Zagazig University Medical Journal
www.zumj.journals.ekb.eg

Manuscript ID ZUMJ-1902-1059 (R2)
DOI 10.21608/zumj.2019.9735.1059

Volume 28, Issue 3, May 2022, Page 401-410

ORIGINAL ARTICLE

Study of Vitamin D Level in Children with Lower Respiratory Tract Infections in Zagazig University Hospitals

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Submit Date	2019-02-20
Revise Date	2019-12-22
Accept Date	2019-12-28

ABSTRACT

Background: Lower respiratory tract infections (LRTIS) remain among of the most important causes of morbidity and mortality among children. Several studies have associated vitamin D deficiency with an increased risk of LRTIS, and vitamin D supplementation has been proposed as a possible preventive measure against RTIS in children. The aim of this work was to assess the association between vitamin D level and acute lower respiratory tract infections in children. **Methods**: This Cross-Sectional Study was conducted on 67 Children with acute lower respiratory tract infections were admitted to Chest and Allergic Diseases Unit, Pediatric department, Zagazig University Hospital during the period from March to October 2018. Complete clinical examination with special concern on chest examination, anthropometric measurement, signs of respiratory distress depended on child's age **Results**: This study included 67 children with acute lower respiratory tract infections, their age ranged from 6months to 10 years. (31.3%) of the study group had pneumonia, (29.9%) bronchopneumonia, (23.9%) bronchiolitis, (9%) pleural effusion and (6%) had hydro-pneumothorax. Regarding disease severity, (41.8%) had mild disease and (58.2%) had severe disease. According to vitamin D level, it was deficient in (49.3%), insufficient in (16.4%) and sufficient in (34.3%). There was a statistical significant negative correlation between vitamin D levels with disease severity. Also, vitamin D was more sufficient in ward patients more than PICU. **Conclusion**: It was concluded that decreased vitamin D levels in children with ALRTIS might play an important role in disease and as a risk factor in severity, recurrence of ALRIS in children.

Keywords; Vitamin D Level, Lower Respiratory Tract Infections, Disease Severity.

INTRODUCTION

Acute lower respiratory infections (ALRIS) contribute to major disease associated mortality and morbidity among children under 5years [1].

In developing countries, on an average, every child has five episodes of acute respiratory infection /year accounting for 30%-50% of the total pediatrics outpatient visits and 20%-30% of the pediatric admissions [2].

The world health organization estimates that in 2013 over 8% of all deaths in the Eastern Mediterranean Region were attributable to Acute respiratory infections[3].

Vitamin D is an essential dietary component for which biological effects occur only as a consequence of it's metabolism into a family of daughter metabolites. Two of these are important for human health, Vitamin D2 (which is synthesized in plants and fungi) and Vitamin D3 (which made in skin exposed to sunlight) [4].

In addition to its important role in skeletal development and maintenance, vitamin D is thought to have roles in the improvement of

https://dx.doi.org/10.21608/zumj.2019.9735.1059

immune function and the reduction of inflammation [5].

There is growing evidence that the effects of vitamin D reach for beyond calcium and bone metabolism, in recent years several immune modulatory effects of vitamin D have been described [6].

Vitamin D deficiency is a common and important nutritional deficiency in children. Clinical and subclinical vitamin D deficiency in children has been reported to be a significant risk factor for sever acute lower respiratory tract infections [7].

Epidemiologic studies have reinforced the hypothesis that Vitamin D deficiency can profoundly mitigate our susceptibility to diverse pathogens. This action was first suspected when it was reported that the incidence of viral infections typically peaked during winter months when epidermal Vitamin D synthesis was lower and serum 25(OH) Vitamin D levels reached a nadir (critical lowest value) [8].

Finally it has been shown that Vitamin D regulates the inflammatory response, altering the pro-inflammatory/anti-inflammatory balance toward an anti-inflammatory phenotype to control the inflammatory burst once triggered [9].

The aim of this work was to assess the association between vitamin D level and acute lower respiratory tract infections in children.

PATIENTS AND METHODS

This Cross-Sectional Study was conducted on 67 Children with acute lower respiratory tract infections were admitted to Chest and Allergic Diseases Unit, Pediatric department, Zagazig University Hospital during the period from March to October 2018.

Inclusion criteria: children of both sex with acute lower respiratory tract infections with age ranged between (6 months to10 years).

Exclusion Criteria: Children with congenital chest wall malformation, active rickets and Children with history of vitamin D or iron supplements intake.

