The Role of Serum Vitamin D Level on Lower Respiratory Tract Infections in Children

Zümrüt Kocabey Sütçü[1], Murat Sütçü[2], Nilgün Selçuk Duru[3], Mahmut Çivilibal[3], Murat Elevli[3]

[1]Clinic of Pediatrics, Süleymaniye Maternity and Children Hospital, *İstanbul, Turkey*
[2]Division of Pediatric Infectious Diseases, İstanbul University İstanbul School of Medicine, *İstanbul, Turkey*
[3]Clinic of Pediatrics, Haseki Training and Research Hospital, *İstanbul, Turkey*

Abstract

Objective: The aim of this study was to evaluate the effect of serum 25 (OH) vitamin D levels on the clinical aspect of acute lower respiratory tract infections (LRTIs) in children.

Material and Methods: Fifty patients (19 female, 32%) who had been internalized in Haseki Training and Research Hospital, Department of Pediatrics with the diagnosis of LRTIs were enrolled in this study. Fifty healthy subjects in the same age group constituted the control group. Serum 25 (OH) vitamin D levels were measured by ELISA method. Prenatal, postnatal factors and nutritional status of children that may influence serum 25 (OH) vitamin D levels were also evaluated.

Results: The mean age of patients was 34.1±24.3 months. The most common type of LRTIs were bronchiolitis (80%) and bronchopneumonia (20%). The degree of severity was grouped as mild (12%), moderate (64%) and severe (24%). Mean serum 25 (OH) vitamin D level was 45.50±21.82 ng/mL in study group and was 55.18±26.83 ng/mL in control group. There was negative correlation between frequency of LRTIs and serum 25 (OH) vitamin D levels (r=-0.522, p= <0.001). Serum 25 (OH) vitamin D levels in patients with severe LRTIs were significantly lower than the mild and moderate group (p values are 0.007 and 0.004, respectively).

Conclusion: Serum 25 (OH) vitamin D levels were inversely proportional with the severity and frequency of LRTIs. *(J Pediatr Inf 2016; 10: 54-9)*

Keywords: Lower respiratory tract infections, 25 (OH) vitamin D, children

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Correspondence Address
Murat Sütçü
E-mail:
sutcu13@yahoo.com

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Introduction

Lower respiratory tract infections (LRTIs) in children today are still amongst the leading causes of morbidity and mortality. Vitamin D deficiency levels is known to be amongst the significant promoter causes of LRTI and the effects of vitamin D levels on the immune system has in recent years been one of the interesting subjects of study (1). Vitamin D inhibits the proinflammatory cytokines and become effective by stimulating the antimicrobial peptide synthesis over the host immune response. Of the peptides, especially the cathelicidin plays an important role against the respiratory system infections in the immune response (2, 3). The relationship of vitamin D with the upper respiratory tract infection, severe pneumonia, respiratory syncytial virus (RSV) and seasonal influenza has been shown by the recent studies (4).

In the present study, the effects of serum 25 (OH) vitamin D levels in children diagnosed with lower respiratory tract infections in our children were investigated.

Material and Methods

Fifty patients (19 female, 32%) who were diagnosed with the LRTIs at the Pediatrics clinics of the Haseki Training and Research Hospital between 1 September and 1 February 2013 were involved in this study. Ethics committee approval and patient consent have not been obtained due to the retrospective nature of the study. Together with serum 25 (OH) vitamin D levels of the patients, the sheer period of breast milk, how long vitamin D has been used for and when it was discontinued, exposure to sun rays, mouthers' use of vitamin during pregnancy and their way of dressing have all been investigated.

It was considered that the value of serum 25 (OH) vitamin D below 20 ng/mL was vitamin D deficiency, values below 20-32 ng/mL, the lack of vitamin D and the value of 32-100 ng/mL, sufficient level of vitamin D (5).

