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ORIGINAL ARTICLE

Vitamin D Status in Infants, Toddlers and Preschool Children with Pneumonia

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ABSTRACT

Background: Pneumonia remains one of the most common causes of hospitalization and is leading cause of morbidity and mortality. Some studies have reported a relationship between serum levels of vitamin D and an increased incidence of pneumonia. The aim of this work was to assess vitamin D in infants, toddlers and preschool children suffering from pneumonia and correlate its level with severity, duration of hospital stay and outcome.
Methods: This cross-sectional study wasconducted on 120 preschool children. They suffered frompneumonia and were admitted to the PICU and Pulmonology Unit, Children's Hospital Zagazig University from July 2021 to June 2022. A complete clinical examination was performed with special concern for anthropometric measurements, a history of sun exposure,a history of Ca and vitamin D supplementation, a previous history of LRTIS,a duration of hospital stay, a chest examination, signs of respiratory distress, CBC, CRP, blood pH and vitamin D.
Results: The study included 51 (42.5%) infants, 53(44.2%) toddlers and 16 (13.3%) preschool children. Their ages ranged from 6 to 56 months. Regarding of severity, 49.2% of patients had severe pneumonia and 50.8% had very severe pneumonia. Vitamin D was insufficient in 14.2%, deficient in 73.3% and severely deficient in 12.5% of the patients. There was a significant relationship between vitamin D and the severity of pneumonia, duration of hospital stay, need for PICU and outcome.
Conclusions: The role of vitamin D in the severity of pneumonia, duration of hospital stay and outcomes in children between 6 and 60 months could be assured.

Keywords: Vitamin D;Pneumonia; Infant;Toddlers;Preschool children

INTRODUCTION

The most common infectious disease among children and one of the leading causes of hospital admissions globally is pneumonia. According to recent epidemiologic studies conducted in wealthy nations for children hospitalized with community-acquired pneumonia (CAP), 30%-70% have respiratory viruses identified, 7%–17% have atypical bacteria, and 2%–8% have pyogenic bacteria.

The respiratory pathogen's epidemiological season and child age significantly affect the etiological spread of CAP [1].Pneumonia is the leading cause of death for children in poor nations, not only being more prevalent than in Europe and North America, but also being more severe. Pneumonia kills greater than 81,000 children under the age of five each year, or 15% of all pediatric deaths [2].

There is increasing evidence that vitamin D has impacts beyond calcium and bone metabolism. It has been shown to have multiple immune modulatory effects [3]. It is thought that vitamin D influences the expression of antimicrobial peptides, such as cathelicidin, in response to bacterial and viral stimuli, hence influencing both the innate and adaptive immune responses. Active vitamin D can be produced by the respiratory airway epithelium [4].

Prior to vitamin D becoming active, alveolar macrophages must be activated[5].Mycobacterial antigen-binding toll-like receptor (TLR) 2/1 ligands stimulate alveolar macrophages, produce 1α-hydroxylase, and elevate 1,25D, which increases the vitamin D-regulated antimicrobial peptide cathelicidin [5].

Additionally, itplays a key role in the balance between T-helper 1 and T-helper 2 (Th1-Th2) cytokines [6,7]. It has been demonstrated that VD increases the levels of anti-inflammatory IL-10 and Th2 cytokines, such as IL-4 and IL-5, and reduces the levels of proinflammatory type 1 cytokines, such as IL-12, interferon-gamma (IFN-γ), IL-6, IL-8, tumor necrosis factor alpha (TNFα), and IL-17 [8]. 1,25(OH)2D stimulates the expression of cathelicidin in both myeloid and epithelial cells. When a lipopeptide from an infectious organism, like M. tuberculosis, stimulates TLR2 in macrophages; the expression of CYP27B1 and VDR increases. When sufficient substrate (25OHD) is present, this leads to the induction of cathelicidin. Since sufficient amounts of vitamin D stimulate the innate immune system, low levels of vitamin D may be linked to respiratory tract infections because they may result in an uncontrollably high level of chemokine synthesis and/or decreased cathelicidin production [9].Severe acute lower respiratory tract infections in children have been linked to both clinical and subclinical vitamin D insufficiency [10]. So,this study sought to evaluate vitamin D levels in children younger than five years aged patients with pneumonia and to establish a correlation between these levels and clinical parameters, length of hospital stay, and outcome.

