

# Okul Öncesi Dönem Down Sendromlu Çocuklarda D Vitamini Eksikliği

## Vitamin D Deficiency in Preschool Children with Down Syndrome

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### Özet

**Amaç:** Bu çalışmada okul öncesi dönem (<6 yaş) Down Sendromlu (DS) çocuklarda D vitamini düzeylerini saptamayı amaçladık.

**Gereç ve Yöntemler:** Çalışmaya Haziran 2015- Ocak 2020 tarihleri arasında polikliniklere başvurmuş; 1-72 ay arası 51'i kız, 70'i erkek olmak üzere toplam 121 DS'li çocuk dahil edildi. Çocukların demografik bilgileri ve eşlik eden hastalıkları tarandı ve kaydedildi. DS'li çocuklar 1 yaş altı olanlar süt çocuğu, 1-3 yaş arası olanlar oyun çocuğu ve 4-6 yaş olanlar ise okul öncesi dönem olmak üzere üç grupta değerlendirildi. Hastaların serum D vitamini düzeyleri [25(OH) D], kalsiyum, fosfor ve serum alkale fosfataz (ALP) değerleri kaydedildi.

**Bulgular:** Çalışmaya dahil edilen hastaların yaş ortalamaları 27.73±19.29 aydı. Çalışmaya dahil edilen DS'li çocukların (n=121) D vitamini düzeyleri süt çocukluğu döneminde (n=34) 33.73±2.83 ng/mL, oyun çocuğu döneminde (n=50) 29.35±2.10 ng/mL ve okul öncesi dönemde (n=37) 21.06±2.03 ng/mL olarak tespit edildi ve 3 grup arasında D vitamini düzeyleri açısından istatistiksel olarak anlamlı fark saptandı (p<0.05). Okul öncesi dönem çocuklarda D vitamini eksikliği ve yetersizliği [25(OH)D seviyesi<30 ng/ml] oranı %75 idi.

**Sonuç:** Sonuç olarak özellikle okul öncesi dönem DS'li çocuklarda D vitamini eksikliği ve yetersizliği oldukça yaygındı. DS'li çocukların serum D vitamini düzeylerinin düzenli olarak kontrol edilmesi ve gereğinde vitamin D desteği önerilerinde bulunulması gerektiğini düşünüyoruz.

**Anahtar kelimeler:** Down Sendromu, Vitamin D, Okul öncesi çocuk.

### Abstract

**Objective:** We aimed to investigate the vitamin D status of preschool children (<6 years) with Down Syndrome (DS).

**Material and Methods:** This retrospective study included 121 children with DS (51 girls-70 boys), aged 1-72 months, and who admitted to our hospitals between June 2015 and January 2020. Children's demographic data and their comorbidities were recorded. The children were evaluated in three groups as infancy under 1 year of age, toddlers between 1-3 years of age, and preschooler between 4-6 years. We also recorded their serum 25-hydroxy-vitamin-D [25(OH)D], calcium (Ca), phosphate (P), and alkaline phosphatase (ALP) levels.

**Results:** The children included in the study had a mean age of 27.73±19.29 months. The children's vitamin D levels were found to be 33.73±2.83 ng/ml for infants (n=34), 29.35±2.10 ng/ml for toddlers (n=50), and 21.06±2.03 ng/ml for preschoolers (n=37), with a statistically significant difference between the groups (p<0.05). The rate of vitamin D deficiency 25(OH)D levels<30 ng/ml was found to be 75% in preschool children with DS.

**Conclusion:** Our findings suggest a prevalence of vitamin D deficiency in preschool children, particularly in those with DS. We recommended that children with DS should be regularly checked for their serum vitamin D levels and given vitamin D supplementation as needed.

**Keywords:** Down Syndrome, Vitamin D, Preschool.

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## INTRODUCTION

Vitamin D is a fat-soluble secosteroid prohormone that is produced on the skin by contact with sunlight. Through various metabolic changes in the body, it transforms into a hormone known as calcitriol, with a key role in the calcium and phosphate metabolism (1). Vitamin D serves plenty of functions in the body. Therefore, its deficiency may cause musculoskeletal symptoms such as bone pain, muscle weakness, gait difficulty, skeletal deformity, in addition to extraskeletal symptoms such as autoimmune diseases, cardiovascular diseases, and neuropsychiatric diseases (2).

Down Syndrome (DS) occurs as a result of trisomy, which occurs due to an extra copy of the whole or part of the long arm of chromosome 21 and is the most commonly known cause of delay in development. DS affects 1 in every 787 liveborn babies (3). DS is often accompanied by distinctive craniofacial features, congenital heart disease and immune, musculoskeletal and endocrine system abnormalities (4,5).

In patients with this syndrome, various environmental and hormonal factors such as hypotonia, low physical activity, poor calcium and vitamin D intake, intrauterine growth restriction, hypogonadism and thyroid dysfunction may contribute to bone mass and quality (6,7). Among all the others, vitamin D may have a crucial role in the health of these people. Vitamin D levels differ with many factors, including exposure to sunlight, dietary intake, and supplement use (8,9).

There is a lack of scientific evidence on the prevalence and severity of vitamin D deficiency in children with DS. Hence, this study aimed to determine prevalence and severity of the vitamin D deficiency in children with DS, from infancy to toddler and particularly during the preschool period, and to raise awareness on the matter.

## MATERIAL AND METHODS

We retrospectively reviewed the data of 305 children with DS, aged 1-72 months, and who applied to the pediatric outpatient clinics between June 2015 and January 2020. We

recorded the serum 25-hydroxy-vitamin D [25(OH)D], calcium (Ca), phosphate (P), and serum alkaline phosphatase (ALP) levels of 121 children with DS (51 girls–70 boys). We also recorded the children's demographic characteristics and data regarding their comorbidities.

Total serum vitamin D levels were measured by nephelometry using commercially available kits. The best indicator of vitamin D status is the serum 25 (OH) D3. Vitamin D deficiency was evaluated at four levels according to serum 25-OH levels as severe deficiency if  $\leq 10$  ng/mL, deficiency if between 11–20 ng/mL, insufficiency if between 21–30, and sufficiency if  $>30$  ng/mL. These values were chosen based on previously established guidelines for bone health (10,11).

The children were divided into three groups as infancy under 1 year of age, toddler between 1-3 years, and preschool between 4-6 years.

## Statistical Analysis

We used SPSS 18.0 software to analyze the data. Descriptive results are expressed as percentages, mean and standard deviations (SD) as appropriate. Conformity to normal distribution and homogeneity were tested using the Shapiro–Wilk test. The Kruskal–Wallis test and the one-way ANOVA test were used for comparisons between groups. P-values  $<0.05$  indicated statistical significance.

## RESULTS

121 children (51 girls – 70 boys) included here had a mean age of  $27.73 \pm 19.29$  months. In terms of Vitamin D status, 13 children had a severe deficiency, 25 had a deficiency, 33 had insufficiency and 50 had sufficiency. The rates of vitamin D deficiency were 41% in the infancy group, 56% in the toddler group, and 78% in the preschool group. Nearly 80% of the children had a comorbid disease, particularly a cardiac anomaly and/or hypothyroidism. **Table 1** shows the prevalence of comorbidities requiring regular follow-up in children with DS.

We found that vitamin D levels were statistically significantly decreased from infancy to toddler and preschool

**Table 1. 25(OH)D status and comorbidities of patients.**

	Total (n:121)		Infancy (n:34)		Toddler (n:50)		Preschool age (n:37)	
	n	%	n	%	n	%	n	%
25(OH)D levels								
$\leq 10$ ng/ml	13	10.8	3	8.8	4	8	6	16.2
11-20 ng/ml	25	20.7	3	8.8	9	18	13	35.1
21-30 ng/ml	33	27.2	8	23.6	15	30	10	27.1
$>30$ ng/ml	50	41.3	20	58.8	22	44	8	21.6
<b>Comorbidities</b>								
No additional diseases	24	19.8	6	17.7	10	20	8	21.7
Cardiac anomaly	65	53.7	22	65	30	60	13	35.1
Hypothyroidism	68	56.1	17	50	26	52	25	67.6
Other	2	1.6	0	0	1	2	1	2.7

age ( $33.73\pm 2.83$ ,  $29.35\pm 2.10$ ,  $21.06\pm 2.03$  ng/ml, respectively;  $p<0.05$ ). There was no significant difference between Ca, P, or ALP values ( $p>0.05$ ) (**Table 2**).

## DISCUSSION

In this study, we determined that vitamin D levels gradually decreased from infancy to toddler and preschool age in children with DS. However, we could only examine the vitamin D levels of 121 of 305 patients with DS that were followed up in our centers. Also, vitamin D deficiency was detected in 58% of children with DS under the age of 6, with this rate being 75% for preschool children.

