Original Article

The Association of Subclinical Vitamin D Deficiency with Severe Acute Lower Respiratory Infection in Children under 5 Years in Duhok

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Abstract

Background: Vitamin D consumption can reduce susceptibility to respiratory tract infections in children. **Objective:** The aim of study was to measure the association of serum 25-hydroxyvitamin D3 with severe acute lower respiratory infections, controlling for demographic and other potential risk factors. **Materials and Methods:** A case–control study conducted from June 2017 to June 2018. Cases were <5 years of age in-patients with severe acute lower respiratory tract infections (LRTIs). Controls were healthy children <5 years old visiting the hospital. The child's demographic and other characteristics were studied. All participants had serum Vitamin D been measured. The cutoff of <10 nmol/l was considered deficiency, 10–30 nmol/l insufficiency, and >30 nmol/l normal. **Results:** The study included 50 cases and 50 controls. The mean serum Vitamin D level in the whole sample was 40 ± 6.7 ng/L (cases were 32.8 ± 27.38 ng/L and controls were 48.23 ± 59.1). The mean erythrocyte sedimentation rate of cases was 19.88 ± 12.8, the mean C-reactive protein 11.22 ± 8.03, the mean white blood cell 13.96 ± 5.13, and granulocyte 45.9%. The rate of Vitamin D deficiency was 14% whereas Vitamin D insufficiency is 48%. Weight-for-age was significantly related to vitamin level. Age of the patient, age of starting solid intake, sun exposure, and educational status of parents were significantly related to severe acute LRTIs. **Conclusions:** No significant association was found between severe acute respiratory tract infections and serum Vitamin D in the current study.

Keywords: Children, granulocyte, respiratory, sun exposure, Vitamin D

Introduction

Lower respiratory tract infections (LRTIs) are of the most important causes of morbidity and mortality in the children.[1] Worldwide, 20% of mortality among under-five is attributed to LRTI and with the inclusion of neonatal pneumonia, 35%–40% of under-five mortality account for 2.04 million deaths annually.[2,3] The predisposing factors for LRTI include young age (<1 year), premature delivery, low birth weight, underlying chronic diseases, malnutrition, failure of breastfeeding, and others.[1] Vitamin D deficiency and LRTI are both significant public health problems in developing countries. Vitamin D plays an important role in both cellular and humoral immunities as well as the pulmonary functions.[4,5] Vitamin D helps the progression of immune function.[6,7] Accordingly, there is an evidence that Vitamin D consumption is likely to reduce susceptibility to LRTI.[8,9] Recent studies support a connection with LRTIs such as pneumonia and bronchiolitis.[10,11] Low levels of serum Vitamin D are associated with a higher incidence of LRTIs and respiratory syncytial virus disease.[12-15] This is common even in countries with plentiful sunshine such as India and Pakistan.[16,17]

The aim of this study was to find out whether Vitamin D deficiency is a risk factor for severe acute lower respiratory infections, controlling for demographic and other potential risk factors.

Materials and Methods

A hospital-based case–control study was conducted in Heevi Paediatric Teaching Hospital in Duhok, Iraq, between June 2017

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and June 2018. Cases were children <5 years of age admitted as in-patients with severe acute LRTIs. A case definition of severe LRTI as given by the World Health Organization (1995) was used to define the cases: lower chest indrawing with respiratory rate >60 breath/min in infants <2 months, >50 breath/min in infants between 3 and 12 months, and >40 breath/min in children between 13 and 60 months. Controls were chosen from healthy children <5 years of age visiting the hospital with their parents during the study. Ethical approval was obtained from the ethical committee at the directorate of Health/Duhok. A structured questionnaire was used to obtain information from both cases and controls. Specimens of venous blood were aspirated from both cases and controls.

A commercial radioimmunoassay kit (I^{125} RIA Kit, Diasorin, UK) was used to measure 25-hydroxyvitamin D in serum to assess Vitamin D status. We chose the cutoff of <10 nmol/l as deficiency, 10–30 nmol/l as insufficiency, and >30 nmol/l as normal. In addition, blood aspirated from cases was tested for erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC) count, and granulocyte percentage. The cases were also sent for chest X-ray.

The statistical calculations were performed using Statistical Package for the Social Sciences version 21 (SPSS, IBM Company, United Kingdom). *T*-test and multiple logistic regression were used for comparison of results. $P < 0.05$ was considered statistically significant.