While children diagnosed with the lower respiratory tract infection were included into the study, patients who had warehouse dose of vitamin D and with chronic diseases were excluded from the study. Fifty healthy subjects who were proved to be healthy as a result of our clinical examinations during the same period and tests and whose serum 25 (OH) vitamin D levels were measured in their routine controls constituted the control group.

Acute LRTI was defined as the disease table including bronchitis, bronchiolitis, pneumonia or any two of all three components of the clinical picture. The patients diagnosed with LRTI were classified according to the evaluation scale inclusive of patients' general condition, respiratory rate, wheezing, and retraction parameters as; "mild" with 1-3 points, "medium" with 4-8 points, and "severe" with 9-12 points or in the presence of apnea (6, 7).

The Statistical Package for the Social Sciences 15.0 software (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. It was specified that when the descriptive statistics of quantitative variables demonstrated the normal distribution of the data distribution, there was mean ± standard deviation; when they did not demonstrate it, there were median, minimum and maximum values. In cases when both group comparisons of the quantitative variables maintained the assumption of normal distribution, the student t test was applied; in the case of failure to maintain the assumption of normal distribution, the Mann Whitney U test was used. In the analysis of qualitative data, on the other hand, the Chi-square test was used and $p<0.05$ was accepted as significant. Comparisons of more than two groups were made with the Kruskal Wallis test. In the case of significant differences, the binary comparisons were evaluated by the Mann Whitney U test and the Bonferroni correction was applied. The relationships between the quantitative variables were evaluated by the Spearman correlation coefficient. In the analyses with a single variable, the values under $p<0.1$ were accepted to be clinically significant and regression analysis was carried out.

Results

Average age of the patients was 34.1±24.3 months and 31 of them were males. Average age of the patients in the control group, on the other hand, was 32.0±21.7 months and 26 were males. No differences were found between the patients and the control group in terms of age and gender ($p=0.804$, $p=0.313$ respectively).

Lower respiratory tract infections diagnosis of the patients was 80% bronchiolitis and 20% bronchopneumonia and it was found that severity of the diseases were 12% mild and 64% medium an 24% severe.

While 25 (OH) vitamin D level average of the patients was 45.50±21.82 ng/mL, it was 45.50±21.82 ng/mL of the control group. It was found that 25 (OH) vitamin D level in the control group was high. Although the difference between the two groups was statistically close to the critical value, it was not accepted as significant ($p=0.051$), (Table 1). It was found that 12% of the patients with LRTI had vitamin D deficiency and 24% lack of vitamin D.

It was found that of the prenatal factors such as mothers' use of vitamins during their pregnancy and their non-revealing dressing styles were 44% and 70% respectively. As far as the sun-ray exposure of the patients were concerned, it was found that the rate of their houses exposed to sun was 75% and that of going for swimming in the summer was 24%. It was found that while 54% of the patients had 400 units and 40% 500 units of vitamin D supplements daily, 6% never took any vitamin D. Average discontinuation of vitamin D ıf the patients was 12.19±4.87 months.

Vitamin D level of the patients decreased as they got older, and the difference was statistically significant ($r=-0.273$, $p=0.006$). While the serum 25 (OH) vitamin D level in patients who had LRTI only once was 60 ng/mL, it was 27 ng/mL in patients who had LRTI four times. As the number of LRTI increased, the serum 25 (OH) vitamin D level decreased ($r=-0.522$, $p<0.001$) (Figure 1). Depending on the severity of the disease, it was 69.82±22.50 ng/mL in the group with mild level of vitamin D, 46.73±18.01 ng/mL in the group with medium level and 30.08±19.74 ng/mL in the group with severe level (Figure 2). There was a

Table 1. General characteristics of the patient and control group and their vitamin D levels

