



The Association Between Lower Respiratory Tract Infections and Vitamin D-Zinc Levels in Children Aged Six Months to Five Years Old

Altı Ay ile Beş Yaş Arasındaki Çocuklarda Alt Solunum Yolu Enfeksiyonları ile D Vitamini ve Çinko Düzeyleri Arasındaki İlişki

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Abstract

Objective: We performed this study to investigate serum vitamin D and zinc levels in lower respiratory tract infections in children aged six months to five years old.

Material and Methods: In this retrospective study, 223 children admitted to the Department of Pediatrics at Kastamonu Training and Research Hospital between November 1, 2021, and March 1, 2022, were included. The study group consisted of 111 children with lower respiratory tract infections. The control group consisted of 112 children who were healthy and had not been diagnosed with lower respiratory tract infections in the last one month. Vitamin D and zinc levels of the patient and control groups were compared in the study. Additionally, the data of inpatients and outpatients, and those with or without the need for intensive care were compared in the patient group.

Results: Serum vitamin D ($p=0.03$) and zinc levels ($p=0.01$) were significantly lower in the study group than in the control group. Vitamin D ($p=0.04$) and zinc levels ($p=0.01$) were significantly lower in the inpatients than the outpatients, and in those with the need for intensive care compared to those without the need for intensive care. As the vitamin D levels of inpatient children decreased, the length of hospitalization was significantly prolonged ($p=0.01$).

Conclusion: A decrease in serum vitamin D and zinc levels leads to an increase in the risk of lower respiratory tract infections and the severity of the disease in children aged six months to five years.

Keywords: Lower respiratory tract infections, vitamin D, zinc

Öz

Giriş: Altı ay ile beş yaş arasındaki çocuklarda alt solunum yolu enfeksiyonlarında serum D vitamini ve çinko düzeylerini araştırmak.

Gereç ve Yöntemler: Retrospektif olarak planlanan bu çalışmaya 1 Kasım 2021 ile 1 Mart 2022 arasında Kastamonu Eğitim ve Araştırma Hastanesi Pediatri polikliniğine başvurmuş altı ay ile beş yaş arasındaki 223 çocuk dahil edildi. Alt solunum yolu enfeksiyonu tanısı almış 112 çocuk çalışma grubunu, sağlıklı ve son bir ay içerisinde alt solunum yolu enfeksiyonu geçirmemiş 111 çocuk kontrol grubunu oluşturdu. Hasta ve kontrol grubunun, hastaneye yatarak tedavi gören ve ayakta tedavi görenlerin, yoğun bakım ihtiyacı olanlar ve olmayanların D vitamini ve çinko düzeyleri karşılaştırıldı.

Bulgular: Çalışma grubundaki çocukların serum D vitamini ($p=0.03$) ve çinko düzeyleri ($p=0.01$), kontrol grubundaki çocuklardan anlamlı şekilde daha düşük bulundu. Hastaneye yatarak tedavi görenlerin D vitamini ($p=0.04$) ve çinko düzeyleri ($p=0.01$) ayakta tedavi görenlere göre anlamlı şekilde daha düşüktü ve yoğun bakım ihtiyacı olanların olmayanlara göre D vitamini ve çinko düzeyleri anlamlı şekilde daha düşük saptandı. Hastaneye yatan çocukların D vitamini düzeyleri düştükçe yatış süreleri anlamlı şekilde uzamaktaydı ($p=0.01$).

Sonuç: Altı ay ile beş yaş arasındaki çocuklarda serum D vitamini ve çinko düzeyleri düştükçe alt solunum yolu enfeksiyonu görülme riski ve hastalık şiddetinde artış bulunmaktadır.

Anahtar Kelimeler: Alt solunum yolu enfeksiyonları, D vitamini, çinko

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Introduction

Lower respiratory tract infection (LRTI), which is the inflammation of the lower respiratory tract caused by microorganisms, is one of the major causes of death in children aged less than five years worldwide. About 15 years ago, the number of children deaths due to LRTI was about two million for each year. Thanks to the developments in prevention and treatment methods, this number has decreased to around 81 thousand (1). There are many factors that cause LRTI in children. Prematurity or low birth weight; age younger than one year; chronic diseases; crowded environments (smoking exposure, etc.), nutritional disorders (zinc deficiency, etc.) and vitamin D deficiency are the most ones (2).