METHODS

After protocol approval by our local ethics committee (ZU-IRB #5754), the patients were recruited for this cross sectional study from the Pediatric Pulmonology Unit and PICU Children's Hospital at Zagazig University from July 2021 to June 2022. We studied 120 children under 5 years of age who were diagnosed with pneumonia. Written informed consent was obtained from the parents of the study patients. According to local hospital protocols, all children were treated with humidified oxygen and intravenous fluids, antibiotics regimen and different mode of ventilator if required The Helsinki Declaration, the World Medical Association's code of ethics for human subject research, adhered to the study protocol.

The inclusion criteria used to identify severity of pneumonia were the updated

World Health Organization,2014 [11] and chest radiographic findings.Age ranged from 6 months to 5 years.

The exclusion criteria included any infant younger than 6 m and any child above 5 years old. Children with congenital or acquired chest wall malformations. Patients who were recently hospitalized. Patients had coexisting chronic lung diseases and congenital heart disease. Individuals with immunosuppressive medications or compromised immune systems at increased risk of developing severe pneumonia.

All patients had a detailed personal history and present history of all symptoms and signs of chest infection at admission (fever, cough, difficulty breathing, tachypnea, central cyanosis, difficultybreastfeeding, drinking, vomiting, convulsion, lethargy, unconsciousness or head nodding. history of drug intake in this illness at home, duration of hospital stay, PICU admission and outcome. Past history of frequency lower respiratory tract infections(LRTIs) treated at home, frequency of previous admission at hospital or not, appropriate time for exposure to sun (more than 30 minutes daily in the sun between 10 AM and 3 PM), seasons at admission , and vitamin D supplementation. The clinical examination involved paying particular attention to the child's age-related respiratory distress indicators, anthropometric measurements, and chest examination. Patients were admitted and divided according to the severity of pneumonia recommended by the WHO [11] for admission into two categories severe and very severe pneumonia. The laboratory test results included a chest x ray, complete blood count, CRP level, and blood pH at admission. In particular research: a direct enzyme-linked immunosorbent assay (ELISA) kit from DRG International, Inc. in New Jersey, United States, was used to quantify the serum 25 hydroxy vitamin D concentration in accordance with the manufacturer's guidelines.There were (13–19%) coefficients of variation (CVs).The level of 25(OH)] was evaluated as follows: <10ng/ml severe deficiency,deficiency: <20 ng/ml, insufficiency21-29ng/ml;sufficiency >30ng/ml, on the basis of on cut- off levels of the Consensus of Italian Pediatric Society[12].

Statistical analysis

SPSS 28 software was used to analyze the data. Qualitative data are expressed as percentages and numbers. To examine the relationships between the frequencies of the qualitative data, Fisher's exact test and the chi-square test ($\chi 2$) were used. The means, standard deviations, medians, and interquartile ranges (IQRSs) of the quantitative variables were used to characterize the data. To compare quantitative data, one-way ANOVA (for normally distributed data) and Kruskal-Wallis test (for nonnormally distributed data) were used. Pairwise comparisons and Bonferroni test were used to identify differences between each of the two separate groups where the difference was significant. The Pearson correlation coefficient denotes a direct or inverse relationship with a (+) or (-) sign, respectively.

RESULTS

This study included 120 patients aged between 6 to 56 months and 44.2% of whom were toddlers. Male represented 55.8% and females represented 44.2% of the patients **[Table1].** Two thirds of the patients (66.7%)

