J Surg Med. 2019;3(8):579-582.
DOI: 10.28982/josam.555486

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Vitamin D status in infancy: What is the solution?

Bebeklikte D vitamini sorunu: Çözüm nedir?

Gökçe Celep [1], Zeynep Hülya Durmaz [2], Hatice Dörtok Demir [2], Yalçıner Erdoğan [1]

[1] Amasya University Medical Faculty, Sabuncuoğlu Şerefeddin Education and Research Hospital, Department of Pediatrics, Amasya, Turkey
[2] Amasya University Medical Faculty, Sabuncuoğlu Şerefeddin Education and Research Hospital, Department of Biochemistry, Amasya, Turkey

ORCID ID of the author(s)
GC: 0000-0001-6250-5096
ZHD: 0000-0002-3260-0030
HDD: 0000-0002-2231-5914
YE: 0000-0002-3476-7395

Corresponding author / Sorumlu yazar:
Gökçe Celep
Address / Adres: Sabuncuoğlu Şerefeddin Eğitim ve Araştırma Hastanesi, Kirazlıdere Mah., Merkez, Amasya, Türkiye
e-Mail: gokce4celep@yahoo.com

Ethics Committee Approval: This study was approved by the Institutional Committee of Scientific Researches of Amasya University Sabuncuoğlu Şerefeddin Education and Research Hospital with (No. 62949364-000-6222/2017, 19/10/2017).
Etik Kurul Onayı: Bu çalışma, Amasya Üniversitesi Sabuncuoğlu Şerefeddin Eğitim ve Araştırma Hastanesi Bilimsel Araştırma Kurumu Kurumsal Komitesi tarafından (No. 62949364-000-6222 / 2017, 19/10/2017) onaylandı.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 8/19/2019
Yayın Tarihi: 19.08.2019

Abstract

Aim: Vitamin D deficiency and insufficiency are common public health problems throughout the world. Besides important multisystemic metabolic effects, vitamin D is necessary for a healthy skeletal system. Various reasons cause vitamin D deficiency in infancy, and supplementation is one of the treatment options. A nationwide supplementation program has been implemented in Turkey since 2005. In this study, we aimed to evaluate the efficacy of this program in our city.

Methods: All infants aged between one and twelve months who were referred to the pediatric outpatient clinics of the hospital and tested for serum 25-(OH)-D levels between January 1, 2015 and December 31, 2016 were enrolled in the study. Patients with chronic illnesses were excluded. Data was obtained retrospectively from the hospital registry. In accordance with the criteria of American Academy of Pediatrics, patients were divided into three groups based on serum 25-(OH)-D levels as follows: 25-(OH)-D<15 ng/ml were considered deficient, 15.1<25-(OH)-D<20 ng/ml were considered insufficient and sufficiency was defined as 25-(OH)-D>20 ng/ml.

Results: The study group consisted of 265 infants. The mean age of the group was 7.53 (2.75) months. Approximately 15% (n=39) of the study group had vitamin D deficiency, 10.5% (n=28) had insufficiency and Vitamin D levels of 74.4% (n=198) of the group were sufficient. Serum 25 (OH) D levels did not differ with gender, age or season (P=0.12, P=0.65 and P=0.09, respectively). Vitamin D levels were sufficient in 78.5% (n=150) of the urban area residents and 69.6% (n=32) of the rural area residents, between which there was no significant difference (P=0.32).

Conclusion: Our results established that supplementation is one of the ways to avoid limitations affecting serum vitamin D levels. Supplementation with 400 IU/day Cholecalciferol is provided during the first year of life by the Turkish Ministry of Health, which we believe rendered gender, age, time of measurement and residential area insignificant in terms of 25(OH) D levels. This supplementation program may solve the problem of vitamin D insufficiency or deficiency among disadvantaged groups.

Keywords: Vitamin D status, Cholecalciferol supplementation campaign, Infancy, Turkey

Öz

Amaç: D vitamini eksikliği tüm dünyada yaygın bir halk sağlığı sorunudur. Vitamin D pek çok sistemi ilgilendiren etkilerinin yanında iskelet sistemi sağlığı için gereklidir. Bebeklik döneminde çeşitli nedenlere bağı olarak D vitamini eksikliği gelişebilir. Yeterlilik sağlamanın yollarından biri destek tedavisidir. Türkiye'de 2005 yılından beri tüm bebekleri kapsayan ulusal bir kampanya ile vitamin desteği ücretsiz olarak sağlanmaktadır. Bu çalışmada amaç kampanyanın ilimizdeki etkinliğini saptamaktır.

