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Original Article

The Relationship Between Serum Vitamin D Level and Severity of Bronchiolitis in Infants Being Referred to in Bandar Abbas Children's Hospital, Iran

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Abstract

Background: The present study aimed to investigate the relationship between the serum vitamin D level and the severity of bronchiolitis in infants.

Materials and Methods: The population of this descriptive-analytical study included all infants within the age range of 1 month to 24 months old with bronchiolitis hospitalized in Bandar Abbas children's hospital in 2018-2019. According to the exclusion and inclusion criteria, patients were entered in the study and diagnosed with bronchiolitis by a pediatric infectious disease specialist. Then, their serum levels of vitamin D were measured as well.

Results: Of the 85 patients, 62.4% and 37.6% were males and females, respectively. The mean serum level of vitamin D was 29.74 ± 13.44 ng/mL. In addition, the mean age in groups with mild-, moderate-, and severe-intensity was 9.27 ± 4.52 months, 5.12 ± 3.95 months, and 3.16 ± 1.16 months ($P < 0.001$), respectively. Further, the Spearman's correlation between age and serum vitamin D levels was r = 0.05 ($P < 0.001$). Based on the results, there was a statistically significant difference between the mean age in the two study groups ($P < 0.001$). Finally, a statistically significant association was found between the severity of bronchiolitis and vitamin D status ($P = 0.007$).

Conclusion: According to the results of the present study, more than half of the infants admitted to the diagnosis of bronchiolitis had insufficient serum levels of vitamin D. There was also a significant association between the severity of bronchiolitis and serum vitamin D levels.

Keywords: Bronchiolitis, Vitamin D, Infants

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Introduction

Acute lower respiratory tract infection, primary pneumonia, and bronchiolitis are the most important causes of mortality and morbidity in children under 5 years of age in developing countries (1). In addition, bronchiolitis is the most common lower respiratory tract infection of viral origin in infants (2). It causes the inflammatory obstruction of small airways (3) and is common in children under two years of age, especially in 2 to 8 months of age (4). The symptoms of bronchiolitis include cough, rhinorrhea, crackles, wheezing, fever, and hypoxemia (5). Further, the causes of this infection are respiratory syncytial virus (RSV), rhinovirus, adenovirus, coronavirus, influenza, and parainfluenza (6, 7). In more than 50% of cases, RSV is the cause of viral bronchiolitis and pneumonia in infants and young children (8-10), and almost all children have the serological evidence of the RSV infection at the age of 2 (11, 12). Most children infected with RSV experience mild illness that requires no hospitalization. However, RSV-induced bronchiolitis is the major cause of hospitalization in infants less than one year of age in the United States (13, 14) and is considered as a major risk factor for asthma in the future (15).

Serum vitamin D levels can affect the incidence and severity of bronchiolitis, especially RSV bronchiolitis because vitamin D also has a non-skeletal activity that may directly or indirectly affect the severity of bronchiolitis (16-18). In addition, vitamin D deficiency at birth, which is defined as vitamin D levels less than 20 ng/mL in the umbilical cord blood, has been reported as a risk factor for lower respiratory tract infection with RSV during the first year of life (19). Although vitamin D status may alter the overall risk of bronchiolitis, there are limited data regarding the effect of vitamin D status on the severity of the acute episode of bronchiolitis (20). This is especially important for children with bronchiolitis who

need to be hospitalized because they have a higher risk of future disability and asthma (21). Therefore, the present study aimed to evaluate the relationship between vitamin D levels in the blood and the severity of bronchiolitis in infants.

Materials and Methods

The present study was a descriptive-analytical study, and the study population included all infants with bronchiolitis hospitalized in Bandar Abbas children's hospital in 2018-2019. The inclusion criteria included Infants in the age range of 1 month to 24 months with the diagnosis of bronchiolitis required hospitalization. On the other hand, patients with a history of wheezing before the disease, history of asthma, immunodeficiency, congenital heart and lung disorders, cystic fibrosis in the patient or first-degree relatives of the patient, history of the regular use of anti-reflux drugs, bronchodilators or anti-inflammatory drugs, prematurity (gestational age less than 37 weeks), and dissatisfaction for participation were excluded from the study. The samples were collected for 1 year after obtaining the ethical code from the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1398.063). Accordingly, 85 infants entered the study, and sampling was done in an accessible and targeted manner. Moreover, the diagnosis of bronchiolitis and the need for hospitalization were performed by a pediatric infectious disease specialist based on history, clinical findings (i.e., wheezing, respiratory distress, and decreased arterial oxygen), and paraclinical procedures.