were admitted frequently in the winter.Most patients (55.8%) had a history of poor sun exposure and 44.2% had a history of infrequent vitamin D supplementation. Approximately 48% had no history of LRTIs and 50% had been admitted to the hospital once, 50.8% had RD grade 4 and very severe pneumonia and 68.3% were admitted to the PICU **[Table2]**. The ranges of TLC (10^3/mm^3) were 12.8 – 22, neutrophil 50-80%, CRP level was (39 – 100) and pH (6.9 – 7.33).The vitamin D level ranged from 7.5 to 23 ng/ml with a mean value of 14.7 ng/ml,73.3% had vitamin D deficiency and12.5% had severe vitamin D deficiency. Chest x ray revealed bronchopneumonia in 19.2% of the patients, lobar pneumonia in 44.2% and complicated bronchopneumonia in 36.7%**[Table 3].**Five percentof the studied patients died and 83.4% of the patients who died were female by the end of the study. The duration of hospital stay ranged from 5 to 12 days with a mean of 7.87 days. The frequency of very severe pneumonia was (50.8%) and 68.3% of the patients admitted to the PICU **[Table 4**].Significant relationships between vitamin D levels and each of TLC,neutrophil, pH,CRP levels and chest x ray findings. A greater percentage of patients with both vitamin D deficiency and severe vitamin D deficiency had complicated pneumonia [**Table 5**].

There was a highly significant relation between vitamin D level and length of hospital stay, and all of the patients who passed away had severe vitamin D deficiencies. **[Table 6].** Vitamin D was found to be a significantly positive correlation related to age, weight, height, and pH. A notably inverse relationships were recorded between vitamin D level and each of CRP levels, WBCs, neutrophil,platelet counts and the duration of hospital stay**[Table 7].**

Table (1): Distribution of studied patients according to baseline data

Parameter	**N=120**	**%**
Gender		
Female	53	44.2%
Male	67	55.8%
Age group		
Infant(>6M-1Y)	51	42.5%
Toddler(>1-3Y)	53	44.2%
Preschool children(>3Y- <5Y)	16	13.3%
	Median (IQR)	**Range**
Age(month)	14(11-18)	6-56
Weight (kg)	9.5(8.5 – 11)	6 – 29
	Mean ± SD	**Range**
Height (cm)	79.98 ± 10.7	66 – 106

Table (2): Distribution of studied patients according to disease-specific data

Parameter	N=120	%
Season at admission		
Autumn	35	29.2%
Summer	5	4.2%
Winter	80	66.7%
History of sun exposure (> 30M/daily 10 AM and 3 PM)		
Good	53	44.2%
Poor	67	55.8%
History of infrequent vitamin D supplementation	53	44.2%
No history of vitamin D supplementation after 6 months	67	55.8%
History of LRTIs treated at home		
No	57	47.5%
Once	53	44.2%
Twice	10	9.3%
History of previous hospital admission		
Once	60	50%
Twice	48	40%
Thrice	12	10%
Grade of RD& Severity of pneumonia		
RD3& Severe pneumonia	59	49.2%
RD4& Very severe pneumonia	61	50.8%
PICU admission	82	68.3%

LRTIs (lower respiratory tract infections),RD (respiratory distress),PICU(pediatric intensive care unit)

Table (3): Distribution of studied patients according to investigations

Parameter	**Mean ± SD**	**Range**
Hemoglobin (g/dl)	9.65 ± 0.87	7.5 – 11.5
Platelet (10^3/mm^3)	340.95 ± 92.7	190 – 610
TLC (10^3/mm^3)	16.02 ± 2.07	12.8 – 22
Neutrophil (10^3/mm^3)	65.14 ± 4.8	50 – 80
CRP level	60.97 ± 11.4	39 – 100
Blood pH	7.23 ± 0.09	6.9 – 7.33
Vitamin D (ng/ml)	14.7 ± 4.13	7.5 – 23
	N	**%**
Severe deficiency	15	12.5%
Deficiency	88	73.3%
Insufficiency	17	14.2%
Chest x ray		
Bronchopneumonia	23	19.2%
Lobar pneumonia	53	44.2%
Complicated bronchopneumonia	44	36.7%

TLC(Total leucocytic count)-CRP(C-reactive protein)

Table (4): Distribution of studied patients according to outcome, severity and duration of admission

Parameter	N=120		Male		Female	
Outcome	N	%	N	%	N	%
Died **Improved**	6 114	5% 95%	1 66	16.6 57.9	5 48	83.4 42.1
Severity of pneumonia						
Severe pneumonia **Very severe pneumonia**	59 61	49.2% 50.8%	46 21	77.9 34.4	13 40	22.1 65.6
PICU admission	82	68.3%	33	41.4	49	58.6
Duration of hospital stay	**Mean ± SD**		**Range**			
	7.87 ± 2.39		5-12			

