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Original Article

Is there a predictive association between vitamin D concentrations and lower respiratory tract infections in infants?

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Abstract

Aim: Vitamin D deficiency have been estimated to be endemic in the worldwide and in each age group and also it is reported that vitamin D has important effects on both natural and acquired immunity and there may be a relationship between deficiency and predisposition to infections The aim of this study is to investigate whether serum vitamin D level are effective in infant lower respiratory tract infection which is one of the most mortal infectious diseases in worldwide.

Material and Methods: In our study, between October 2016 and January 2018 in Department of Pediatrics, the data of 418 infants with LRTI and their ages ranging from 5 to 24 months and were examined retrospectively. Vitamin D levels were studied in 106 of this patients.

Results: In group-1, the mean duration of vitamin D supplementation was 4.9 months, while the mean in group-2 was 8.6 months. Breastfeeding time was 3.27 months in group 1 while it was 5.71 months in group 2. Both the duration of breastfeeding and the duration of vitamin D supplementation were shorter in group 1 than in group 2.Those difference between the groups was in terms of statistically significant ($p< 0.05$)

Conclusion: Vitamin D deficiency in infants may be associated with LRTI, and even vitamin D deficiency may be a predisposing factor for severe LRTIs and also the frequency and severity of LRTIs can be reduced with optimal serum levels of vitamin D.

Keywords: Infant; LRTI; Vitamin D.

INTRODUCTION

Lower respiratory tract infections (LRTI: bronchiolitis and pneumonia) are among the most important causes of morbidity and mortality in childhood (1-5). Approximately two million children under five years of age die each year from LRTI. Studies have shown that LRTI is the cause of a high rate like 15-40% of all child deaths (1,3-5). According to data from the United States, LRTI is the still leading cause of death by caused of infections in all age groups.In the same data, it was reported that among the 10 million patients who were admitted to the hospital annually in the US, to 2.3 million of them were diagnosed pneumonia, 500 thousand of them were hospitalized and 45 thousand of them lost their lives (5).

Because of difficult that to differentiate pneumonia from acute bronchiolitis in infants, the definition of 'acute lower respiratory tract infection' including these two diseases is also used.In children hospitalized due to lower respiratory tract infections, frequency of LRTI is between 29 to 38% in all pediatric age groups, while this rate is between 33 to 50% in infants (3,4,6). According to the 2003 data of the Ministry of Health in Turkey, LRTIs are responsible for 48.4% of the causes of infant deaths in the 0 to 1 age group and 42.1% of the causes of toddler deaths in the 1 to 4 year age group. The source of LTRI agents can be direct human

The source of LTRI agents can be direct via human or pets such as bird, cat and the main transmission route is droplet infection, it is often encountered in winter and spring months.Pneumonia and its prognosis are not considered to be a homogeneous disease what as associate of clearly of cause - disease - clinical features, due to as there are many factors affecting the clinical signs and prognosis of pneumonia (1-3).

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Can vitamin D deficiency be one of these factors? In fact, vitamin D deficiency have been estimated to be endemic in the worldwide and in each age group and also it is reported that vitamin D has important effects on both natural and acquired immunity and there may be a relationship between deficiency and predisposition to infections (4-6). Inaddition the discovery of vitamin D receptors in all immune system components and especially may be affect the maturation-differentiation-migration stages of antigen presenting cells supports the idea that this vitamin is an important immunomodulator (1-4,7-9). Because of, stages of growth and development are very quickly in infancy period, breastfeeding time and duration of vitamin D supplementation should be two years. Whereas, breastfeeding time and vitamin D supplementation duration of the patients both in study and control group had lower than normally. For this reason, vitamin D levels of these patients who had not yet rickets clinic have been evaluate in terms of early diagnosis of rickets , in routine child health visit.

The aim of this study is to investigate whether serum vitamin D level are effective in infant lower respiratory tract infection which is one of the most mortal infectious diseases in worldwide.

MATERIAL and METHODS

In our study, between October 2016 and January 2018 in Faculty of Medicine, Department of Pediatrics, and data of 418 infants whose ages ranging from 5 to 24 months and with LRTI were examined retrospectively. Vitamin D levels were studied in 106 of this patients.

Demographic data, hospitalization season, vitamin D serum levels, serum C-reactive protein (CRP), leukocyte (WBC) levels, hospitalization time and intensive care support requirements of these patients were recorded.

Patients who vitamin D deficiency detected were evaluated in terms of that simultaneous ca, p, alp, pth serum levels. These laboratory findings were supported vitamin D deficiency and no detected rickets and hypoparathyroidism.

Vitamin D supplementation were not given in the hospitalization time.

The study group consisted of 106 patients who had serum vitamin D levels and they were treated for LRTI (Group 1).