	GROUP		p
	Study group (n=50)	Control group (n=50)	
Gender (n (%), male)	31 (%62)	26 (%52)	0,31
Age (month, mean±SD)	34.1±24.3	32.00±21.71	0.80
Height (cm, mean±SD)	89.96±17.19	93.01±21.01	0.16
Weight (kg, mean±SD)	13.08±4.51	16.52± 5.75	0.084
Birth weight (gr, mean±SD)	3084.69±426.98	2984.69±685.12	0.42
Gomez (%, mean±SD)	92.90±9.95	94.15±10.18	0.28
Amount of daily vitamin D support (gtt, mean±SD)	2.5±1	3.7±1.3	<0.001
Duration of vitamin D intake (month, mean±SD)	8.2±4.2	12.±3.9	0.25
Duration of only breastfeeding (month, mean±SD)	4.1±1.5	5.1±1.7	<0.001
Duration of stopping breastfeeding (month) (month, mean±SD)	12.4±6.7	15.3±6.8	0.22
Level of 25 (OH) vitamin D (ng/mL, mean±SD)	45.50±21.82	55.18±26.83	0.051

SD: Standard Deviation

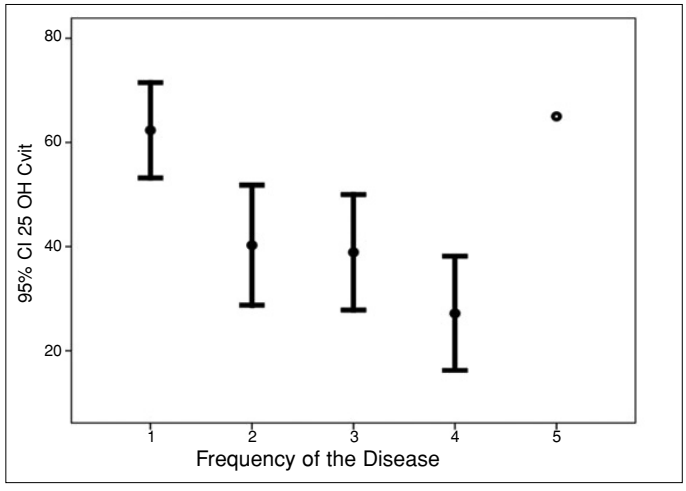

Figure 1. Number of recurrent LRTI and vitamin D levels and confidence intervals

LRTI: Lower Respiratory Tract Infections

significant difference in the opposite direction between the severity of the disease and the serum 25 (OH) vitamin D levels and as the severity of the disease increased, it was found that 25 (OH) vitamin D levels were low (r=-0.530, p<0.001), (Table 2). It was found that the serum 25 (OH) vitamin D levels in the group with severe degree of disease were significantly low in comparison to groups with medium and mild levels (p=0.007 p=0.004 respectively). There was also significant difference in terms of the serum 25 (OH) vitamin D levels in the groups with medium and mild levels (p=0.022).

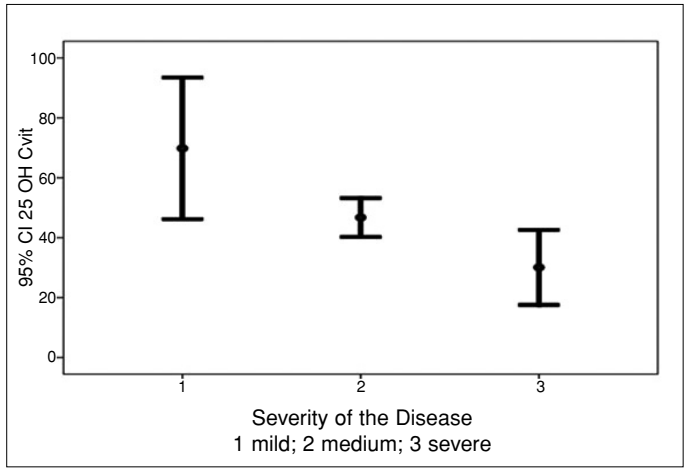

Figure 2. Severity of the disease and vitamin D levels and confidence intervals

Table 2. Relationship of the serum 25 (OH) vitamin D level of the study group cases with the general features

	Rho	p
Age	-0.273	0.006
Height	-0.175	0.223
Weight	-0.108	0.454
Birth weight	0.051	0.725
Gomez	0.418	0.003
Duration of breastfeeding	-0.166	0.249
Discontinuation time of vitamin D	0.542	0.001
Frequeny of the disease	-0.522	<0.001
Severity of the disease	-0.530	<0.001

While a positive relationship was found between the serum 25 (OH) vitamin D levels and Gomez scores (r:0.418, p=0.003) and vitamin D discontinuation periods of the patients (r=0,542, p=0,001), a negative relationship was detected with the age of the patients (r=-0,273, p=0,006) (Figure 3). While the average serum 25 (OH) vitamin D of the patients vitamin D supplement of 500 units was55,72±22,77, that of those patients with 400 units was 39,88±19,10 and no significant difference was found (p=0,016). The serum 25 (OH) vitamin D levels of the three patients who did not receive any vitamin D supplement was 28,03±8,20 ng/mL. There was no significant difference between the average serum 25 (OH) vitamin D levels of the cases and gender as well as diagnostic groups (p=0,348, p=0,382). While the average serum 25 (OH) vitamin D levels of the mothers with a non-reveal-

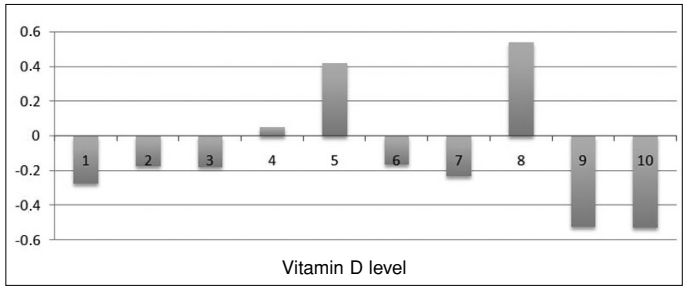

Figure 3. Vitamin D level correlation analysis

Table 3. Multivariate Lineer Regresyon Analysis of the factors that determine the vitamin D level

	B	Beta	p
Age (month)	-0.450	-0.384	0.002
Severity of the disease	-8.043	-0.224	0.066
Sun exposure of the house	-26.366	-0.505	<0.001
Discontinuation time of vitamin D (month)	1.184	0.252	0.031

ing dressing style was 40.71±20.49, it was 56.70±21.33 in those without that style and it was significantly low (p=0.022). Furthermore, the average serum 25 (OH) vitamin D levels of the patients with house exposed to sun rays was higher (53.11±19.64) than those whose houses were not exposed (23.87±10.07) to sun rays (p<0.001).

The variables of age, severity of the disease, the Gomez score, the way of dressing of the mother, the rate of exposure to sun rays, the dose of vitamin D and time of discontinuation which were all clinically significant in analyses with single variables were subjected to regression analysis. It was found that the variables of age, the rate of exposure to sun rays and the time of discontinuation of vitamin D were the most important factors that defined the levels of serum 25 (OH) vitamin D (Table 3).

Discussion

Epithelial cells of the respiratory system are able to synthesize the active vitamin D; therefore, it contributes to the strengthening of the local immune system by enabling the growth of cathelicidin and the activation of toll-like receptor (8, 9). It was shown that susceptibility to respiratory tract infections and frequency increased in cases with low level of serum vitamin D (10). In the present study, average age was 34.1±24.3 months and of the 50 patients, 31 were males. 80% of the cases were diagnosed with bronchiolitis and 20% with bronchopneumonia. The fact that the diagnosis of LRTI was mostly composed of bronchiolitis was linked to the age of patients and period of the season when the study was carried out.

