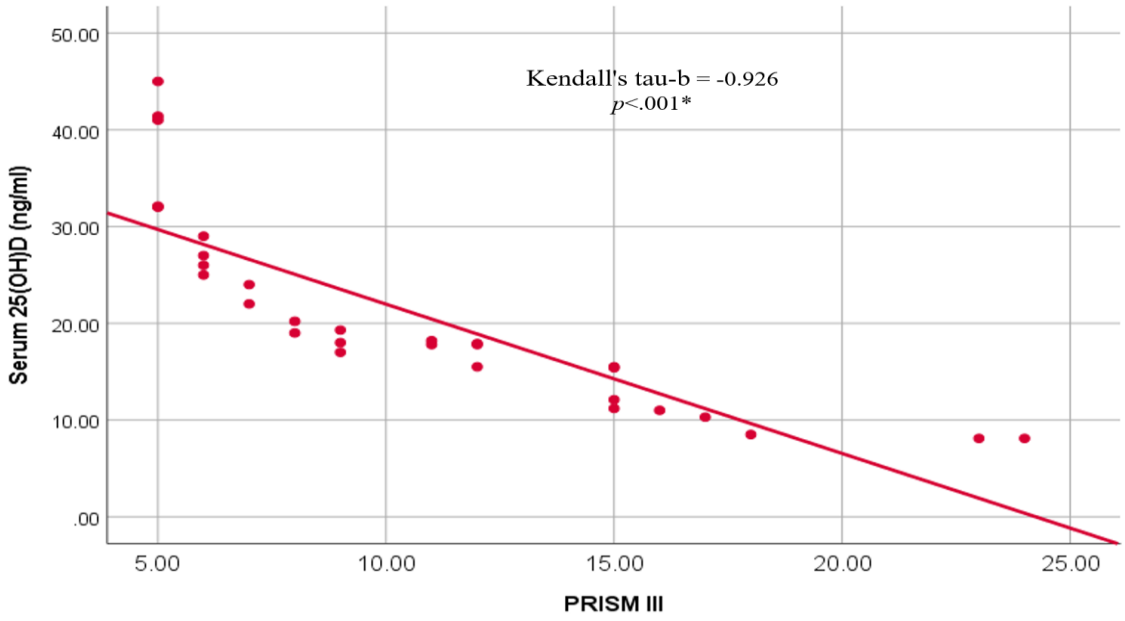

Figure (1): Correlation between PRISM III and Serum 25(OH)D (ng/ml)

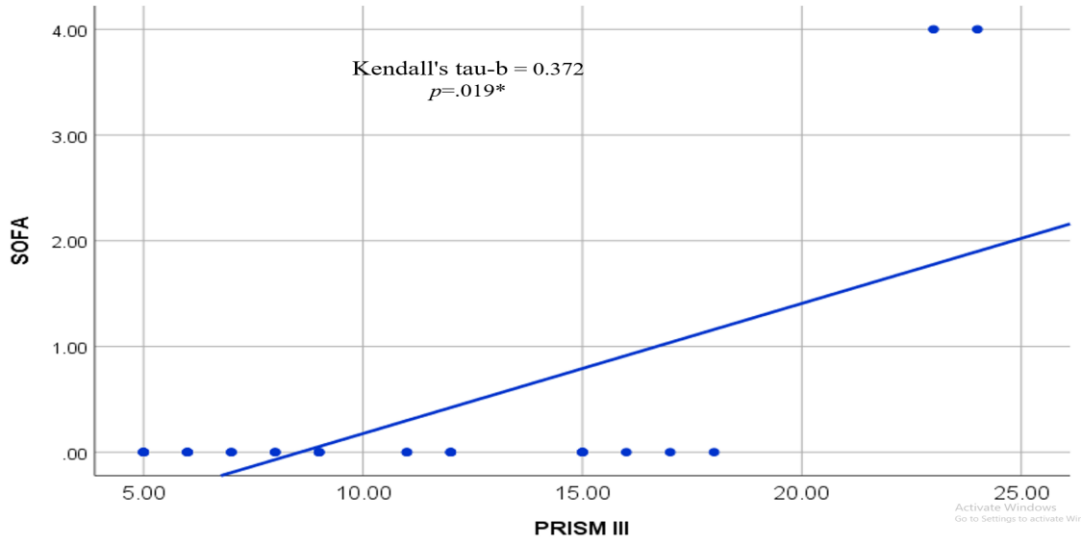

Figure (2): Association amongst PRISM III and CV-SOFA

Discussion

Vitamin D is indispensable for skeletal development and maturation. Numerous recent studies, on the other hand, have demonstrated that vitamin D is also crucial for immunity and shortage in this nutrient is linked to infections [11]. Vitamin D has been linked to anti-proliferative ,anti-inflammatory impacts and deficiency in this nutrient may elevate the mortality risk related to cardiovascular, autoimmune and malignant diseases [12]. The mechanisms described above are mediated by vitamin D receptors distributed all over body tissues [13].