Many factors such as age, gender, ethnicity, season, exposure to sunlight, socioeconomic level, diet and prophylactic use of vitamin D have significant effects on vitamin D levels (3). The level of vitamin D affects the humoral and cellular immunity and lung functions. It is possible to produce active vitamin D with epithelial cells of the lower respiratory tract. Accordingly, the toll-like receptor stimulates alveolar macrophages and the active form of vitamin D is produced. With active vitamin D, an increase in cathelicidin (an antimicrobial peptide) occurs. Decrease in proinflammatory cytokines (IL-6, IL-8, IL-12, IL-17, IFN- γ and TNF- α), increase in anti-inflammatory cytokines (IL-4, IL-5, IL-10), natural killers (NK) increase in the cytotoxic activity of cells and inhibition of the activity of lung dendritic cells are the other major functions of vitamin D (4,5).

Zinc, an essential trace element with a direct antiviral effect, is very important for the normal development and functioning of innate immunity elements such as NK cells and neutrophils. It also has a direct effect on the production of IFN- γ (6). Low body stores and poor intestinal absorption in children cause them to be more susceptible to zinc deficiency. In our study, the association between LRTI and vitamin D- zinc levels in children aged six months to five years was investigated.

Materials and Methods

Our retrospective study included 223 children aged six months to five years between November 1, 2021 and March 1, 2022. A hundred and eleven children diagnosed with LRTI were the study group. The control group included 112 healthy children who had not been diagnosed with LRTI in the last one month. Rickets and bronchial asthma; liver or kidney diseases; immunosuppressant drug therapy; vitamin D treatment (excluding prophylaxis taken between 0-1 years of age) and not checking vitamin D and zinc levels in examinations were determined as exclusion criteria.

Demographic data (age, gender) of the patients, inpatients, length of hospitalization and data on laboratory tests were obtained through the hospital information system. Vitamin D and zinc levels of the patients were examined and recorded at the time of admission to the hospital. The level of vitamin D > 30 ng/mL was considered to be normal. The level of 20-30 ng/mL was considered to be insufficiency and <20 ng/mL was considered to be vitamin D deficiency (7). The normal range of zinc level was accepted as 60-135 mg/dL (8).

Vitamin D and zinc levels of the study and control groups were compared in our study. In addition, the study group were divided into two groups as outpatients and inpatients. Inpatients were also divided into two groups as those with or without the need of intensive care (IC).

Statistical Analysis

Frequency, percentage, mean and standard deviation values were used for presenting descriptive statistics. Normal distribution was checked with the Kolmogorov-Smirnov test. Age, length of hospital stay, levels of vitamin D and zinc in the patient groups were analyzed by the independent sample t-test. The correlations between the proportional values according to the groups were examined by chi-square analysis. $p < 0.05$ was considered statistically significant and SPSS 25.0 program was used for analysis. G*Power Version 3.1.7. was used to determine the power level and effect size of the study. The study had a power of over 95% and an effect size of 0.46.

Results

In our study, we concluded that there was no significant difference between the study and control groups in terms of demographic data (age and gender) ($p = 0.83$) (Table 1). We found a significant difference between the groups in terms of vitamin D levels ($p = 0.03$). Accordingly, the rate of those with vitamin D deficiency was higher in the study group than the control group. The rate of those with vitamin D insufficiency and those with normal vitamin D levels was higher in the control group than the study group (Table 1).

We determined a significant difference in serum zinc levels between the study and control groups ($p = 0.01$). The mean serum zinc levels of the study and control groups were 86.18 ± 12.39 and 98.41 ± 13.45 respectively. The mean serum zinc level of the study group was significantly lower than the control group (Table 1).

We found that there was a significant difference in vitamin D ($p = 0.04$) and serum zinc levels ($p = 0.01$) between inpatient and outpatient children in the study group. Vitamin D and zinc levels were significantly lower in inpatient children compared to outpatients.

Table 1. Comparison of the study and control groups

	Study group (n= 111)	Control group (n= 112)	p
Gender (n, %)			
Male	59 (53.2)	60 (53.6)	0.83
Female	52 (46.8)	52 (46.4)	
Mean age (months)	22.7 ± 13.49	22.6 ± 13.46	0.95
Vitamin D level (n, %)			
Deficiency	44 (39.7)	4 (3.6)	0.03*
Insufficiency	32 (28.8)	47 (42.0)	
Normal	35 (31.5)	61 (54.4)	
Zinc level (µg/dL)	86.18 ± 12.39	98.41 ± 13.45	0.01**

*Pearson's Chi-square test, ** Independent sample t-test.

Table 2. Comparison of vitamin D and zinc levels of inpatients who need and did not need intensive care

	Inpatients with the need of IC	Inpatients without the need of IC	p
Vitamin D level (n,%)			
Deficiency	16 (84.2)	21 (53.8)	0.04*
Insufficiency	0 (0.0)	16 (41.0)	
Normal	3 (15.8)	2 (5.2)	
Zinc level (µg/dL)	74.65 ± 11.01	86.78 ± 11.63	0.01**

*Pearson's Chi-square test, ** Independent sample t-test.