All children were subjected to a detailed history including personal history, present history stressing on (fever, cough, dyspnea, grunting, cyanosis, and refusal of feeding), feeding history, sun exposure, Socioeconomic status, scores were classified into very low, low, middle , and high levels , according to Socioeconomic status level of **Fahmy & El-Sherbeni scale [10].** Adequate sun exposure was taken as spending >30 minutes per day in sunlight between 10 AM and 2 PM**.**

Complete clinical examination with special concern on chest examination, anthropometric measurement, signs of respiratory distress depended on child's age.

To score the clinical status of the patients we used scoring system depends on physical signs as nasal flaring, respiratory rate, retractions of accessory muscles of respiration, wheezing and general status. Each point is given a score from 0 to 3. **[11]**

Laboratory investigations: Complete blood count, CRP. Chest X ray. Specific investigation: Serum 25 hydroxyvitamin D levels was measured using the ELISA method.

Venous blood samples were collected aseptically from all children who participated in the study by venipuncture using a 2ml evacuated glass tubes. Blood was allowed to clot at room temperature (20 C). Then centrifugation was done for 15 min. It was stored at -20 C till assessment was done.

The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is proportional to the concentration of 25- Dihydroxy vitamin D (25-OH-D) . we calculate the concentration of 25-Dihydroxy vitamin D (25-OH-D)in the samples by comparing the OD of the samples to the standard curve.

Vitamin D status in relation to [25(OH)] level was done as follows: Vitamin D Deficiency: <20 ng/ml, Insufficiency: 21-29 ng/ml, Sufficiency: >30 ng/ml. **[12]** Based on World Health Organization Criteria.

Written informed consent was obtained from all children' parents, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical

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Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were collected, tabulated and analyzed by SPSS 20 software. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD , the following tests were used to test differences for significance;. difference and association of qualitative variable by Chi square test (X^2) . Differences between quantitative independent groups by t test. The significance level was considered at $P < 0.05$.

RESULTS

Table (1), showed the mean age of the study group was (2.5±2.6) years. **Table (2),** showed that (43.3%) of studied group had history of ALRTIs, (55.2%) had good sun exposure, about (61.2%) were exclusively breast fed for the 1st 6 months and most of our studied cases were admitted to the ward while (31.3%) of them were PICU admitted. **Table (3),** showed the clinical and laboratory data of the studied group. **Table (4),** showed that there was no statistical significant in vitamin D level among different diagnosis in the studied group. **Table (5),** showed that there was a statistical significant in vitamin D status between mild and severe cases where (69.7%) of deficient vitamin D had severe disease and only (30.3%) had mild disease. **Table (6),** showed that that severe cases were more frequent among young children and all the severe cases had low family social status, other patients characteristics were not related to disease severity.

Table (1): socio-demographic data of the studied group.

Variable	The studied group (67) mean ± SD (Range) median	
Age (years):	2.5±2.6 (6months-10 years) 1.6	
Variable	**NO (49)**	**%**

Table (2): Clinical history of the studied group

Variable	NO(67)	%
Age of starting weaning (months):		
Not started	41	61.2%
7	5	7.5%
8	6	9.0%
10	1	1.5%
12	11	16.4%
14	1	1.5%
18	2	3.0%
Previous attack of ALRTs	38	56.7%
No	29	43.3%
Yes		
Sun exposure		
poor	30	44.8%
good	37	55.2%
Exclusive breast feeding in the 1st 6 months		
Yes	41	61.2%
No	26	38.8%
Disease severity		
Mild	28	41.8%
Severe	39	58.2%

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Variable	NO(67)	%
Admission		
PICU	21	31.3%
Ward	46	68.7%

Table (3): Clinical examination and investigations of the studied group:

Variable	The studied group(49) mean ± SD (Range) median
Temperature(°C)	38.4±1.2 (36-40) 38.5
Height or length (cm)	82.1±20.9 (60-140) 80
Weight (kg)	11.7±5.6 (5.5-30) 10
OFC(cm)	27.9±22.4 (0.0-50) 43
WBC(×10^3/ul)	13.5±7.1 (3-43.1) 12.4
Hb(g/dl)	10.2±1.2 (7-12.8) 10.1
Platelets(×10^3/ul)	451.5±211.2 (108-1294) 447
CRP(mg/l)	49.0±59.4 (0.31-271) 22.6
Vitamin D(ng/ml)	25.2±26.1 (1-89.2) 20.6