Results

The study included 50 cases and 50 controls. The mean age of cases was 2.04 ± 0.44 years, of controls was 2.78 ± 1.1 years. The mean serum Vitamin D level in the whole sample was 40 ± 6.7 ng/L (in cases 32.8± -27.38 ng/L vs. 48.23 ± 59.1 in controls) and the $P = 0.277$. The mean ESR of cases was 19.88 ± 12.8, the mean CRP was 11.22 ± 8.03, and the mean WBC was 13.96 ± 5.13 with granulocyte percentage of 45.9%. The rate of Vitamin D deficiency is 14%, while Vitamin D insufficiency is 48%. The relation between serum Vitamin D level and different characteristics of cases was studied in Table 1.

Most of the cases with very low level of Vitamin D had their weight-for-age below 5th centile, while most of those with low levels of Vitamin D had weight-for-age between 5th and 50th centiles with significant relation ($P = 0.006$). No significant association was found for the other variables.

As shown in Table 2, there was no significant relation between serum Vitamin D level and the imaging and laboratory tests.

The characteristics of cases and controls are shown in Table 3. Both the age of the participants and the age of starting solid food intake were significantly different.

The sociodemographic characteristics of cases and controls are shown in Table 4. The education status of both parents and the sun exposure was significantly associated with severe LRTIs.

Table 1: The relation of serum Vitamin D level to characteristics of all participants

Variable	<10 ng/l, *n* (%)	10-<30 ng/l, *n* (%)	= or >30 ng/l, *n* (%)	*P*
Age (years)				
<6 months	6 (20.7)	12 (41.4)	11 (37.9)	0.42
6 months-<1 year	2 (10)	9 (45)	9 (45)	
1-<3 years	6 (19.34)	15 (48.38)	10 (32.28)	
3-5 years	0 (0)	12 (60)	8 (40)	
Immunization				
Up to date	14 (14.14)	47 (47.67)	38 (38.19)	
Not up to date	0 (0)	1 (100)	0 (0)	
Breastfeeding duration				
<6 months	9 (16.7)	26 (51.85)	14 (31.45)	0.76
6 months-<1 year	3 (9.09)	16 (48.48)	14 (42.43)	
1-2 years	1 (25)	1 (25)	2 (50)	
No breastfeeding	1 (10)	4 (40)	5 (50)	
Starting solids				
4 months	4 (10.2)	21 (53.8)	14 (36)	0.3
6 months	3 (8.5)	16 (45.7)	14 (45.8)	
>6 months	0 (0)	1 (100)	0 (0)	
Not started	7 (18.4)	10 (26.3)	18 (55.3)	
Weight for age				
Below 5th centile	10 (33.3)	11 (36.6)	9 (30.1)	0.006
Between 5th and 50th centiles	2 (3.6)	30 (54.5)	23 (41.9)	
Above 50th centile	2 (13.3)	7 (46.6)	6 (40.1)	
Height or length for age				
Below 5th centile	8 (25)	12 (37.5)	12 (37.5)	0.143
Between 5th and 50th centiles	6 (11.7)	27 (52.9)	18 (35.4)	
Above 50th centile	0 (0)	9 (56.2)	8 (43.8)	

Table 2: The relation of imaging and laboratory tests to serum Vitamin D level in cases

	<10 ng/l, *n* (%)	10-<30 ng/l, *n* (%)	= or >30 ng/l, *n* (%)	*P*
Chest X-ray				
Bronchopneumonia	6 (39)	7 (40)	5 (27.7)	0.364
Bronchiolitis	2 (20)	3 (30)	5 (50)	
Lobar pneumonia	2 (25)	5 (62.5)	1 (12.5)	
Normal	2 (14.28)	5 (35.7)	7 (50.02)	
Mean ESR	18.4±7.9	17.57±12.8	24.13±14.7	0.49
Mean CRP	12.1±8.6	10.8±7.93	11.25±8.2	0.755
Mean WBC	11.9±6.02	13.51±4.53	15.9±4.97	0.322
Granulocyte percentage	47.55±15.55	43.02±18.11	49.16±16.63	0.44

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, WBC: White blood cell

Table 3: The characteristics of cases and controls

Characteristic	Cases, *n* (%)	Controls, *n* (%)	*P*
Age			
<6 months	19 (65.5)	10 (34.5)	0.006
6 months-<1 year	13 (65)	7 (35)	
1 <3 years	13 (41.9)	18 (58.1)	
3-5 years	4 (20)	16 (80)	
Immunization			
Up to date	49 (49.5)	50 (50.5)	0.305
Not up to date	1 (100)	0 (0)	
Breastfeeding duration			
<6 months	27 (50)	27 (50)	0.09
6 months-<1 year	12 (37.5)	20 (62.5)	
1-2 years	4 (100)	0 (0)	
No breastfeeding	7 (77.7)	3 (22.3)	
Starting solids			
4 months	12 (30.7)	27 (69.3)	0.001
6 months	16 (45.6)	19 (54.4)	
>6 months	0 (0)	1 (100)	
Not started	22 (88)	3 (12)	
Weight for age			
Below 5th centile	15 (50)	15 (50)	0.095
Between 5th and 50th centiles	23 (41.8)	32 (58.2)	
Above 50th centile	12 (80)	3 (20)	
Height for age			
Below 5th centile	14 (43.7)	18 (56.3)	0.349
Between 5th and 50th centiles	24 (47)	27 (53)	
Above 50th centile	12 (70.5)	5 (29.5)	

Discussion

It is proposed that the deficiency of Vitamin D is endemic and is present in about 1 billion people worldwide.[18] In childhood, both deficiency and insufficiency of Vitamin D are important health problems with variable prevalence in studies conducted in different countries.[19,20] In a Greek study, the rate of Vitamin D deficiency was 14%;[19] in an American study, deficiency rate was 14% and insufficiency 63%;[20] whereas in another study, deficiency rate was 12% and insufficiency rate was 40%.[21]

In this study, among all the participants, the rate of Vitamin D deficiency is 14%, while Vitamin D insufficiency is 48%, and results are comparable. Although the mean Vitamin D level in cases is lower than what was found in controls, this difference was not found significant in this study. Similar results were found in other studies. A Turkish study found no significant correlation between Vitamin D level and the severe LRTIs in children.[1] A Canadian study found no difference in vitamin D levels between the case and control groups though more children with severe lower respiratory tract infections were vitamin D deficient.[22] Similarly, An Australian study found that Children hospitalized with lower respiratory tract infections were less likely to have vitamin D insufficiency compared with children hospitalized for other conditions.[23] A Turkish study found that the association between lower respiratory tract infections and vitamin D did not prove a causal association.[24]

In contrast to the current and the aforementioned studies many studies point to a causal relationship and severe LRTI in children.[14,25-30] Despite the nonsignificant association of Vitamin D deficiency and severe LRTI in this study, which can be probably because of the small sample size still the Vitamin D level in patients is lower than in controls.

Serum Vitamin D level was significantly correlated to weight for age, which indicates that Vitamin D deficiency is a part of global nutritional deficiency that leads to poor weight gain. Similar results were found in other studies.[31,32] The sun exposure uncovered has been associated with a better Vitamin D level, and this is a fact that Vitamin D is synthesized in the skin from sun exposure. This is in agreement with other studies that proved a similar relationship.[27,31,33] Not starting solid intake has been found significantly associated with severe LRTI in this study. These solids are rich sources of Vitamin D and are proposed to have a protective role against severe LRTI. The same idea has been stressed by another study.[31] No significant relation was found between Vitamin D level and each of ESR, CRP, WBC count, and granulocyte percentage in accordance with a Turkish study that found a similar result.[1]

Conclusions

No significant correlation was found between severe acute respiratory tract infections and serum Vitamin D in the current study. Further studies with larger series should be achieved for definite results.

Table 4: Sociodemographic characters of cases and controls

	Cases, *n* (%)	Control, *n* (%)	*P*
Father's education			
Illiterate	8 (36.6)	14 (63.4)	0.002
Primary	17 (60.7)	11 (39.3)	
Secondary	22 (64.7)	12 (35.3)	
University	3 (18.75)	13 (81.25)	
Mother's education			
Illiterate	13 (34.2)	25 (65.8)	0.046
Primary	17 (65.3)	9 (34.7)	
Secondary	13 (61.6)	8 (38.4)	
University	7 (46.7)	8 (53.3)	
Smoking			
Yes	30 (49.1)	31 (50.9)	0.964
No	20 (51.3)	19 (48.7)	
Family history of LRTIs			
Yes	9 (69.2)	4 (30.8)	0.332
No	41 (47.1)	46 (52.9)	
Heating source			
Electrical	4 (66.7)	2 (33.3)	0.875
Kerosene	5 (55.5)	4 (44.5)	
Both	41 (48.2)	44 (51.8)	
Sun exposure			
Uncovered	22 (34.9)	41 (65.1)	0.001
With clothes	3 (42.8)	4 (57.2)	
With swaddle	4 (66.7)	2 (33.3)	
No	21 (87.5)	3 (12.5)	

LRTIs: Lower respiratory tract infections

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Conflicts of interest

There are no conflicts of interest.

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