Table 3. The relationship between the vitamin D levels of hospitalized children and the length of hospital stay

	Length of hospitalization (day)	p
Vitamin D level (n, %)		
Deficiency	7.53 ± 1.42	0.01*
Insufficiency	6.69 ± 0.79	
Normal	5.00 ± 0.16	

*Pearson's Chi-square test, ** Independent sample t-test.

We found that the vitamin D ($p= 0.04$) and zinc levels ($p= 0.01$) of inpatient children with the need of IC were significantly lower than those without the need of IC (Table 2).

We concluded that there was a meaningful correlation between the vitamin D levels of inpatients and the length of hospitalization. Accordingly, it was observed that as the vitamin D level in children increased, the length of hospitalization decreased significantly ($p= 0.01$) (Table 3).

Discussion

In our study, we aimed to determine the changes in vitamin D and zinc levels in children aged six months to five years with LRTI. Accordingly, we concluded that vitamin D and zinc levels were lower in children with LRTI than healthy children. In addition, we found that vitamin D and zinc levels were lower in inpatients than in outpatients. According to our results vitamin D and zinc levels were lower in those with the need of IC compared to those without the need of IC. As the level of vitamin D increased in inpatients the length of hospitalization was shortened.

In some studies, it has been determined that active vitamin D is synthesized from epithelial cells of the respiratory system and it affects the production of antimicrobial peptides such as cathelicidin and defensin (9,10). Cathelicidin is an antimicrobial peptide that increases pathogen clearance. This peptide especially protects against infections caused by microorganisms such as mycobacterium tuberculosis and respiratory syncytial virus. Therefore, it is accepted that children with low serum vitamin D levels are more vulnerable to LRTI (11,12).

In our study, we found an association between vitamin D deficiency and LRTI in children aged six months to five years. Similar to our results, Inamo et al. determined an association between clinical severity of LRTI and vitamin D deficiency (13). Roth et al. concluded that vitamin D deficiency was associated with LRTI in children aged 1-18 months (14). Moreno-Solis et al. conducted their study with 48 infants and found that there was a correlation between vitamin D deficiency and the severity of LRTI (15). Özdemir et al. proved that low serum vitamin D level was among the causes of recurrent respiratory tract infections (16).

Leis et al. conducted their study with 197 children less than five years of age and concluded that LRTI was four times more common in children who did not receive 800 IU vitamin D supplementation compared to those who received it (17). Larkin et al. recommended vitamin D supplementation for children aged <5 years with the risk of LRTI (18). On the contrary, Iqbal et al. concluded that there was no correlation between the severity of viral LRTI and vitamin D deficiency (19). Similarly, two studies in Canada (20,21) and Ismail et al. (22) suggested that vitamin D deficiency was not associated with the severity of LRTI in children aged six months to three years.

In our study, we concluded that 84.2% of the inpatients with need of IC had vitamin D deficiency. Similarly, Yalaki et al. (23) proved that 77.1% of children with the need of intensive care due to LRTI had vitamin D deficiency. Remmelts et al. (24) determined that there was a correlation between vitamin D deficiency and the risk of IC admission-30-day mortality in the inpatient children with LRTI.

In our study children with LRTI had significantly lower serum zinc levels than healthy children. Similar to our results, many studies proved that the serum zinc levels were significantly lower in children with LRTI than healthy children (2,25,26). This can be associated with the negative effects of zinc deficiency on the immune system. The fact that LRTI mediates the effects of cytokines such as zinc, interleukins and TNF- α can also be accepted as another reason for the lower zinc level (25). In a study conducted in 2009, a 15-20% decrease was observed in the incidence of LRTI in zinc supplemented preschool children (27).

Conclusion

Our study concluded that children under five years of age had an increased risk of LRTI and a severe clinical course as their vitamin D and zinc levels decreased.

Limitations

Our study has two main limitations. First, it was conducted retrospectively. Second, the pre-LRTI vitamin D and zinc levels of the children were not included in the study. We suggest further studies to determine whether the vitamin D and zinc supplementation after discharge will be beneficial for the inpatient children. One of the limitations of our study is that vitamin D deficiency was detected more frequently in the control group.

Ethics Committee Approval: Ethics Committee approval was received from Kastamonu University Clinical Research Ethics Committee (Decision no: 2022-KAEK-5, Date: 26.01.2022).

Informed Consent: Patient consent was obtained.

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