Yöntemler: Çalışmaya hastanenin Çocuk Sağlığı ve Hastalıkları polikliniklerine 1 Ocak 2015- 31 Aralık 2016 tarihleri arasında başvuran, 1-12 aylıkken 25- hidroksi- D düzeyi çalışılan tüm sağlıklı bebekler dahil edilmiştir. Altta yatan kronik hastalığı olanlar çalışma dışı bırakılmıştır. Veriler kayıt sisteminden geriye dönük olarak elde edilmiştir. Katılımcılar Amerikan Pediatri Akademisi'nin belirlemiş olduğu kriterlere dayanarak serum 25 (OH) D düzeylerine göre gruplara ayrılmıştır. Bu gruplar sırası ile "eksiklik: <15 ng/ml", "yetmezlik: 15,1-20 ng/ml" ve "yeterlilik: >20 ng/ml" olarak belirlenmiştir.

Bulgular: Çalışmada 265 bebek değerlendirilmiştir. Yaş ortalaması 7,53 (2,75) aydır. Bebeklerin %14,7'sinde (n=39) D vitamini eksikliği, %10,5'inde (n=28) yetersizliği saptanmıştır. Grubun %74,4'ünde (n=198) yeterli düzey sağlanmıştır. Cinsiyete, yaşa veya ölçüm yapılan mevsime göre gruplar arasında 25 (OH) düzeyleri açısından anlamlı fark saptanmamıştır (sırasıyla P=0,12; P=0,65 ve P=0,09). Kentsel bölge sakinlerinin %78,5'inde (n=150), kırsal kesimde yaşayanların %69,9'unda (n=32) 25 (OH) D düzeyleri yeterli olup, aralarında anlamlı fark saptanmamıştır (P=0,32).

Sonuç: Vitamin desteği D vitamini eksikliğini kolaylaştıracak etmenlerin yok edilmesini sağlayan etkin bir yoldur. Türkiye Cumhuriyeti Sağlık Bakanlığı tarafından sağlanan günlük 400 IU dozundaki Kolekalsiferol desteği ile cinsiyet, yaş, ölçüm zamanı, yaşanılan yer gibi olumsuz etki oluşturabilecek değişkenler bertaraf edilebilmektedir. Aynı uygulamanın hassas gruplar için de uygulanabileceği düşünülmektedir.

Anahtar kelimeler: D vitamini düzeyi, Ulusal D vitamini desteği kampanyası, Bebeklik dönemi, Türkiye

How to cite / Atıf için: Celep G, Durmaz ZH, Demir HD, Erdoğan Y. Vitamin D status in infancy: What is the solution? J Surg Med. 2019;3(8):579-582.

Introduction

Insufficient or deficient vitamin D is a common, important pediatric health problem throughout the world as well as in our country, despite our warm and sunny climate [1,2]. In the first year of life infants carry the risk of vitamin D deficiency (VDD) since breast milk cannot supply sufficient amounts [3,4]. Vitamin D is mainly synthesized in the skin under direct sunlight. VDD or vitamin D insufficiency (VDI) becomes inevitable unless adequate sunlight exposure and/ or vitamin D supplementation are provided. These problems result in poor bone health and multi-systemic problems related to cardiovascular, respiratory, and nervous systems as well as immunity [5]. A nationwide vitamin D supplementation campaign for providing free vitamin D drops for every infant in primary health care centers began in 2005. The recommended dose is 400 IU/day from the neonatal period to at least 1 year of age, preferably until 3 years old [5,6]. All infants were given free vitamin D (Cholecalciferol solutions that contain 133 IU vitamin D3 in one drop) drops and recommended to receive 400 IU (3 drops) daily to avoid vitamin D insufficiency (VDS). Following this campaign, the incidence of nutritional rickets, which used to be a crucial public health problem, decreased [7].