The fact that level of 25 (OH) vitamin D whose half-life is nearly 20 days is the best parameter for the evaluation of the vitamin level and about the pool of vitamin D in the body (11, 12). Previous studies reported a relationship between the low or deficient levels of serum vitamin D in children and the LRTI. In their study they carried out with Ethiopian children, Muhe et al. (13) demonstrated a strong correlation between the nutritional rickets cases and pneumonia. In another study, it was shown that the LRTI frequency in children (<10 ng/mL) with asymptomatic vitamin D deficiency increased 11 times. Furthermore, it was stated that signs or symptoms of infection appeared before the skeletal system symptoms (14). In the present study, while the average serum 25 (OH) vitamin D level in children who had LRTI was 45.50±21.82 ng/mL, it was found that it was 55.18±26.83 ng/mL in the control group. The average serum 25 (OH) vitamin D levels of both groups were at a sufficient level. However, the average serum 25 (OH) vitamin D level of the study group was lower in comparison to the control group. In our study, 12% of the patients with lower respiratory tract infection had vitamin D deficiency and 24% lack of vitamin D.

Although the serum 25 (OH) vitamin D level of 32-100 ng/mL were within normal range, it was not specifically clear which values over the serum vitamin D level were effective against infections. In an adult study, it was found that viral respiratory tract infections were low in patients whose 25 (OH) vitamin D level was over 38 ng/mL (15). In the present study, we tried to determine the level of 25 (OH) vitamin D effective in preventing the LRTI in children, but since the number of patients was limited, it was not evaluated. There is a need for randomized controlled studies with many cases on this subject.

While the relevant literature does not contain sufficient number of studies on the recurrent LRTI and the level of vitamin D, the level of vitamin D in the frequently recurrent tonsillopharyngitis cases in Turkey was investigated and it was found that the level of vitamin D in the study group was significantly lower than the control group (16). It was found in our study that as the number of recurrent LRTI increased, vitamin D level of the cases decreased. Although these findings make us think that there might be a relationship between the frequently recurrent LRTI and vitamin D, they also emphasize that there is a need for randomized controlled studies with many more cases.

The degrees of illness of the 50 patients with lower respiratory tract infection were 12% mild, 64% medium and 24% severe. McNally et al. (17) found vitamin D deficiency in patients who had LRTI and needed to be monitored in the pediatric intensive care unit and this deficiency might be linked to the severity of the disease. Similarly in the

present study, depending on the severity of the disease, the serum 25 (OH) vitamin D levels were 69.82±22.50 ng/mL in the mild group, 46.73±18.01 ng/mL in the medium group, and 30.08±19.74 ng/mL in the severe group. As the recurrent LRTI frequency increased in patients, the level of vitamin D decreased.

Vitamin D is affected by many factors such as age, gender, season, ethnic origin, socio-economic level, exposure to sun rays, the Gomez score, state of health, pubertal stage, total energy intake and diet (18). While a positive relationship (p=0.006) was found between the serum 25 (OH) vitamin D levels and age of the patients, a positive relationship was detected with the vitamin D levels and the Gomez score as well (p=0.003). The 25 (OH) vitamin D levels of the mother with non-revealing dressing styles in comparison to those with revealing dressing styles and those with direct exposure to the sun rays in comparison to those without exposure to sun rays were significantly low. Furthermore, the time to discontinue vitamin D was another significant factor that affected the level of serum vitamin D, and it was found that the level in those patient who took vitamin D for a long time was higher (p=0.001).

In their placebo-controlled adult study, Avenell et al. (19) reported that 800 unit daily vitamin D supplement decreased the rate of infections 10-15%. In the present study, it was found that the serum 25 (OH) vitamin D levels of cases who took 500 units of vitamin D was significantly high (p=0.016). It has recently been suggested that the daily vitamin D requirement is 800-1000 units (20). In the current situation, the daily vitamin D supplement aims to be a precaution for rickets rather than preventing infections.

In conclusion, it was found that the serum 25 (OH) vitamin D level in the study group who had LRTI in our study was lower in comparison to the control group. As the level of vitamin D decreased, the severity of the disease and the number of recurrent LRTIs increased. According to the results of the present study, vitamin D supplement should be given to the mothers during their pregnancy and to their children in order to prevent the development of LRTI and the frequency of the disease.

Ethics Committee Approval: Ethics committee approval was not received due to the retrospective nature of this study.

Informed Consent: Written informed consent was not received due to the retrospective nature of this study.

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