Vitamin D is a prohormone that plays a role in the neuromuscular and skeletal system by regulating the serum calcium/phosphorus balance (12). However, the effects of vitamin D are not limited to the musculoskeletal system. Recent data suggests many organs (e.g., osteoblasts, lymphocytes, mononuclear cells, brain, pancreas, small intestine, colon, heart, skin, gonad, prostate, and breasts) to commonly contain these receptors (12,13). Vitamin D levels are important for the musculoskeletal system, both for normal muscle tone and strength and for normal development and mineralization of the skeletal system. Vitamin D levels have particular importance in patients with DS, who commonly present with musculoskeletal pathologies such as hypotonia and osteoporosis (4).

The serum 25 OH vitamin D levels of infants are correlated with those of their mothers during the first eight weeks of life, after which sunlight becomes more determinant (14). In our country, each newborn infant is given 400 IU vitamin D supplement orally from the first day of life until 1 year of age, under the regulation of the Ministry of Health. After 1 year, the daily need is determined as 600 IU, recommended to be given by food and/or oral vitamin D supplementation (15). One study on vitamin D levels in childhood and adolescence in 2015 has emphasized that 61% of all children included had vitamin D deficiency, with vitamin D levels decreasing with increased age (16). In the present study, we found that vitamin D levels were higher during infancy, but increased deficiency was observed in toddler and preschool period. Children with DS may be less exposed to sunlight, particularly during toddler and preschool period due to hypotonia and delay in development. Therefore, physicians who follow children with DS should have a higher awareness of vitamin D deficiency and consider oral supplementation when necessary.

Dogan et al. (16) found preschool children to have a mean vitamin D level of  $23.86\pm 10.64$  ng/ml. Kartalet al. (17) conducted a similar study on healthy preschool children and found them to have a mean vitamin D level of  $35.9\pm 15.4$  ng/ml. In the present study, we found preschool children with DS to have a mean vitamin D level of  $21.06\pm 2.03$  ng/ml. Stagi et al. compared children with DS aged between 2-12 years with a healthy control group and found that the group with DS had significantly lower vitamin D levels. Considered as the first comprehensive evaluation of 25(OH)D levels in children and adolescents with DS, this study highlighted a very high prevalence of vitamin D deficiency in children with DS at different age groups, suggesting vitamin D deficiency to be a significant health problem in these patients (18). To the best of our knowledge, our study is the first to evaluate the prevalence of vitamin D deficiency in preschool children with DS in our country. In this study, we found that the rates of children with DS and below 30 mg/ml vitamin D levels were 41% in the infancy group, 56% in the toddler group, and 78% in the preschool group. Moreover, in comparison to other groups, preschool children were determined to have significantly lower vitamin D levels.

In our patient group, there was quite a high rate of hypothyroidism and some cardiac anomalies (common in children with DS). In fact, even the patients undergoing continuous follow-up for these comorbidities did not have sufficient vitamin D levels.

There has been very little attention on bone health in children with DS. Most clinicians who treat children with DS do not check vitamin D levels on a consistent basis. The most important limitations of our study were its retrospective design, absence of a healthy control group and our lack of information on whether these patients received regular vitamin D supplementation. However, we think that this study will raise awareness in physicians dealing with this group of patients, particularly since the rates of vitamin D deficiency are very high in patients who are followed up for DS, even when they are regularly checked for other comorbidities. At the same time, prospective controlled studies with healthy control groups are needed. There is also need for studies examining the effects of Vitamin D levels on the motor development and bone density of DS patients.

In conclusion, we recommend that children with DS should be regularly followed for their vitamin D levels and given vitamin D supplementation as needed.

**Table 2. Serum 25(OH)D, Ca, P, ALP levels and p values**

	Total (n=121)	Infancy (n=34)	Toddler (n=50)	Preschool (n=37)	P value
Sex (n:F/M)	51/70	15/19	25/25	11/26	>0.05
25(OH) D (nl/ml)	$27.98\pm 19.29$	$33.73\pm 2.83$	$29.35\pm 2.10$	$21.06\pm 2.03$	0.002*
Ca (mg/dl)	$9.39\pm 0.73$	$9.6\pm 0.12$	$9.2\pm 0.12$	$9.3\pm 0.23$	>0.05
P (mg/dl)	$4.92\pm 0.91$	$5.12\pm 0.23$	$4.94\pm 0.12$	$4.73\pm 0.90$	>0.05
ALP (U/L)	$197.66\pm 102.9$	$252\pm 28.4$	$166\pm 10.6$	$187\pm 9.81$	>0.05

**Competing Interests**

The authors declare that they have no competing interest.

**Financial Disclosure**

There are no financial supports.

**Author Contribution**

All authors contributed equally to the article.

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