Serum 25- hydroxy vitamin D (25 (OH) D) is the primary metabolite of active vitamin D. Its half-life is longer than calcitriol (approximately three weeks vs 4-6 hours), which makes it a more reliable parameter to evaluate vitamin D status [8]. Serum 25 (OH) D concentration depends on direct sunlight exposure, seasons, latitude, skin pigmentation, clothing, maternal status, supplementation, or conditions that impair vitamin D metabolism and malabsorption. The cut-off value for 25 (OH) D is usually based on parathormone (PTH) levels to keep bone remodeling under control. Sufficient vitamin D level is the value that keeps PTH levels within normal ranges according to age [9]. Different authors or associations define vitamin D status with minor variations. The American Academy of Pediatrics (AAP) classified vitamin D status in the pediatric population using the following 25(OH) D levels: Severe deficiency : <5 ng/ml, deficiency: <15 ng/ml, insufficiency: 15 - 20 ng/ml, sufficiency: 20-100 ng/ml, excess: 101-150ng/ml, and intoxication: 150 ng/ml [10]. The Endocrine Society defined vitamin D status with a consensus statement: Deficiency: <30 nmol/ml (<12ng/ml), insufficiency: 30-50 nmol/l (12-20 ng/ml) and sufficiency: >50 nmol/ml (>20 ng/ml) as 1 ng/ml = 2.5 nmol/l. Here, the cut off value was <30 nmol/ml (<12ng/ml) to prevent nutritional rickets [11].

This study was designed to detect the efficacy of the supplementation programmed in our city based on AAP criteria ten years after the supplementation campaign began.

Materials and methods

This cross-sectional study with retrospective design was conducted in a small city located at 36^0 57' 06''- 36^0 31' 53'' longitude east and 41^{0}04' 54''- 40^0 16' 16'' latitude north, in the middle Black Sea region. [12]. The climate is sunny between May and October with minimal air pollution [13]. All infants aged between one and twelve months who were referred to the pediatric outpatient clinics of the hospital and tested for serum 25-(OH)-D levels between January 1, 2015 and December 31, 2016 were enrolled in the study. Patients with chronic illnesses and those in need of regular drug therapy except iron supplementation were excluded. None had failure to thrive or developmental delay. Data was obtained retrospectively from the hospital registry. Serum levels of 25 (OH) D levels (normal range: 20-100 ng/ml) were measured by electrochemiluminescence with the Roche modular analytical E 170, through venous blood samples. The specificity and sensitivity of the method is 98% and 95% respectively with coefficient of variation (CV) value 6.8. Venous blood samples were obtained from all patients after physical examination between 8.30-12.00 AM, per hospital rules. For the evaluation of results the participants were divided into groups according to their serum 25(OH) D levels based on the American Academy of Pediatrics (AAP) criteria. 25-(OH)-D<15 ng/ml were considered deficient, 15.1<25-(OH)-D<20 ng/ml were considered insufficient and sufficiency was defined as 25-(OH)-D >20 ng/ml.

This study was approved by the Institutional Committee of Scientific Researches of Amasya University Sabuncuoğlu Şerefeddin Education and Research Hospital with (No. 62949364-000-6222/2017, 19/10/2017).

Statistical analysis

Statistical analyses were performed with SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL, USA). The data were presented as frequencies, medians and minimum–maximum, range or mean (SD) by descriptive statistics, as needed. The variables were evaluated using visual (histograms, probability plots) and analytical methods (Kolmogorov Simirnov test) to determine normal distribution. As the serum 25 (OH) D levels were not normally distributed, Kruskall Wallis test was conducted to compare its levels among different groups and Mann Whitney U test was performed to test the significance of pair-wise differences using Bonferroni corrections to adjust for multiple comparisons. The Chi-square test or Fisher's exact test was used to compare variables among various groups. A P-value of less than 0.05 was considered statistically significant.

Results

The study group consisted 147 (55.3%) males and 118 (44.7%) females (n=265). The mean age of the group was 7.53 (2.75) months (1-12 months). 83 (31.3%) patients were younger than 6 months. 46 (19.4%) and 191(80.6%) patients lived in rural and urban areas, respectively.