Table (5): Relation between vitamin D level and investigated data of studied patients

Parameter	Severe deficiency	Deficiency	Insufficiency	F	p
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Hemoglobin (g/dl)	9.43 ± 1.21	9.69 ± 0.83	9.61 ± 0.71	0.598	0.551
Platelet (10^3/mm^3)	378 ± 116.13	332.44 ± 82.1	352.29 ± 116.82	1.716	0.184
TLC (10^3/mm^3)	17.45 ± 2.22	15.96 ± 2.05	15.08 ± 1.39	5.768	0.004*
Bonferroni posthoc	P_1 0.026*	$P_2$0.297	P_3 0.033*		
Neutrophil (10^3/mm^3)	68.17 ± 3.41	65.0 ± 4.92	63.22 ± 4.12	4.651	0.011*
Bonferroni posthoc	P_1 0.049*	$P_2$0.46	P_3 0.01*		
CRP	70.3 ± 10.77	61.9 ± 10.35	47.94 ± 4.22	22.244	<0.001**
Bonferroni posthoc	P_1 0.008*	P_2<0.001**	P_3<0.001**		
Blood pH	6.95 ± 0.12	7.24 ± 0.09	7.32 ± 0.01	9.689	<0.001**
Bonferroni posthoc	P_1<0.001**	$P_2$0.001*	P_3<0.001**		
	N=15 (%)	**N=88 (%)**	**N=17 (%)**	χ^2	p
Chest x ray **Bronchopneumonia** **Lobar pneumonia** **Complicated bronchopneumonia**	 3 (20%) 5 (33.3%) 7 (46.7%)	 19 (21.6%) 33 (37.5%) 36 (40.9%)	 1 (5.9%) 15 (88.2%) 1 (5.9%)	MC	0.008*

*p<0.05 is statistically significant, F one way ANOVA test, χ2Chi square test **p≤0.001 is statistically highly significant,

MC (Monte Carlo test) SD(standered deviation)CRP(c-reactive protein),TLC(Total leucocytic count)

Table (6): Relation between vitamin D and duration of admission and outcome of studied patients

Parameter	Severe deficiency	Deficiency	Insufficiency	χ^2	p
	N=15 (%)	**N=88 (%)**	**N=17 (%)**		
Outcome **Died** **Improved**	6 (40%) 9 (60%)	0 (0%) 88 (100%)	0 (0%) 17 (100%)	24.302	<0.001**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	t	p
Duration of hospital stay	10.0 ± 1.31	8.05 ± 2.28	5.06 ± 0.24	14.155	<0.001**
Bonferroni posthoc	$P_1$0.002*	P_2<0.001**	P_3<0.001**		

p1 difference between severe deficiency and deficiency p2 difference between deficiency and insufficiency p3 difference between severe deficiency and insufficiency *p<0.05 is statistically significant F one way ANOVA testχ^2Chi square test **p≤0.001 is statistically highly significant *p<0.05 is statistically significant,SD (slandered deviation), χ2Chi square test

Table (7): Correlation between vitamin D level and the studied parameters

Parameter	**r**	**P**
Age (month)	0.466	<0.001**
Weight (kg)	0.544	<0.001**
Height (cm)	0.514	<0.001**
Blood pH	0.652	<0.001**
Hemoglobin (g/dl)	0.147	0.109
Platelet (10^3/mm^3)	-0.219	0.016*
TLC (10^3/mm^3)	-0.447	<0.001**
Neutrophil (10^3/mm^3)	-0.307	<0.001**
CRP level	-0.725	<0.001**
Duration of hospital Stay	-0.867	<0.001**

r Pearson correlation coefficient **p≤0.001 is statistically highly significant *p<0.05 is statistically significant
CRP(c-reactive protein),TLC(Total leucocytic count)

DISCUSSION

The most prevalent infectious disease that is easily recognized and treated by pediatricians is CAP. However, because a precise diagnosis and suitable therapy are frequently in inaccurate, it leads to needless medical resource loss, excessive antibiotic administration, and hospitalization[1].