All infants participating in the study were given 3 mL of blood samples required to measure the serum levels of 25 hydroxyvitamin D by the nurse in the infectious disease ward, and the samples were sent according to the instructions provided by the reference laboratory and partner in the research project. Then, the patients were divided into two groups based on serum vitamin D levels with insufficient serum levels (less than 30 ng/mL) and normal levels (≥30 ng/mL) according to 22. To determine the severity of bronchiolitis, patients were rated according to Table 1 and classified into three groups with mild (less than 7), moderate (8 to 14 points), and severe (15 to 21 points) intensity. This scoring system consists of 7 factors, each of which obtains 1 point to 3 points (23). The severity of bronchiolitis was measured by the assistant specialist of the pediatric center, and finally, the information was recorded in a researcher-made checklist.

Statistical Procedures

The data were analyzed using the SPSS package (version 22.0) and descriptive tests such as frequency, percentage, mean, and standard deviation. Moreover, Mann-Whitney U-test, Fisher's exact test, Kruskal-Wallis, Spearman's correlation coefficient, logistic regression, and odds ratio (OR) were run to analyze the data. The level of significance was set at $P \leq 0.05$.

Results

Of the total studied population, 53 (62.4%) and 32 (37.6%) cases were male and female infants, respectively. The mean age of the total study population was 6.05 ± 4.41 months, and this mean was 5.94 ± 3.98 and 6.25 ± 5.23 in male and female populations, respectively ($P = 0.650$). In addition, 22 (25.9%), 57 (67.05%), and 6 (7.05%) infants were in the group with mild-, moderate-, and severe-intensity bronchiolitis, respectively. Further, 46 (54.1%) infants had insufficient vitamin D levels while 39 (45.9%) cases had normal vitamin D levels. Based on the results (Table 2), no significant statistical association was found between gender and bronchiolitis severity ($P = 0.463$). On the other hand, a statistically significant difference was reported (Table 3) between the mean age in the group with mild, moderate, and severe bronchiolitis ($P < 0.001$). In other words, the mean age differences between mild and moderate ($P = 0.002$), mild and severe ($P < 0.001$), and severe and moderate groups (0.030) were significant. The results (Table 3) also revealed a statistically significant difference between the mean age in the group with insufficient and normal vitamin D levels ($P < 0.001$).

The association of the severity of bronchiolitis with vitamin D status (levels <30 and ≥30 ng/mL) was measured using the Fisher's test and the results (Table 4)

Table 1. Standard Bronchiolitis Severity Score

Items		Score 1	Score 2	Score 3
Respiratory rate	1-2 month(s)	60 ≤	61-69	≥70
	2 months -1 year>	50 ≤	51-59	≥60
	1 year>	40 ≤	41-44	≥4
Cyanosis		Normal	Peripheral	Central
SpO2		94-100%	90-93%	89% ≤
Sensorium		Mild irritable but easy to console	Difficult to console	Lethargy/ drowsy
Nasal flare/retraction (SC, IC, and SCS) Max: 4		1	2	3 or 4
Feeding		Normal	≥50%	<50%
Air entry/wheeze		Normal, scattered rhonchi/crepitation, end expiratory	Fair, rhonchi/rales in both inspiration and expiration	Poor, grunt, rhonchi, and crepitation

Note. SpO2: oxygen level or saturation; SC: *subcostal*; IC: *intercostal*; SCS: suprasternal and supraclavicular.

Table 2. The Relationship Between Gender and Severity of Bronchiolitis

Gender	Severity of Bronchiolitis						*P* Value
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
Male	16	30.2	33	62.3	4	7.5	0.463
Female	6	18.8	24	75	2	6.2	

Table 3. Comparison of Mean Age Based on Bronchiolitis Severity and Vitamin D Status

Variable	Sub-group	Age (months)		*P* value
		Mean	Standard Deviation	
Severity of bronchiolitis	Mild	9.27	4.52	<0.001
	Moderate	3.95	5.12	
	Severe	1.16	3.16	
Vitamin D status	<30 ng/mL	4.17	3.15	<0.001
	≥30 ng/mL	8.28	4.69	

Table 4. The Relationship Between Vitamin D Status and Severity of Bronchiolitis

Vitamin D Status	Severity of Bronchiolitis						*P* Value
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<30 ng/mL	7	31.8	33	57.9	6	100	0.007
≥30 ng/mL	15	68.2	24	42.1	0	0	

demonstrated a significant association ($P=0.007$).