The mean serum concentration of 25 (OH) D was 28.37 (12.49) ng/ml (3.30-94.5; median: 29.60 ng/ml) and none of the patients showed clinical signs of rickets. According to AAP classification, 14.7% (n=39) of the study group had VDD, 10.5% (n= 28) had VDI and 74.4% (n=198) had VDS. 9.8% (n=26) of the participants had VDD according to the Endocrine Society consensus statement (2015).

Vitamin D levels were 28.18 (12.23) ng/ml among the <6-month-old group and 28.45 (12.64) ng/ml among 6-12-month-old group. Deficiency was detected in 16.9% (n=14) of the younger group and 13.7% (n=25) of the older group. Age as a variable caused no significant difference between two groups (P=0.65).

The mean concentration of 25(OH) D levels were 28.40 (13.30) ng/ml in males and 30.10 (11.2) ng/ml in females; it did not differ with gender (P=0.12). 25(OH) D levels were sufficient in 80.5% (n=95) of the females and 70.1% (n=103) of the males. 10.2% (n=12) of the males and 18.4% (n=27) of the males had deficiency.

The serum levels of 25(OH) D were also compared among seasons. The mean concentration of 45 patients who were tested during winter was 24.32 (11.63) ng/ml. This value was 27.82 (12.66) ng/ml during spring, 30.73 (13.15; range: 4.2-73.0; median: 30.7) ng/ml during the summer and 28.81 (11.31) ng/ml during autumn. There was no significant difference in terms of serum 25(OH) D levels between seasons (P=0.09).

Mean concentration of serum vitamin D levels in those living in urban and rural areas were 28.88 (10.99) ng/ml and 28.40 (14.02) ng/ml, respectively. Vitamin D levels were sufficient in 78.5% (n=150) urban area residents and 69.6% (n=32) in rural area residents. There was no significant difference between two groups (P=0.32).

Vitamin D levels were also evaluated considering birth seasons. 50 of the participants were born in the winter, 47 in spring, 69 in the summer and 71 in autumn. The main concentration of 25 (OH) D levels were 31.88 (10.38); 25.60 (11.67); 27.22 (11.37); 30.24 (12.07), respectively. Approximately half of the vitamin D-deficient infants (48.4%; n=15) were born during summer, while 83.1% (n=59) of the autumn-born infants had sufficient serum vitamin D levels. Infants born in the summer and autumn had significantly better vitamin D levels (P<0.001). The vitamin D levels of all patients with respect to different variables are shown in Table 1.

Table 1: Distribution of vitamin D levels with regards to different parameters

Vitamin D Status	Deficiency n (%)	Insufficiency n (%)	Sufficiency n (%)	Total n	P-value
Gender					
Girls	12 (10.2)	11(9.3)	95 (80.5)	118	0.12
Boys	27 (18.4)	17 (11,6)	103 (70.1)	147	
Age (months)					
1-6 months	14 (16.9)	10 (12.0)	59 (71.1)	83	0.65
7-12 months	25 (13,7)	18 (9.9)	139 (76.4)	182	
Residence					
Rural area	9 (19.6)	5 (10.9)	32 (69.6)	46	0.32
Urban area	22 (11.5)	19 (9.9)	150 (78.5)	191	
Seasons of evaluation					
Winter	10.2 (22.2)	6 (13.3)	29 (64.4)	45	0.09
Spring	13(16.7)	7 (9)	58 (74.4)	78	
Summer	9 (10.7)	10 (11.9)	65 (77.4)	84	
Autumn	7 (12.1)	5 (8.6)	46 (79.3)	58	
Seasons of birth					
Winter	2 (4)	6 (12)	42 (84)	50	<0.001
Spring	9 (19.1)	7 (14.9)	31 (66)	47	
Summer	15 (21.7)	4 (5.8)	50 (72.5)	69	
Autumn	5 (7)	7 (9.9)	59 (83.1)	71	

Discussion

The main source of Vitamin D in the body is the photo conversion of 7- dehydrocholesterol to pre-vitamin D3 in the skin under direct sunlight [14]. The dietary intake is negligible in breastfed infants because the breast milk content of vitamin D is very low [3,4]. Formulas contain 400 U/ l vitamin D, and unless the infant consumes enough formula, deficiency becomes inevitable [3,5]. Insufficiency of maternal resources causes inadequate transplacental transition which contributes to poor vitamin D levels during infancy [15]. During the first year of life, direct sunlight exposure may be limited because of weather conditions or cultural habits. Supplementation seems to be the only way to avoid these limitations and the recommended dosage of 400 IU/ day is adequate if compliance is achieved. In this study group 74.4% of the participants had sufficient vitamin D levels. Comparison with respect to gender, age and seasons caused no difference, but mean concentration of 25 (OH) D changed significantly according to birth seasons.