The control group are designed with 65 patients in the same age group who were randomly selected and they had no acute or chronic disease and their serum vitamin D levels were studied (Group 2).

Vitamin D level were considered as normal above 20 ng / mL,as mild deficient between 10-20 ng/mL and as severe deficient below 10 ng/mL.

Patients who with any the causes of frequent lower respiratory (i.e immun defificiency, cystic fibrosis), chronic systemic disease or immunodeficiency other than LRTI, aged younger than 5 months and above 24 months, received vitamin D supplementation in the last 3 months were excluded from the study.

Groups were between compared patients of age, gender, hospitalization season, vitamin D levels.

In addition, the duration of hospitalization of patients who had vitamin D levels above 20 ng / mL, between 10-20 ng / mL and below 10 ng / mL, were compared.

Ethics approval

The study was carried out with the approval of Mustafa Kemal University Medical Faculty Ethics Committee, dated 08/02/2018 and numbered 04.

Statistical analysis

Data were analyzed using SPSS for Windows 18.0 version (SPSS Inc., Chicago, IL, USA). The differences between the groups were examined by student's t test. Categorical variables were evaluated by Chisquaretest. P <0.05 was considered significant.

RESULTS

The mean age of the group-1 patients was 11.4 months. 46.23% (n: 49) were female and 53.77% (n: 57) were male.

The mean age of the group-2 patients was 13.1 months. 44.61% (n: 29) were female and 55.39% (n: 36) were male.

No statistically significant difference was found between the groups in terms of demographic data (p>0.05) (Table 1).

Admissions season to hospital, in group 1; 43.39% (n: 46) in winter, 22.64% (n: 24) in autumn, 20.75% (n: 22) in spring, 13.20% (n: 14) in summer and in group-2, 44.61% (n: 29) in winter, 23.07% (n: 15) in autumn, 18.46% (n: 12) in spring, 13.84% (n:9) in summer. Coexisting vitamin D deficiency and LRTI most commonly seen in winter. This data was found statistically significant (p< 0.05) (Table 1).

The mean D-vitamin levels of the patients in Group-1 were 10.56 ng / mL and the patients in group-2 were 24.87 ng / mL.Statistically significant difference was found between the groups in terms of Serum vitamin D levels (p <0.05) (Table 1).

In group 1, the mean duration of hospitalization of patients who with vitamin D levels above 20 ng/mL was 4.1 days, between 10-20 ng/mL was 5.9 days, while those with vitamin D levels below 10 ng/mL were 8.3 days. Statistically significant difference was found between the vitamin D deficiency and severe deficiency groups(p <0.05) and alsostatistically significant difference was found between vitamin D level normal and severe deficiency groups (p <0.05). Despite the duration of hospitalization of patients who with vitamin D levels between 10-20 ng/mL was longer than above 20 ng/mL but this findings were no statistically significant(p>0.05).

As remarkable, vitamin D levels of patients (all patients of 5%, n:3) who was required intensive care treatment were below 10 ng/mL.

In group-1, the mean duration of vitamin D supplementation was 4.9 months, while the mean in group-2 was 8.6 months.Breastfeeding time was 3.27 months in group 1 while it was 5.71 months in group 2.

Both the duration of breastfeeding and the duration of vitamin D supplementation were shorter in group 1 than in group 2. Those difference between the groups was in terms of statistically significant (p< 0.05) (Table 1).

Table 1. Features of patients

	Group 1 n (%)	Group 2 n (%)	p
Number of patients	106	65	
Gender			
Male	57 (53.77)	36 (55.39)	>0.05
Female	49 (46.3)	29 (44.61)	>0.05
Mean age(months)	11.4	13.1	>0.05
Admission season			
Autumn	24 (22.64)	15 (23.07)	>0.05
Winter	46 (43.39)	29 (44.61)	>0.05
Spring	22 (20.75)	12 (18.46)	>0.05
Summer	14 (13.20)	9 (13.84)	>0.05
Mean D vitamin Levels(ng/mL)	10.56	24.87	0.028
D vitamin level			
Normal	24 (22.64)	34 (52.31)	0.032
Mild deficiency	57 (53.77)	28 (43.08)	>0.05
Severe deficiency	25 (23.58)	3 (4.61)	0.01
Vitamin D supplementation			
In lactation (month)	4.9	8.6	0.042
Breastfeeding time (month)	3.27	5.71	0.048