According to the logistic regression test, the chance of vitamin D sufficiency (≥30 ng/mL) in the moderate bronchiolitis group was 0.339 (OR = 0.339, $P=0.042$) compared to the mild-intensity group while that of the severe bronchiolitis group was zero compared to the mild bronchiolitis group.

Discussion

Numerous studies have shown that infants with low levels of 25 hydroxy (OH)-vitamin D taken from the umbilical cord blood are at a higher risk for acute nasopharyngitis (24), lower respiratory tract infections (25-27), and RSV bronchiolitis (19). Additionally, evidence represents the role of the effects of calcium and vitamin D homeostasis on innate and acquired immunity thus vitamin D deficiency is associated with an increased risk of acute respiratory infections in both children and adults. Some immune system cells such as dendritic cells and macrophages have vitamin D receptors, which stimulate the production of human cathelicidin protein-18. This increases the capacity of phagocytes and activates anaphylactoid factors for the migration of neutrophils and monocytes to the site of the infection (28).

In the present study, the ratio of male to female was 1.65 and the mean age was about 6 months. In a study by Beigelman et al (29), the mean age was 4.3 months and 61% of cases were male patients. In the present study, 25.9%, 67.05%, and 7.05% had mild, moderate, and severe bronchiolitis, respectively. In addition, 54.1% had vitamin D levels less than 30 ng/mL. In another study by Fairchok et al (22), 66% of vitamin D was less than 30 ng/mL. In the current study, the mean serum level of vitamin D among the study population was 29.74 ng/mL. Similarly, Beigelman et al (29) reported that the average amount of the level of serum 25 OH-vitamin D was 36.8 ng/mL. In the present study, a statistically significant relationship was found between the severity of bronchiolitis and age so that the lowest mean age was related to the severe bronchiolitis group while the highest mean belonged to the group with mild bronchiolitis. Accordingly, age is inversely related to the severity of bronchiolitis and more severe bronchiolitis occurs at younger ages.

In the present study, the serum levels of vitamin D in the study population was increased by increasing the age average. In the above-mentioned study, the group of children with vitamin D deficiency was younger compared to participants who had more vitamin D, and the average amount of vitamin D deficiency was equal to 20 ng/mL. This association was also found in the present study, which may be due to vitamin D deficiency in breast milk. According to the report by Fairchok et al (22), infants with insufficient vitamin D develop more severe viral respiratory disease. Breastfeeding is linked to vitamin D deficiency, and the use of vitamin D supplementation during pregnancy can reduce the risk and severity of respiratory disorders in infants. In the present study, the chances of vitamin D adequacy (≥30 ng/mL) in the moderate bronchiolitis group were significantly lower compared to the mild bronchiolitis group, and those of the group with severe bronchiolitis were zero compared to the mild bronchiolitis group. Clinical findings have shown an increase in viral respiratory infections in infants and children with insufficient levels of 25 OH-vitamin D (24-27). The results of a prospective study of 28 Japanese children hospitalized with a lower respiratory tract infection demonstrated a significant association between vitamin D deficiency with excess oxygen and ventilation with the ventilator (30). In addition, Garg et al (1) reported that subclinical vitamin D deficiency is an important risk factor for the acute lower respiratory tract infection in children under 5 years of age. However, Beigelman et al (29) concluded that vitamin D deficiency is uncommon in children hospitalized with bronchiolitis RSV.

It is recommended that more detailed studies be performed prospectively including higher sample sizes to investigate the effects of vitamin D deficiency on the severity of bronchiolitis in infants. It is best to do studies with a stronger methodology such as a case-control method in order to measure the serum levels of vitamin D in healthy, asymptomatic children compared with the study group. It is also suggested that future studies consider the nutritional status of the infant (breastfeeding and the like). Therefore, the most important limitations

of the present study were the low sample size, the lack of a control group, and the lack of the study of infant nutrition.

Conclusion

According to the results of the present study, more than half of the infants admitted to the diagnosis of bronchiolitis had insufficient serum levels of vitamin D. There was also a significant association between the severity of bronchiolitis and serum vitamin D levels. Therefore, the level of vitamin D should be regularly checked in infants, and supplements be prescribed if needed.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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Ethical Statement

The study was approved by the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1398.063). Patients' information was kept confidential throughout the research procedure.

Authors' Contribution

All authors contributed to the proposal and design of the study, the acquisition of the data, as well as data analysis and interpretation. Furthermore, they cooperated on drafting the article and revising it critically for important intellectual content, along with approving the final version of the study for submission.

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Informed Consent

The present study was conducted after obtaining informed consent from all participants.

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