The data of this study was classified according to AAP criteria and "deficiency" was defined as serum 25 (OH) D levels below 15 ng/ml. 14.7% of the participants were vitamin-D-deficient. A study from an industrialized city in north western Turkey reported that the mean 25 (OH) D level was 42.5 (25.8) ng/ml in infants aged between 84 and 365 days (263 (116)), and that 2.2% of all participants had vitamin D deficiency (<15ng/ml) [16]. Another study from Turkey defined deficiency as serum 25 (OH) D<20ng/ml, thus calculating deficiency rate as 57% [17]. In Hong Kong, the participants of a study did not receive vitamin D supplementation and the median serum 25(OH) D concentration at 3 months was 58 (IQR, 32-75) nmol/L. Among 155 infants, 52 (33.5%) had vitamin D deficiency, defined as serum 25(OH) D <50 nmol/L (<20 ng/ml) [18].

Deficiency starts prenatally because of poor vitamin D levels of pregnant women and 25 (OH) D levels of the cord blood are critically low even in sunny countries [15,19,20]. Turkish Ministry of Health recommends that vitamin D supplementation begin within the first days of life. Every infant is provided with 400 IU (3 drops) of Cholecalciferol solutions [6,16]. In this study group all participants were younger than one year and 74.4% of them had sufficient 25 (OH) D levels. Although supplementation is recommended throughout the whole life, after the first year, it is usually given up and a negative correlation emerges between 25 (OH) D levels and age [21]. Şahin et al. [1] reported sufficient vitamin D statuses in the first year of life but declared that the deficiency rate increased after the second year.

In this study 10.2% of the females and 18.4% of the males had deficiency, and the difference between genders was not significant. In the study of Sahin et al. [1], mean serum vitamin D levels were 30.5 (18.1) ng/ml in females and 34.7 (16.5) ng/ml in males in the first year of life. A study from İzmir had close results with a deficiency rate of 42.9% in males and 15.9% in females in a sample of 100 infants [17]. Many studies find that gender is key factor with increasing age, i.e. the increased deficiency rate among adolescent girls' [1,21].

As the main source of Vitamin D is skin synthesis under direct sunlight, seasons may cause significant changes in serum levels of 25 (OH) D [14]. Between February and May, the level is lower than other times of the year according to the data mining study of Şahin et al. [1]. In this study, the period of serum vitamin D level assessment had no significance, but season of birth proved important. In autumn-born-infants, sufficiency rate was higher than other seasons. Deficiency was frequent in infants born during winter. VDD in early infancy is related to maternal 25 (OH) D levels and studies showed that mothers who had given birth in summer and autumn had higher vitamin D levels [15]. Here, maternal 25 (OH) D levels of participants were not evaluated, which is one of the important limitations of this study. Unless patients lived at the same latitude, urban or rural areas of residence were not significant. This result was also compatible with a study from Ankara reflecting the data of a large cohort [22].

Limitations

This study has several limitations as it was retrospective and based on hospital registry. The type of vitamin D supplementation, dosage, sunlight exposure and nutritional habits of the participants were not taken in consideration. Vitamin D levels of the mothers and supplementation history during pregnancy are not known. Parathormone, calcium, phosphorus and alkaline phosphatase levels are not evaluated. The clinical statuses or bone mineral densities of the participants were not evaluated to directly predict bone health [23].

Conclusion

Our study established that supplementation is one of the ways to avoid limitations affecting serum vitamin D levels. Supplementation with 400 IU/day Cholecalciferol is provided during the first year of life by the Turkish Ministry of Health, which we believe rendered gender, age, time of measurement and residential area insignificant in terms of 25(OH) D levels. Studies show that these parameters become prominent when supplementation is given up with age or because of medical or financial reasons. Supplementation should be offered throughout the whole life to solve the public health problem of vitamin D deficiency or insufficiency.