DISCUSSION

In the pediatric age group, one fourth of the outpatients and one third of the inpatients are diagnosed with LRTI. LRTI is the firstly between causes of leading to child mortality under 5 years of age where in undeveloped and developing countries due to by the effect malnutrition (3,4,6, 8). According to WHO data, respiratory infections are responsible 28% of the deaths of children who die due to preventable and treatable reasons every year in worldwide (4, 5, 8-11). Because of there are no specific symptoms, physical examination and laboratory findings of lower respiratory tract infections, that it may be especially difficult to diagnose infants.In infants, fever, irritability, cough, respiratory distress and family history, as well as, their of feeding and their relation with environment should be evaluated (4-6,10). Sometimes, fever may be the only symptom of LRTI in the infant period but tachypnea is the more common symptom and finding. As a matter of fact, sometimes tachypnea may be the only finding without fever.In addition to tachypnea, detection of that vocal fremitus, mathite, decline of respiratory sounds, bronchial respiration sounds and crepitatedrales are the findings of physical examination supporting LRTIs (4,6,9,11,12). However, most common symptom in patients with mild deficiency was fever while the most common symptom in patients with severe deficiency was tachypnea. It may be the cause of confused diagnosis of infectious diseases such as LRTI in infants with severe deficiency who had especially tachypneawithout fever. Therefore, we think that, it might be beneficial detect of the level of vitamin D in routine laboratory tests in diagnosis of these patients.

Vitamin D deficiency was found to be between 12-32% and 40-82% especially in undeveloped and developing countries. In addition, it was reported that the incidence of LRTI was higher in these countries due to low socioeconomic status and nutritional deficiency (2,3,6,7,9-12). Remarkably, the incidence of LRTI increases in the winter months when the incidence of vitamin D deficiency increases due to sun rays reach to skin less and the natural nutrients can't support the daily vitamin D requirement (3,8,9,2,13).

In the literature suggest that breastfeeding should be continued until two years. However, since D vitamin not enough in human milk, D vitamin supplementation should be given in infant period average one years. Otherwise D vitamin deficiency might becommonly seen (7,12).

In a study which examining the relation between vitamin D level and LRTI were compared vitamin D levels between the LRTI and healthy infants. In this study reported that, vitamin D levels were lower in infants with LRTI than healthy infants and vitamin D deficiency is found associated with LRTI in early childhood. In the literature, There are also studies reporting that, vitamin D deficiency adversely affects both severity and incidenceof LRTI and also increases the intensive care and oxygen therapy requirements in this patients (2,3,6,10,13-15).

There are few studies on the relationship between vitamin D deficiency and LRTI, especially involving infants.Studies have shown that vitamin D deficiency was increased the severity and frequency and also number of admission the emergency units in children with asthma (3,8,13,15,16). Our study is one of the few studies conducted infants with LRTI. D vitamin deficiency increase number of episodes, severity of asthma in the disease and admission to emergency unit. Because of there are no cases with asthma in this study, it was no considered relationship between asthma and vitamin D deficiency. This data suggests that vitamin D deficiency increases the severity and frequency of LRTI.

The relationship between immune system and vitamin D are among the most investigated subjects.The immune system-related effects of vitamin D are found linked regulation of cell proliferation and differentiation (2,12, 15,17-20). There are different theories about the roles of vitamin D in body defense mechanisms. Some of these theories include that protect the respiratory tract from invasion of microorganisms, activating hydrogen peroxide

secretion from monocyte cells and increasing the potential for oxidative bursting and increase immune cells to fight against infections. It is also reported in the literature that it has immunomodulatory functions (10,15,17,19,20). In animal models and in vitro studies Show that vitamin D increases the production of Interleukin 4 (IL-4), Interleukin 5 (IL-5) and Interleukin-10 (IL-10) from proinflammatory T helper cells (Th1 and Th17 responses), and in this way it has been shown to support the functions of Th2 and regulator T cells (4,6,11-17).

Some studies showed that vitamin D increases the antibacterial function of bronchial epithelial cells and therefore it is possible to use this vitamin by inhalation to patients with cystic fibrosis who be required frequent antibiotic use and frequent hospitalization (8,14,16,18).

Reported in some studies that, invasive pneumococcal-meningococcal infections more commonly seen patients with vitamin D deficiency although rickets not seen (2,14, 8,19). These data suggest that vitamin D deficiency may be the cause of recurrent-resistant respiratory tract infections in immature infants (2-5,10,14,17).

It was limitations in this study that, there are no long-term follow-up of patients with vitamin D deficiency.

Remarkably, Vitamin D deficiency is seen as an important health problem which causes susceptibility to infections especially in childhood.

CONCLUSION

This study suggests that vitamin D deficiency in infants may be associated with LRTI, and even vitamin D deficiency may be a predisposing factor for severe LRTIs and also the frequency and severity of LRTIs can be reduced with optimal serum levels of vitamin D.We think that, the supplementation of vitamin D there should be in the treatment protocols of LRTI in infants who had vitamin D deficiency and LRTI, especially in winter months. Nevertheless, it is recommended that there are require studies with larger series and longer follow-up for accurate results.

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