Many researchers have focused on vitamin D and its role in different disorders, including susceptibility to infections and autoimmune illnesses. Vitamin D deficiency is regarded as a serious health issue; however, in clinical practice fewer and fewer of its symptomatic manifestations are observed. The pediatric age group is considered a "gray area" where vitamin D treatment is frequently given without a reliable assessment of the patient's condition [13].

The purpose of this study was to measure the serum vitamin D level in infants, toddlers, and preschoolers who were either in the Pediatric Pulmonology Unit or the PICU had pneumonia. Additionally, we aimed to link the level of vitamin D to clinical, laboratory, imaging, length of hospital stay,

and outcomes. A total of 120 patients with pneumonia participated in this cross-sectional study.

In our study, the ages of the patients ranged from 6 to 56 months and 44.2% of the patients suffering from pneumonia were toddlers whereas 42.5% were infants and 13.3% were preschool children.

In our study the percentages of males to females were 55.8% (67) male and 44.2% (53) female. Jackson et al., confirmed our findings that males had an ALRIS that was1.5 (95% CI: 1.0 to 2.3) times greater than that of females; however, only one included report was from Africa [14].Additionally, Ismail et al. reported that the male frequency was more than the female frequency in the pneumonic group[15]. According to the severity of pneumonia and its relationship with sex, our study revealed that 40 (65.6%) females and 21 (34.4%) males suffered from very severe pneumonia. On the other hand, 46 patients (77.9%) were male and 13 patients (22.1%) were female and had severe pneumonia. So, greater percentage of female patients (58.6%) needed PICU than male patients (41.4%). In agreement with Naheed et al. who reported that a greater percentage of hospitalized preschool females than males had extremely severe pneumonia [16].

The mortality rate for female children hospitalized with very severe pneumonia was five times greater than that of male children. Likewise, in a study by Del Rosal et al, in Madrid, Spain, the number of female pneumonic patient deaths was four times higher than the number of male deaths [17]. Some doctors clarified that this idea might result from parents of sick children were seeking' treatment for boys more than for girls before being admitted to the hospital [16]. On the other hand, Yancey et al. reported that after surgical removal of the reproductive organs, there was no difference in the susceptibility of mycoplasmas in the lungs of male and female mice, and there was a gender difference in the severity of disease along the airways [18].

The ccurrent study recorded that vitamin D levels in pneumonic patients below 5 years ranged from 7.5 to 23ng/ml with a mean value of 14.7 ng/ml. In contrary to another study in Egypt carried out by Ismail et al. reported that no significant difference in vitamin D levelsbetween the pneumonic and control groups, with both groups having vitamin D concentration > 20 ng/ml[15]. Ismail et al. explained that children from different governorates in the same country, particularly Egypt, exhibited significant heterogeneity in their levels. This explained the difference in blood levels of vitamin D depending on sun exposure [15].

A total of 85.8% of the patients were vitamin D deficient based on cut off levels of Consensus of the Italian Pediatric Society [12]. The majority of patients (73.3%) had vitamin D deficiency, 12.5% had severe vitamin D deficiency and 14.2% had vitamin D insufficiency. The vitamin D level may be an indicator of the severity of presentation among children under 5 years old age with pneumonia. In contrast to finding from another study conducted in Egypt, Abdo et al. reported that 49.3% of the study group had decreased vitamin D, 16.4% had inadequate vitamin D while 34.3% had adequate vitamin D [19].In agreement with to our results a study performed by Kim et al. reported that 80% of CAP patients were deficient in vitamin D [20]. Also, another study carried out by Roth and collagues who noted that, irrespective of age, a startlingly high proportion of patients have inadequate levels

of this vitamin [21]. Moreover, Selvarajan et al. declared that the majority of people worldwide are vitamin D deficient [22].

We noted a strong relation between the severity of pneumonia and vitamin D levels. Additionally, the current study revealed a strong relation between vitamin D levels and the need for a PICU, blood pH, length of hospital stay, and prognosis. Patients in the PICU who had severe pneumonia or very severe pneumonia also had considerably lower levels of vitamin D. In agreement with research conducted in Egypt by Abdo et al. who reported that low vitamin D levels in kids with ALRTIs may be a major cause in the illness and a risk factor for how severe ALRIs is in kids [19]. Aregbesola et al reported that in comparison to those with the highest levels of vitamin D, those with the lowest levels had a significant 2.6-fold (95%CI: 1.4, 5.0) increased chance of contracting pneumonia. They concluded that the probability of incident pneumonia was inversely correlated with the serum 25(OH)D concentration [23].

According to our research, vitamin D deficiency and severe deficiency were linked to previous history of LRTIs treated at home and past history of repeated hospital admissions; however, the group with vitamin D insufficiency experienced the least number of LRTIs attacks and the shortest length of hospital stay Özdemir et al. concurred with our findings, which indicated that infants with recurrent respiratory infections had considerably lower serum 25(OH) D levels [24]. Additionally,Abdo et al. revealed that lower vitamin D levels in kids were linked to recurrence of ALRTIs in Egypt [19].

According to our research, toddlers (50%) made up the majority of patients in the vitamin D deficient group patients, followed by infants (44.3%).The majority of patients in the severely deficient group were infants. The relationship between age and vitamin D level was statistically significant and positive. Similarly, work by Bénet et al. may be explained by lower vitamin D levels after six months of life caused by a mother's milk supply that is inadequate in addition to a lack of body reserve [25].In additions to explaining of Weiler, stated that this age group has reduced exposure to sunlight outside [26].

Agree with Corsello et al. stated that oral vitamin D supplements should be given to all infants during their first year of life. Beyond this age, when proposing whether or not supplementation is necessary, physicians and scientific societies should always take geographic and cultural heterogeneity into account [13]. These findings can be explained by parents' ignorance, carelessness, and lack of awareness of the importance of vitamin D as a micronutrient, particularly by mothers.
According to the current study, prevalence of pneumonia in the preschool group had decreased to 13.3%. Additionally, preschool-aged children made up the majority of the vitamin D insufficiency group in our study (14.8%), and 44.2% of them took their vitamin D dosages infrequently. Preschoolers have higher vitamin D levels than other pneumonic patients which can be explained by Chen et al. who conducted earlier research in China and other Asian nations and revealed that while vitamin D sufficiency was lower in Hangzhou than in other East Chinese cities, preschoolers had the lowest percentage of deficient vitamin D (11.4%). Chen et al. revealed that dietary habits, strenuous exercise, activity, and sun exposure may contribute to these results [27].

A noteworthy significant relationship was observed in our investigation between the

vitamin D level and the history of sun exposure as well as the season of admission. The current results can be explained by our behaviors and beliefs during cold weather, such as overdressing children and restricting or completely eliminating their time spent in the sun Chen et al. validated our theory that sun exposure, food, and supplementation are the main sources of vitamin D. They also provided a complex link between the severity of pneumonia, vitamin D status, and sun exposure to explain our results. Vitamin D levels are influenced by sun exposure and changes in lifestyle choices and total UVB ray exposure, which are influenced by age, skin type, family traditions, and geography [27]. Additionally, Ahmed et al. concluded that the percentage of body surface area exposed to sunlight was the only factor that significantly affected the odds of ALRTIs, and that this proportion was connected with the risk of ALRTIs [28].

The degree of respiratory distress is used to classify the severity of pneumonia according to the WHO case criteria, which are utilized primarily in developing nations [11]. The results of the present study revealed substantial relations between vitamin D levels and of RD grade, pneumonia severity, blood pH, length of hospital stay, requirement for the PICU and prognosis. Carloni et al.; explained our findings by pointing out that people with low vitamin D have a higher frequency of respiratory tract infections, which may be caused by a decrease in cathelicidin production or an increase in chemokine production that triggers an uncontrollable inflammatory response [6]. Additionally, Lipińska-Opałka et al, reported that vitamin D regulates the innate and adaptive immune response and is important for maintaining the proper ratio of T-helper 1 to T-helper 2 (Th1-Th2) cytokines [7]. Finally, Bleakley et al. had been demonstrated that vitamin D elevates the levels of anti-inflammatory IL-10 and Th2 cytokines, such as IL-4 and IL-5, and lowers proinflammatory type 1 cytokines, such as IL-12, interferon-gamma (IFN-γ), IL-6, IL-8, tumor necrosis factor alpha (TNFα), and IL-17 [29].

Our findings were corroborated by a substantial relationship between vitamin D levels and each of TLC (range: 12.8 x 10^3 - 22 x 10^3), neutrophil (range: 50% to 80%) and CRP levels (39 - 100). A notably, inverse relationships were observed between vitamin D and each of WBCs, neutrophils and CRP levels. According to the current investigation, the etiology is mostly thought to be bacterial in nature because finding concomitant neutrophilia, a high CRP, and radiographic consolidation. Suspicion of a viral etiology may be excluded as evidenced by negative CRP, and the lack of concomitant lymphocytosis or lymphopenia. Bernstein et al, confirmed our findings, which showed that determining the serum CRP level could be useful in differentiating between viral pneumonia and bacterial pneumonia. They proposed that compared with children with nonbacterial pneumonia, children with bacterial pneumonia had a higher likelihood of having blood CRP concentrations over 35 - 60 mg/l (3.5 - 6 mg/dl) [30]. Additionally, Lakhani and Muley, reported that the sensitivities of CRP, ESR and TLC in the diagnosis of CAP were 90.9%, 72.7% and 48.5% respectively [31].However, Popovsky and Florin et al, reported that the overlapping clinical characteristics of the bacterial and viral etiologies of pneumonia, as well as other lower respiratory tract diseases, make the diagnosis of pneumonia in children difficult. S. pneumoniae is the most frequent typical

bacterial infection, whereas viral pathogens are the most prevalent cause of pneumonia [32].

On the other hand, Principi and Esposito, declared that acute phase reactants may be useful in tracking the progression of the illness, assessing the effectiveness of treatment, and determining when to stop treatment.They should not be the only factor used to discriminate between the bacterial and viral etiologies of CAP [33].

According to the current study, the range of Hb was 7.5 to-11.5 with a mean of 9.65. There was no beneficial correlation between the HBs of pneumonic patients and vitamin D. We concur with the finding of Ismail et al, who reported that children with pneumonia had a declining in the mean Hb value below 10 g/dl, which was a significantly different from that of control group (11.6 g/dl, $p < 0.001$)[15]. Additionally, Feldstein et al, reported anemia in kids with LRTIS who were hospitalized. They described how infection-related anemia results in impaired haem production due to a barrier in the release of iron from macrophages to growing normoblasts [34]. Rashad et al, who showed that poor tissue oxygenation is the primary pathophysiological deficiency in ARTIS, and anemia independently reduces oxygen supply, leading to increased illness and hospitalization [35].As well as Smith and Tangpricha documented association between vitamin D and anemia which referred to vitamin D potentiates and enhances erythropoiesis and diminishes pro-inflammatory cytokines by its effect on inhibition mRNA of hepcidin[36].

According to chest x-ray results from the present study, 36.7% of the patients had complicated bronchopneumonia and 44.2% of the patients had lobar pneumonia. Only 19.2% of patients had bronchopneumonia. The chest x-rays results and the vitamin D levels were significantly related. Lobar pneumonia was more common in the insufficient group (88.2%) than in the severe deficient and vitamin D deficient groups (33.3% and 37.5%, respectively). A greater proportion of patients with severe vitamin D deficiency (46.7%) and vitamin deficiency (40.9%) had complicated bronchopneumonia. The current study is backed by that of Rimpovaa et al. who conducted an association between profound deficiency of vitamin D and children cases with pulmonary complications as pneumothorax, necrotizing pneumonia, hydrothorax and parapneumonic effusion. They referred that to impair immune response in lung parenchyma and deficiency of vitamin D [37].

The limitation of this work includes lack of published literatures about normal level of vitamin D for Egyptian children.So further national studies could be needed to assess vitamin D level for all stages of childhood should be done.

Conclusion: It is possible that vitamin D status may have a significant impact on the severity of pneumonia, PICU need, recurrence of LRTIs, length of hospital stay, and overall prognosis in children aged 6 to 60 months. Widespread health education could raise awareness of the benefits of vitamin D supplements, vitamin D rich foods, and appropriate sun exposure.

Conflict of interest: None.

Financial Disclosures: None.

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