References

1. Sahin ON, Serdar M, Serteser M, Unsal I, Ozpinar A. Vitamin D levels and parathyroid hormone variations of children living in a subtropical climate: a data mining study. Ital J Pediatr. 2018 ;44(1):40.
2. Lips P. Vitamin D status and nutrition in Europe and Asia. J Steroid Biochem Mol Biol. 2007;103(3-5):620-5.
3. Ala-Houhala M, Koskinen T, Terho A, Koivulo T, Visakarpi J. Maternal compared with infant vitamin D supplementation. Arch Dis Child 1986;61(12):1159-63
4. Reeve LE, Chesney RW, DeLuca HF. Vitamin D of human milk identification of biologically active form. Am J Clin Nutr. 1982;36(1):122-6.
5. Antonucci R, Locci C, Clemente MG, Chicconi E, Antonucci L. Vitamin D deficiency in childhood: old lessons and current challenges. J Pediatr Endocrinol Metab. 2018;31(3):247–60.
6. Hatun S, Ozkan B, Bereket A. Vitamin D deficiency and prevention: Turkish experience. Acta Pediatr. 2011;100(9): 1195-9.
7. Ozkan B, Doneray H, Karacan M, Vançelik S, Yildirim ZK, Özkan A, et al. Prevalence of vitamin D deficiency rickets in the eastern part of Turkey. Eur J Pediatr. 2009;168(1):95-100.
8. Holick MF. Vitamin D status:measurement, interpretation and clinical application. Ann Epidemiol. 2009; 19(2): 73–8.
9. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline, J. Clin. Endocrinol. Metab. 2011;96(7):1911–30.
10. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M, Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008;122(2):398–417.
11. Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. J Clin Endocrinol Metab. 2016;101(2):394–415.
12. Amasya Valiliği: Amasya Genel Bilgiler: http://www.amasya.gov.tr/cografi-konum. accessed in January 2019
13. Amasya Valiliği. Genel bigiler. https://www.mgm.gov.tr/veridegerlendirme/il-ve-ilceler-istatistik.aspx?m=AMASYA, accessed in January 2019
14. Zittermann A, Gummert JF. Nonclassical vitamin D action. Nutrients. 2010;2(4):408–25.
15. Nicolaidou P, Hatzistamatiou Z, Papadopoulou A, Kaleyias J. Low vitamin D status in mother–newborn pairs in Greece. Calcif Tissue Int. 2006;78(6):337-42.
16. Mutlu GY, Kuşdal Y, Özsu E, Çizmecioğlu FM, Hatun S. Prevention of Vitamin D deficiency in infancy: daily 400 IU vitamin D is sufficient. Int J Pediatr Endocrinol. 2011;(1):4.
17. Gülez P, Korkmaz HA, Özkök D, Can D, Özkan B. Factors Influencing Serum Vitamin D Concentration in Turkish Children Residing in İzmir: A Single-Center Experience. J Clin Res Pediatr Endocrinol. 2015;7:294-300.
18. Chan KC, Tam WH, Chan MH, Chan RS, Li AM. Vitamin D deficiency among healthy infants in Hong Kong: a pilot study. Hong Kong Med J. 2018;24 Suppl 3(3):32-5.
19. Güven A, Ecevit A, Tarcan A, Tarcan A, Özbek N. Yenidoğan bebeklerde kordon kanı vitamin D düzeyleri. Çocuk Sağlığı ve Hastalıkları Dergisi. 2011;54:55-61.
20. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr. 2005; 81(5):1060- 4.
21. Karagüzel G, Dilber B, Çan G, Ökten A, Değer O, Holick MF. Seasonal vitamin D status of healthy schoolchildren and predictors of low vitamin D status. J Pediatr Gastroenterol Nutr. 2014;58(5):654-60.
22. Akman A O, Tümer L, Hasanoğlu A, İlhan M, Çaycı B. Frequency of vitamin D insufficiency in healthy children between 1 and 16 years of age in Turkey. Pediatrics International. 2011;53(6):968–73.
23. Yenilmez E, Çetinkaya RA. Evaluation of initial results of naïve HIV-infected patients regarding bone health. J Surg Med. 2019;3(5):384-9.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine