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# *Original Articles*

## Vitamin D Status of Children in a University Hospital in West Turkey

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**Abstract** ***Objectives:*** An optimal vitamin D status is important for the growth and development of bones in children and adolescents. We aimed to determine the frequencies of 25-hydroxyvitamin D (25(OH)D) deficiency and insufficiency in children and adolescents. ***Patients:*** A total of 556 children aged 0 to 18 years were included in the study. Serum 25(OH)D, calcium, phosphorous and alkaline phosphatase levels were measured. ***Results:*** Prevalence of low vitamin D status (<30.0 ng/mL) was 63.5% for children aged 0 to 18 years; 219 children (39.3%) had vitamin D deficiency (<20 ng/mL), while 134 of them (24.10%) had vitamin D insufficiency (20 ng/mL ≤ insufficient <30 ng/mL). The prevalence of vitamin D deficiency was higher among girls compared with boys, in adolescents compared with childhood stages and in autumn compared with other seasons. ***Conclusions:*** 25(OH)D deficiency/insufficiency was found to be very common in the studied population. Routine screening and supplementation to prevent vitamin D deficiency in at-risk groups during winter and autumn months when vitamin D synthesis is scarce, may be required.

**Key words** Children; Prevalence; Rickets; Vitamin D

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## Introduction

Vitamin D is an essential fat soluble vitamin and unique hormone that is mainly provided from synthesis in the human skin by natural exposure to sunlight.[1]

Few foods including fatty fish (salmon, tuna, mackerel), egg yolks, and some mushrooms have vitamin D in nature, and in some parts of the world, milk, cheeses, yogurt and cereals are fortified with vitamin D to supply the daily requirements, but their contributions to the total amount of daily vitamin D needs for the human body are often inadequate to satisfy them.[2-4]

The key function of vitamin D is to help maintain the body's level of calcium-phosphate by increasing their intestinal absorption for the mineralisation of bone. Beyond its main role in calcium homeostasis, vitamin D may be involved in diverse physiological and pathological processes in the human body.[4,5]

In adults, observational studies showed associations

between low concentrations of 25-hydroxyvitamin D (25(OH)D) and increased risk of cancer, cardiovascular diseases, glucose metabolism disorders, infectious diseases, multiple sclerosis, hypertension, mood disorders, declining cognitive function, and obesity.[5,6] These conditions are major public health problems worldwide. Low 25(OH)D concentrations were not identified as the cause of these diseases but were suggested as biological markers of deteriorating health and severity of disorders.

An optimal vitamin D status is important for the growth and development of bones in children and adolescents.[7] The prevalence of vitamin D deficiency is still high, even in low-latitude and industrialised countries, and vitamin D deficiency in childhood is reemerging as major public health issue. In 2005, the initiation of nationwide campaign of free vitamin D supplementation decreased its prevalence from 19% to 6% in Turkey.[7] Few studies have been conducted to evaluate the prevalence of 25(OH)D deficiency in children and teenagers in our country.[8-13]

The aim of this study was to evaluate the vitamin D status of children aged 0 to 18.99 years living in the province of Denizli (37.7667 N, 29.0833 E) located in the Aegean part of Turkey.

## Methods

Study population: This study was performed using data from the University Hospital registry in Denizli province, located in the west of Turkey, between January 2013 and December 2013. Participants were recruited from children aged 0 to 18.99 years who visited Tertiary Medical Center consecutively for health and growth status check-ups. Individuals who had chronic conditions such as liver diseases, renal diseases, gastrointestinal system problems, and those on treatment with anticonvulsants or systemic glucocorticoids causing vitamin D deficiency were excluded. The study was approved by the Institutional Review Board of Pamukkale University Hospital, and informed consent was obtained from their parents. Children were grouped into 4 categories – infant (0-12 months), toddler and preschooler (1-5 years), school-aged (6-11 years) and teenager (12-18 years) and 4 seasonal groups as follows: spring (from March to May), summer (from June to August), autumn (from September to November), and winter (from December to February).

The cut-off levels used to define vitamin D status are controversial. We defined vitamin D deficiency as serum 25(OH)D levels less than 20 ng/mL (50.0 nmol/L); vitamin D insufficiency, as ≥20 ng/mL to <30 ng/mL; and vitamin D sufficiency, as ≥30 ng/mL to be consistent with the published data.[14] Low vitamin D status was defined as 25-OH-D levels <30.0 ng/mL (75.0 nmol/L)

## Assays

Serum 25(OH) D concentrations were measured using an automated Vitamin D2-D3 HPLC Analyser (25 OH Vitamin D2-D3 HPLC Analysis Kit; Zivak Technologies, Gebze, Turkey). Total calcium, inorganic phosphate, alkaline phosphatase (ALP), intact parathyroid hormone (PTH) were analysed by a routine analyser (Cobas 8000; Roche Diagnostic, Manheim, Germany).

## Data Analysis

SPSS (Statistical Package for Social Sciences) for Windows statistical software version 18.0 was used for all calculations. Data distribution was analysed using the Kolmogorov-Smirnov test. Categorical variables were assessed using the $\chi^2$ test. The Kruskal-Wallis test was used to compare means among groups more than two, while those between two groups were done with the Mann-Whitney U test (variables not normally distributed). The lower and upper limits of the 95% confidence interval was calculated according to method described by Robert Newcombe.[15] Data were expressed as mean±SD. In all analyses, a p-value ≤0.05 was considered significant.

## Results

A total of 556 children (253 male, 303 female) with a mean age of 6.26±6.18 years were included in this study. Out of the study population, 72 (12.9%) were infants, 248 (44.6%) were toddlers-preschoolers, 87 (15.6%) were school-aged children, and the remaining 149 (26.7%) were teenagers. Biochemical characteristics and 25(OH) D levels for male and female children are illustrated in Table 1. Substantial proportion of children had low levels of serum 25(OH)D and the overall ratio of low vitamin D status was 63.5% for children aged 0 to 18 years (Table 1). Among these children, 219 (39.3%) had vitamin D deficiency (<20 ng/mL) and 134 (24.10%) had vitamin D insufficiency. Clinical vitamin D deficiency was not found in any children. Mean vitamin D levels were higher in the infants and toddler-

preschoolers groups than upper age groups (Table 2). Vitamin D deficiency and insufficiency were more prevalent in teenagers and vitamin D deficiency were significantly more common in girls. The lowest mean vitamin D levels were detected in autumn and in teenagers (Tables 2 and 3, Figures 1a and 1b). The differences between gender, seasons, and childhood stages were significant ($p<0.05$, $p<0.05$, $p<0.001$ respectively; Tables 1-3). In the correlation analysis, Serum 25(OH) D levels were negatively correlated to PTH ($r=-0.269$, $p<0.001$) and age ($r=-0.453$, $p<0.001$), but positively to calcium levels ($r=0.315$, $p<0.001$), and phosphorus levels ($r=0.231$, $p<0.001$).

## Discussion

This study was conducted to assess vitamin D levels of children and adolescents who were brought to a medical facility located in the Aegean part of Turkey for routine check-ups and growth status assessments. A limited number of reports on the vitamin D status of Turkish children have been published to date. Those studies examined different childhood age groups such as infancy, adolescence, or 1-16 years of age. Our study population was one of the largest populations examined in Turkey, to our knowledge; however, it differs from other study populations in that it includes all ages and stages of childhood, from infancy to the end of adolescence. The results of the study showed that children, even those who lived in the sunny region of Turkey and supplemented with vitamin D during the first year of life, had a significantly high ratio of vitamin D deficiency/insufficiency, with the highest percentages appearing in teenagers. Vitamin D deficiency was significantly more common in girls, and seasonal variation was observed, with increased incidence in autumn and winter that decreased from spring to summer.

Vitamin D plays one of the crucial roles to achieve optimal

**Table 1** Biochemical characteristics (mean±SD) and the prevalence of low serum 25(OH)D levels for male and female children

| | **Study population n:556(%) (%95CI)** | **Male n:253(%) (%95CI)** | **Female n:303(%) (%95CI)** | ***p*** |
|---|---|---|---|---|
| Age (years) | 6.26±6.18 | 4.82±5.38 | 7.47±6.52 | <0.001 |
| D vitamin levels±SD ng/mL | 27.21±15.90 | 28.71±15.67 | 25.96±16.01 | <0.05 |
| Calcium, mg/dL | 9.99±0.84 | 9.96±0.98 | 10.01±0.69 | 0.587 |
| Phosphorus, mg/dL | 5.11±0.97 | 5.15±1.01 | 5.08±0.95 | 0.640 |
| ALP, IU/L | 248.86±245.17 | 255.79±183.83 | 242.80±288.79 | <0.05 |
| PTH, pg/mL | 38.76±29.08 | 37.82±36.59 | 39.49±21.82 | 0.06 |
| D vitamin levels <20 ng/mL | 219 (39.3)(35.3-43.6) | 82 (32.4)(26.9-38.4) | 137 (45.1)(39.7-50.8) | <0.05 |
| D vitamin levels <30 ng/mL | 353 (63.5)(59.3-67.4) | 153 (60.47)(54.1-66.4) | 200 (66.0)(60.3-71.2) | 0.134 |

25(OH)D: 25-hydroxyvitamin D, PTH: parathyroid hormone, ALP: alkaline phosphatase, SD: standard deviation.
$p<0.05$, statistically significant

**Table 2** The prevalence of low serum 25(OH)D levels in childhood stages

| | **Study population n:556(%) (%95CI)** | **Infancy n:72(%) (%95CI)** | **Toddlers-Preschoolers n:248(%) (%95CI)** | **Schoolers n:87(%) (%95CI)** | **Teenagers n:149(%) (%95CI)** | ***p*** |
|---|---|---|---|---|---|---|
| Mean D vitamin levels±SD | 27.21±15.90 | 38.74±18.00 | 31.18±14.71 | 21.24±11.07 | 18.49±13.27 | <0.001 |
| D vitamin levels <20 ng/mL | 219 (39.3) (35.4-43.5) | 10 (13.8) (7.0-23.71) | 61 (24.6) (19.4-30.5) | 47 (54.0) (43.0-64.6) | 101 (67.7) (59.5-75.0) | <0.001 |
| D vitamin levels <30 ng/mL | 353 (63.5) (59.3-67.4) | 26 (36.1) (25.3-48.3) | 129(52.0) (45.6-58.3) | 70 (80.4) (70.2-87.8) | 129 (86.5) (79.8-91.4) | <0.001 |

CI: confidence interval, 25(OH)D: 25-hydroxyvitamin D, SD: standarddeviation.
$p<0.05$, statistically significant.

peak bone mass during childhood and adolescence, when peak bone mass in skeletal development is accrued.[16] Vitamin D deficiency and associated states are reemerging as major public health issues worldwide and include all age groups and ethnicities, even in industrialised and low-latitude countries, and about 1 billion people worldwide are estimated to have low vitamin D levels.[1,17] The reported prevalence in childhood periods ranged from 9% to 97% based on the definition criterion, the season, and the latitude of the study population on country. The highest prevalence of vitamin D deficiency was reported from Middle East in neonates, children and adolescent girls and adults.[18-21]

In our country, the prevalence of low vitamin D levels was different among regions and populations. Halicioglu et al found the prevalence of vitamin D deficiency (≤20 ng/mL) and insufficiency (20-29.9 ng/mL) in exclusively breastfed infants supplemented daily with 400 IU of vitamin D as 28% and 38.5%, while Akman et al reported the prevalence of vitamin D deficiency to be 14.5% and vitamin D insufficiency to be 22.5% in the 1-7 year age group.[9,10] Hatun et al and Olmez et al found the prevalence of vitamin D deficiency in healthy Turkish adolescent girls at the end of winter to be 65% and 40%, respectively.[11,12] Andiran et al reported that overall rate of deficiency (≤20 ng/mL) was 40% in their study population and adolescent girls had the highest prevalence of 64.8%.[8] One of the latest studies conducted by Karaguzel et al on vitamin D status in Turkey showed that the proportion of vitamin D deficiency (<20 ng/mL) in adolescent children was 82%, and girls had lower 25(OH)D levels than boys in northeastern Turkey.[13]

**Table 3** Seasonal prevalence of low serum 25(OH)D levels and mean monthly 25(OH)D levels in the children

| | **Spring n:207(%) (%95CI)** | **Summer n:52(%) (%95CI)** | **Autumn n:81(%) (%95CI)** | **Winter n:216(%) (%95CI)** | ***p*** |
|---|---|---|---|---|---|
| D vitamin levels±SD | 27.78±15.35 | 30.81±12.62 | 23.55±15.15 | 27.17±17.19 | <0.05 |
| | April 24.59±14.10 | July 34.42±12.04 | October 23.41±14.61 | January 29.89±15.23 | 0.01 |
| | May 32.90±16.81 | August 31.32±15.52 | November 24.34±12.66 | February 30.73±19.28 | |
| | June 28.40±14.93 | September 27.58±11.00 | December 22.92±17.26 | March 23.34±15.31 | |
| D vitamin levels<20 ng/mL | 69 (33.3)(27.2-40.0) | 8 (15.3)(8.0-27.5) | 45 (55.5)(44.7-65.8) | 97 (44.9)(38.2-51.8) | <0.001 |
| D vitamin levels<30 ng/mL | 129 (62.3)(55.5-68.6) | 26 (50.0)(36.8-63.1) | 60 (74.0)(63.5-82.3) | 138 (63.8)(57.2-70.2) | 0.058 |

CI: confidence interval, 25(OH)D: 25-hydroxyvitamin D, SD:standard deviation.
p<0.05, statistically significant

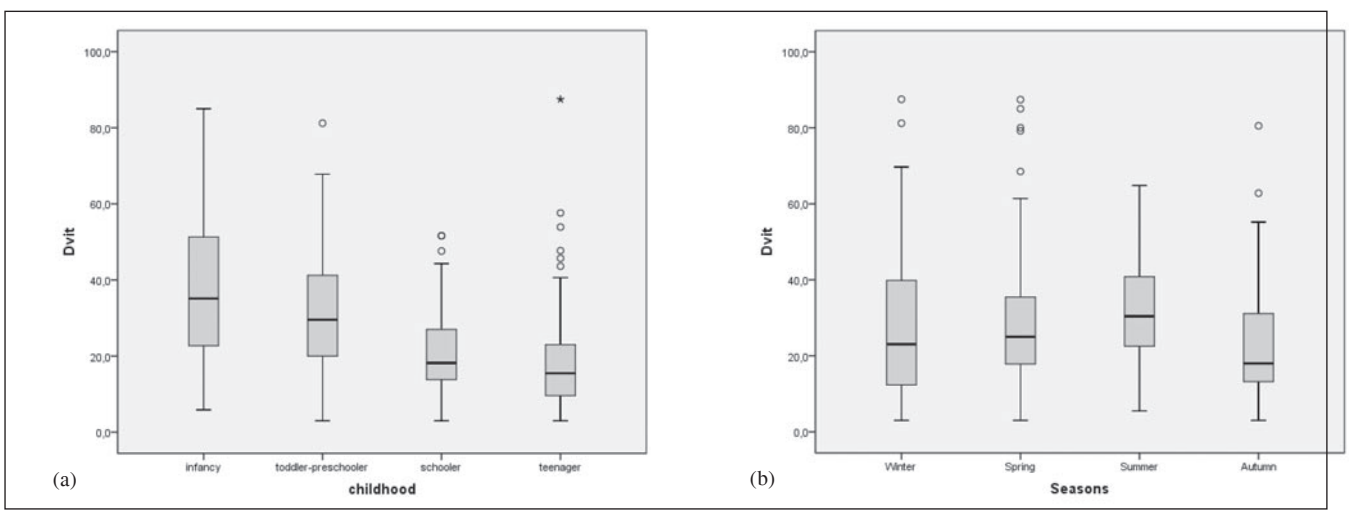


**Figure 1** Box plot of serum 25-OH-D levels according to the chilhood stages (a) and the seasons (b).

The study showed the overall proportion of vitamin D deficiency/insufficiency was 63.5%. Even though the lowest ratio was seen in the infant group, it was still high in consideration of the free vitamin D supplementation campaign carried on since 2005. The highest prevalence of vitamin D deficiency/insufficiency was detected in adolescent children as 86.5%, and 70.5% of girls, and 61.7% of boys in adolescence were vitamin D deficient. Our results show a high prevalence of hypovitaminosis D, similar to reports from other provinces and countries around the world.[22,23]

In Turkey, maternal vitamin D deficiency, unsupplemented and prolonged exclusive breastfeeding, limited and inadequate sunlight exposure, time spent indoors, and the effects of air pollution during autumn and winter time, socio-cultural factors (overcrowded families, smaller houses, lower family incomes, and lower parental education levels, a religious dress code in adolescents girls), low vitamin D intake, and obesity may play major roles in vitamin D status.[7,24-26]

Apart from all these, competitive entrance examinations for high school and university in Turkey lead children to attend preparatory classes and reduce their time spent in outdoor activities, and all of which would certainly contribute to low vitamin D status in adolescents.

This study has some limitations: (1) the subjects enrolled were not randomly selected, so our study population may not represent the whole population of children of the region; and (2) vitamin D supplementation, sunlight exposure, diet information were missing to interpret the observed ratio of vitamin D deficiency.

This study showed that vitamin D deficiency and insufficiency in Turkey represent an ongoing and important public health issue, not only in infancy but in all childhood periods, with the highest prevalence seen during adolescence which is also a crucial period for the achievement of peak bone mass.

## Conclusion

Taking into consideration of the positive effects of vitamin D on growing bones and non-bone health outcomes, it might be rational to speculate that the vitamin D supplementation started for newborns should be extended to children of all ages, and that routine screening and supplementation should be provided to prevent vitamin D deficiency in at-risk groups during winter and autumn months, when vitamin D synthesis is scarce.

## Conflict of Interest

The authors declare that they have no conflict of interests.

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