The presence of low vitamin D levels has been related to higher levels of severity in grownup cases, as demonstrated by severity scoring systems like SOFA or PELOD [17]. In adult individuals, the level of 25(OH)D at the time of intensive care unit admission has been linked to various outcomes, involving short, long-term overall survival, period of mechanical ventilation, cardiovascular involvement and infection [15, 16]. Nevertheless, research on its prevalence, effects on results and severity in pediatric critical individuals remains limited [7,4].

Regarding demographic data, the current study showed no statistically significant variance amongst critically ill children & control groups as regard gender, age, weight, weight Z-score, height, height Z-score, BMI and BMI Z-score (p>0.05). In concordance with the current research **Ibrahim et al.** revealed

that was noted no statistically significant variance amongst critically ill children and control group as regard age, sex, weight and BMI (p>0.05) [17].

Depending on the level of serum 25(OH)D between the studied groups, our findings revealed that the patient group had significantly lower serum 25(OH)D level in comparison to the control group (20.85±9.87 ng/ml versus 28.66±11.94 ng/ml, respectively; p=0.007) a statistically significant difference was seen amongst the two groups.

In agreement with our results **El-Gendy et al.** revealed that the levels of 25(OH)D in individuals with sepsis accepted to PICU were lower than in pediatric controls (16.61±8.46 vs. 23.15±8.57 ng/ml respectively; P = 0.001) [18].

The PRIM III score is one of the scoring systems that is frequently utilized to quantify critical disease in the pediatric age and provide an objective evaluation of the degree to which a person is under the influence of illness [19].

Taking into consideration the mortality risk for children (PRISM) III score, the current study showed that the mean PRISM III was 10.73±5.35 among the patients group. A comparison between patients with different diagnosis showed that there was no association between diagnosis and mean PRISM III score, the lack for significance may be because of the inadequate sample size of the current research.

In accordance with the present research **de Araujo et al.** found no relation of case type & underlying disease with risk of death assessed by PRISM [20].

Contrasted to the outcomes of the current research, **Pirzadeh et al.** found a significant link among the underlying condition and the fate of children who were severely ill. In children had an underlying disease, respiratory signs are related with poor results [21].

Concerning the relation between PRISM III and outcome, the results of our research revealed that the PRISM III Score was considerably greater among individuals who had passed away compared to individuals who had been discharged (p =0.005).In agreement with our results **García-Soler et al.** demonstrated that higher PRISM III Score was significant risk factor of mortality among kids with critical illness [22].

As well, **Kaur et al.** revealed that high PRISM III Score was significantly associated with mortality among children with critical illness [19].

Regarding the relation amongst PRISM III and Serum 25(OH)D, our research demonstrated that was noted a statistically significant negative correlation amongst PRISM III and Serum 25(OH)D (ng/ml) (p<.001).In line with our research **El-Gendy et al.** noted a significant negative correlation amongst vitamin D level and PRISM III score (P = 0.02), CV-SOFA score (P = 0.001), duration of ventilation (P = 0.003) and PICU stay (P < 0.001) [18].

On the other hand, **Ibrahim et al.** did not found any significant association amongst 25(OH) vitamin D and the PRISM III, the requirement for mechanical ventilation or the use of inotropes. It is possible that the reasons for the disagreement with the current research are due to differences in the sample size, the reason for admission and the season [17].

Concerning the correlation between PRISM III and Cv-SOFA, our results demonstrated that a statistically significant positive correlation is noted amongst PRISM III and CV-SOFA (p=0.019).

In concordance with our results **Dang et al.** showed that there was a statistically significant negative correlation between PRISM III and Serum 25(OH)D (r = −0.397, P = 0.0001) and SOFA (CV-SOFA) (r = −0.193, P = 0.0008) at PICU admission in critically ill children.[10].

As well, **Baloch et al.** showed that CV-SOFA score was positively related to Pediatric Risk of Mortality III 24 score (r=0.712, p=0.001) in pediatric ICU. [23].

Conclusion : Serum 25(OH)D was negatively correleatd with PRISM III score in critically ill children admitted to PICU .

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