Table (4): Relation between diagnosis and vitamin D level in the studied group

Diagnosis	Vitamin D mean ± SD (Range)	F-test	p-value
Pleural effusion	6.6±7.6 (1-20.6)	2.2	0.08
Bronchopneumonia	32.1±27.9 (1-89.2)		
Pneumonia	16.9±22.2 (1-80.2)		
Bronchiolitis	32.9±25.3 (1-78.7)		
Hydro-pneumothorax	30.6±40.2 (1-86.2)		

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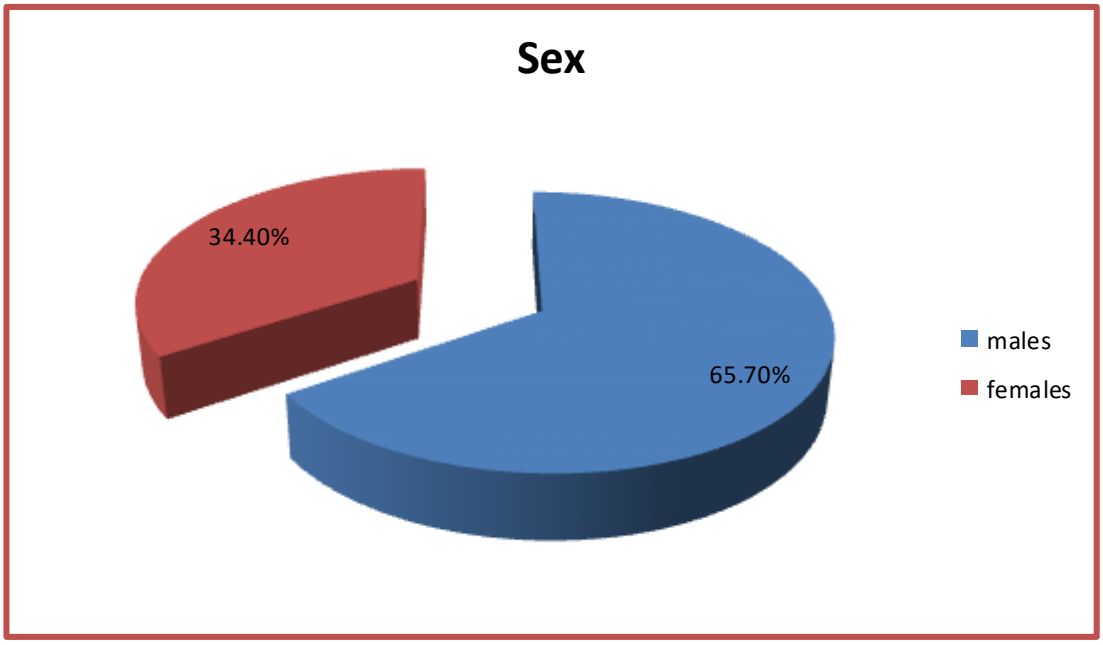
Table (5): Relation between disease severity and vitamin D status in the studied group

Disease severity	Mild diseases No(28) %	Severe diseases No (39) %	χ^2	p-value
Deficient (33)	10 30.3	23 69.7	4.6	**0.01***
Insufficient (11)	7 63.6	4 36.4		
Sufficient (23)	11 47.8	12 52.2		

Table (6): Relation between disease severity and patients' characteristics in the studied group.

Variable	Mild diseases No(28) %	Severe diseases No (39) %	χ^2	p-value
Age grouping			6.4	**0.04***
<1 year (22)	14 63.6	8 36.4		
1-5 years (36)	11 30.6	25 69.4		
5-10 years (9)	3 33.3	6 66.7		
Sex			3.5	0.06
male (44)	22 50.0	22 50.0		
female (23)	6 26.1	17 73.9		
Family social status			6.5	**0.03***
poor (6)	0.0 00.0	6 100.0		
low (42)	17 40.5	25 59.5		
moderate (19)	11 57.9	8 42.1		
Previous attack of ALRTS			1.1	0.2
No (38)	18 47.4	20 52.6		
Yes (29)	10 34.5	19 65.5		
Sun exposure			1.5	0.2
poor (30)	15 50.0	15 50.0		
good (37)	13 35.1	24 64.9		



Figure(1): Pie chart for sex distribution in the studied group

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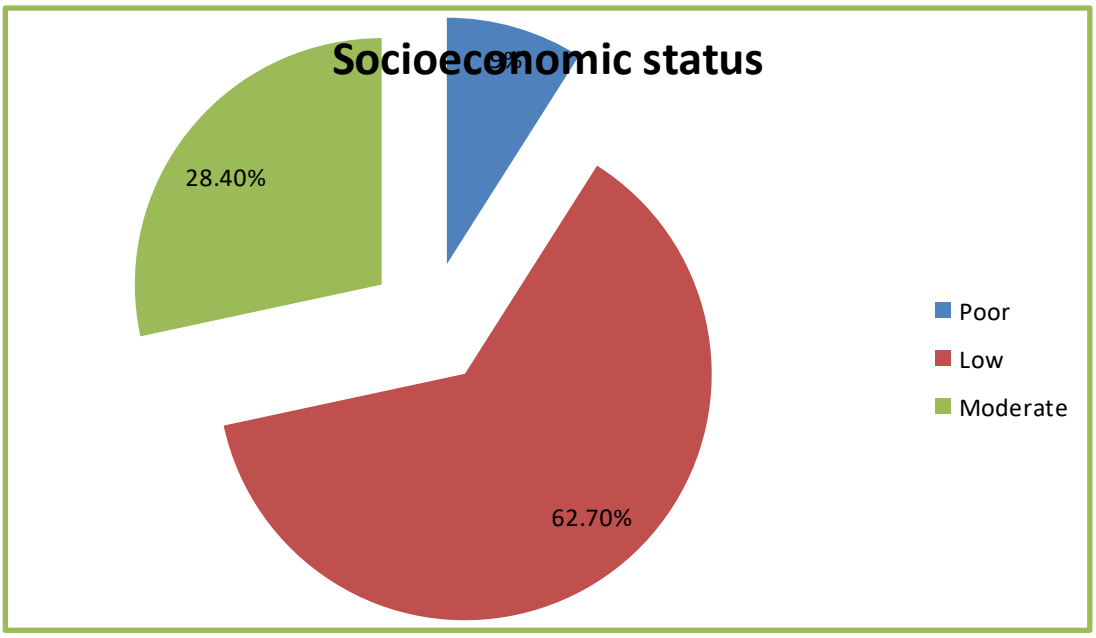
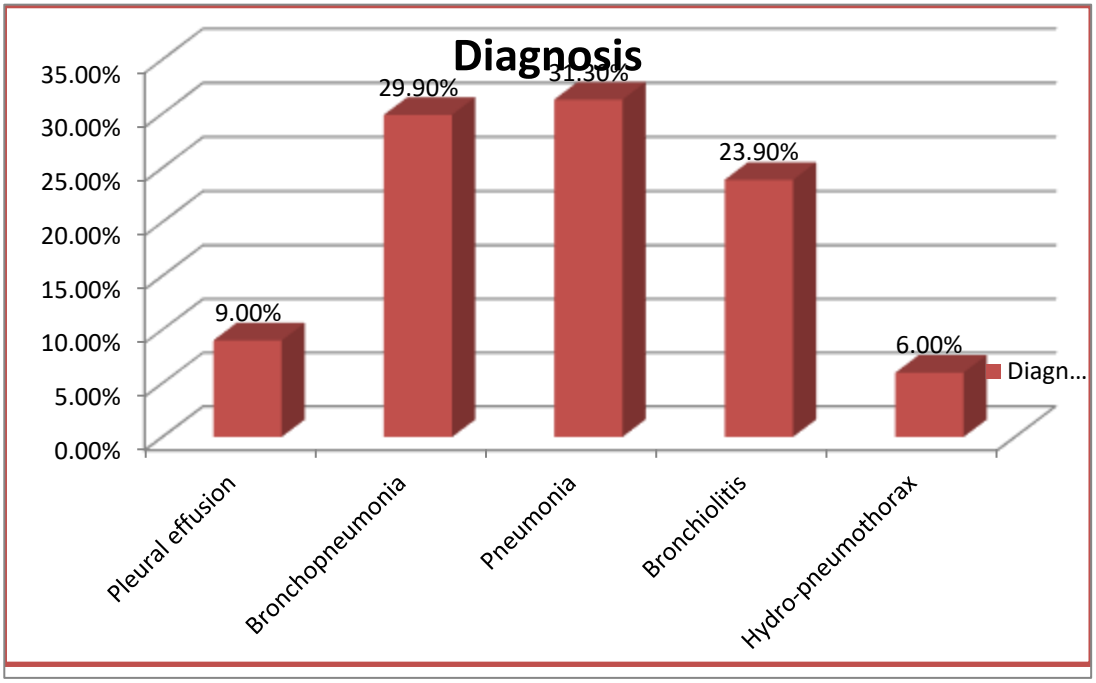


Figure(2): Pie chart for socio-economic status in the studied group



Figure(3): Bar chart for diagnosis in the studied group

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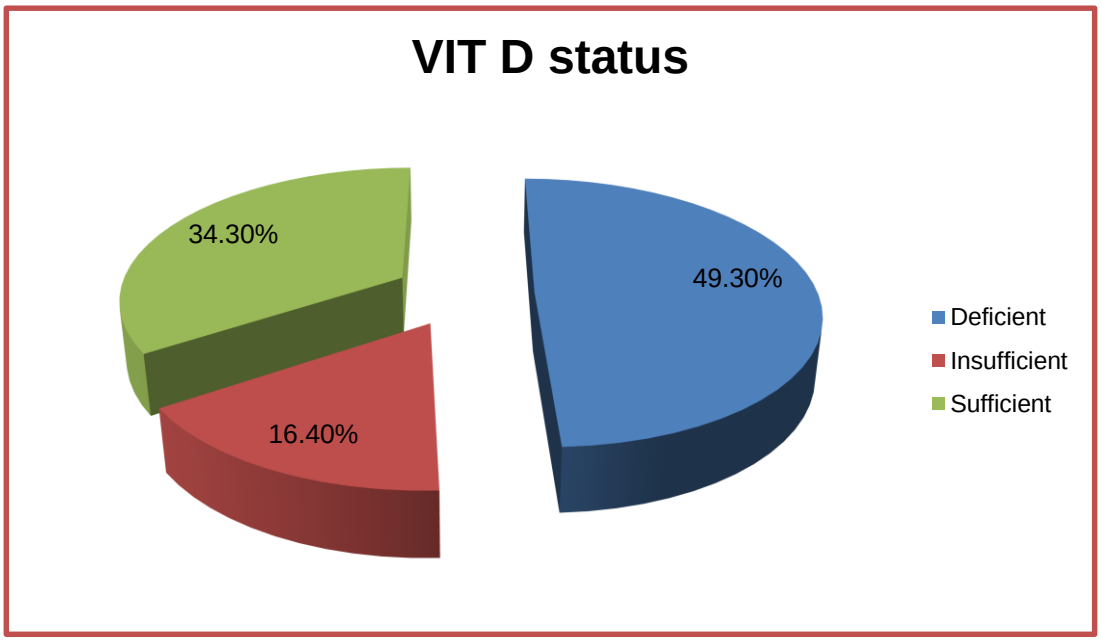

Figure(4): Pie chart for vitamin D status in the studied group.

DISCUSSION

Vitamin D plays a fundamental role in regulating calcium and phosphorus homeostasis and, in particular, the pathways involved in bone mineralization and bone mass acquisition. Besides these classic skeletal actions, recent studies have demonstrated that vitamin D exerts other significant extraskeletal actions, with a possible role in the pathogenesis of several pathological conditions, including infectious and autoimmune diseases [13].

Vitamin D has extensive influence on gene expression affecting the immune system and the inflammatory cascade. Multiple cell types of the respiratory epithelial cells, macrophages, monocytes, and dendritic cells posses both the enzyme (CYP27B1) required to convert inactive circulating 25(OH)D to active 1,25(OH)D and it's receptors the vitamin D receptor(VDR) [14].

The aim of this work is to assess the association between Vitamin D level and lower respiratory tract infections in children. A total of 67 patients, recruited from the department of pediatrics, Chest and Allergic Disease Unit at Zagazig University Hospital. Patients were subjected to full history taking including; patient demographic information as age, gender, diagnosis, dieteric history as regard duration of breast feeding, time of weaning, housing and sun exposure, socioeconomic status, history of recurrent LRTIs along with complete physical examination, and routine laboratory investigations including; complete blood count, CRP, chest X ray in addition to serum 25 hydroxyvitamin D levels.

In our study the mean age was found to be 2.5±2.6 years (53.7%) of them ranged from 1 to 5 years, (32.8%) less than 1year, and (13.4%) ranged from 5 to 10 years.(Table 1). In our study male and female percentages in the study group were (67.7%) males and (34.4%) females.(figure 1). According to socioeconomic status (62.7%) of study group had low socioeconomic status, (28.4%) had moderate socioeconomic status, while only (9%) were of high socioeconomic status.(figure 2). A results came in agreement with the study of **El Sakka et al. [15]**, who reported that (53.17%) had low socioeconomic status.

We found that (43.3%) had previous attacks of ALRTIs, (55.2%) were well exposed to sun (Adequate sun exposure was taken as spending >30 minutes per day in sunlight between 10AM and 2PM) [16].

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Ahmed et al. [17] in his study of 50 Nigerian children concluded that in multiple conditional logistic regression, the only variable that significantly influenced the odds of ALRTIS was that the less percentage of body surface area exposed to sunlight was associated with risk of ALRTIS.

Breast milk represents the best food to satisfy children's nutritional needs, although it contains insufficient amount of vitamin D (<50 IU/L) [18].

In our study (61.2%) were exclusively breastfed in first 6months.(Table 2). In our study we found that (58.2%) of the study group had severe disease and (41.8%) had mild disease. Most of our studied group cases admitted to the word while (31.3%) were PICU admitted. As regard our pateints they were classified according to their clinical diagnosis and X-ray finding into (31.3%) pneumonia, (29.9%) bronchopneumonia, (23.9%) bronchiolitis, (9%) pleural effusion, and (6%) had hydropneumothorax.(figure 3). By clinical examination we found that temperature (axillary) ranged from (36-40°C), WBC of study group ranged from (3 to 43.1×10^3/ul), Hb ranged from (7 to 12.8g/dl), platelet ranged from (108 to 1294×10^3/ul), CRP ranged from (0.31 to 271mg/l). (Table 3). Considering vitamin D status in relation to [25(OH)D] level was done as following:Deficient <20 ng/ml, Insufficient 21-29 ng/ml and Sufficient >30 ng/ml.

In our study we found that vitamin D was deficient in (49.3%) of the study group, (16.4%) had insufficient vitamin D, while (34.3%) had sufficient vitamin D, this was agreement with **Elsakka et al [15],** who stated that (55.2%) for vitamin D deficient and (8.3%) for vitamin D insufficient.(figure4).

We studied the relation of diagnosis with vitamin D level in our patients and we didn't find statistically significant difference in vitamin D level between different diagnosis. (Table 4).

Similar results were obtained by **Sismanlar et al [19],** who found no significant correlation between the diagnosis and vitamin D level, (P> 0.05). In our study we found significant relation between degree of vitamin D deficiency and disease severity; (69.7%) of deficient vitamin D cases had severe disease and only (30%) had mild disease (Table 5).

This was agreement with **Madhu et al [20],** who stated that (63.3%) of vitamin D deficient cases had severe respiratory finding, while (37.7%) had mild respiratory finding, and children with severe respiratory finding had lower vitamin D level as compared with milder symptoms which was statistically significant with a P value of (0.0001).

Similar results were obtained by **Elsakka et al. [15],** who stated that; vitamin D level has significant negative correlation with the severity of ALRTIS (P value 0.001).

Comparisons between disease severity and patients characteristics revealed that was statistically significant difference between mild and sever cases in age grouping and socioeconomic status, our study revealed that disease severity increased in older age (69.4%) of age group from 1 to 5 years were severe and (66.7%) of the age group from 5 to10 years were severe disease as expected, (100%) of poor socioeconomic status had severe disease while (42.1%) of moderate socioeconomic status had severe disease. (Table 6). Regarding sex, sun exposure and previous attack of ALRIS, they were not significantly related to the disease severity.

Similar results were obtained by **Elsakka et al [15],** who stated that; gender was not a risk factor for ALRTIS . But on the contrary, they reported that family social level was not a risk factor for the severity of ALRTIS and history of previous attacks of ALRTIS was significant risk factor for the severity of ALRTIS.

CONCLUSION

We can conclude that decreased vitamin D levels in children with ALRTIS might play an important role in disease and as a risk factor in severity, recurrence of ALRIS in Egyptian children. Health education about the importance for proper sun exposure and food rich in vitamin D. More trials should be done for vitamin D supplementation in ALRTIS patients which may improve prognosis of

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cases. Prophylactic use of vitamin D supplementation in patients with LRTIs.

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To Cite

Jaber, N., Sarhan, D., Abdo, A., elshal, A. Study of Vitamin D Level in Children with Lower Respiratory Tract Infections in Zagazig University Hospitals. *Zagazig University Medical Journal*, 2022; (401-410): -. doi: 10.21608/zumj.2019.9735.1059