Nobel Med 2022; 18(3): 161-166

ALTERATIONS IN 25(OH) VITAMIN D CONCENTRATIONS AND SEASONAL DIFFERENCES ACCORDING TO AGE GROUPS IN TURKEY

Murat Kaytaz[1], Hacer Eroğlu İçli[2], Emre Akkaya[1], Evin Ademoğlu[1], Sema Genç[1]

[1]*Istanbul University Istanbul Faculty of Medicine, Department of Biochemistry, Çapa, Istanbul, Türkiye*
[2]*Bakırköy Mazhar Osman Mental Health and Neurological Diseases Education and Research Hospital, Istanbul, Türkiye*

ABSTRACT

Objective: *We aimed to establish reference ranges of 25(OH) vitamin D levels in childhood and adults including age-sex-specific partition, also to evaluate the seasonal variations.*

Material and Method: *The study comprised one hundred eighty-one thousand six hundred sixteen venous blood samples from residual material of the Istanbul Public Health Laboratory workflow. The study group was stratified according to age groups; Group 1; 0-2, group 2; 3-10 years, group 3; 11-20 years, group 4; 21-50 years group 5; 51-70 years and group 6; over 70 years of age.*

Results: *25(OH) vitamin D concentration of all study group was 21.7±13.3 ng/mL, being significantly lower in women compared with men (21.35±13.52 ng/mL vs 22.54±12.5 ng/mL, p=0.008). In entire group, the deficiency rate was 43.8%, and 44.0%, the insufficiency rate was 29.4% and 34.8%, and severe deficiency rate was 11.4% and 4.9% for women and men respectively. The severe deficiency, insufficiency and sufficiency rates were significantly different between females and males (p=0.000 for all). The lowest deficiency rate was in 0-2 age group, 25.2% and 14.6%, and the highest in 11-20 year age group (57.2% and 54.4%). The deficiency rates were significantly different except the subjects over 70 years. The vit-D levels of March was significantly lower than October (p=0.001).*

Conclusion: *Serum 25 (OH) vit-D levels contribute greatly to clinical practice throughout the lifetime. Serum vit-D determination should be measured periodically especially in childhood, adolescence and adulthood, and legally mandatory food supplementation may meet a great contribution for public health.*

Keywords: *25(OH) vitamin D deficiency, age groups, seasonal variation.*

CORRESPONDING AUTHOR: Sema Genç Istanbul University Istanbul Faculty of Medicine, Department of Biochemistry, Çapa, Istanbul nsgenc@hotmail.com

MK https://orcid.org/0000-0001-8355-8285 | HEİ https://orcid.org/0000-0002-9775-1710 | EA https://orcid.org/0000-0002-3117-4359

EA https://orcid.org/0000-0003-2933-3119 | SG https://orcid.org/0000-0002-2577-9263

DELIVERING DATE: 02 / 06 / 2021 • **ACCEPTED DATE:** 22 / 10 / 2021

TÜRKİYE'DE YAŞ GRUPLARINA GÖRE 25(OH) VİTAMİN D KONSANTRASYONLARINDAKİ DEĞİŞİMLER VE MEVSİMSEL FARKLILIKLAR

ÖZET

Amaç: Bu çalışmada Türk çocukları ve erişkinlerinin yaş ve cinse özgü 25 (OH) D vitamini düzeylerinin değerlendirilmesi ve yaz ve kış aylarındaki değişimin gösterilmesi amaçlandı.

Materyal ve Metot: İstanbul Halk Sağlığı Laboratuvarı'na başvuran yüz seksen bir bin altı yüz on altı kişi (0-95 yaş) çalışma grubunu oluşturdu. Çalışma grubu; 0-2 yaş; 3-10 yaş; 11-20 yaş; 21-50 yaş; 51-70 yaş; 70 yaş üstü ve kadın ve erkek olarak klasifiye edildi.

Bulgular: Tüm çalışma grubunun 25 (OH) D vitamini konsantrasyonu 21,7±13,3 ng/mL olup, kadınlarda erkeklere göre anlamlı derecede düşük bulundu (21,35±13,52 ng/mL vs 22,54±12,5 ng/mL, *p*=0,008). D vitamini eksiklik prevalansı kadınlarda ve erkeklerde sırasıyla %43,8 ve %44,0, yetersizlik oranı %29,4 ve %34,8, şiddetli eksiklik oranı %11,4 ve %4,9'du. (tümü için *p*<0,001). Yaş grupları içinde en düşük eksiklik oranı %25,2 ve %14,6 ile 0-2 yaş grubunda iken en yüksek 11-20 yaş grubunda (%57,2 ve %54,4) bulundu. Eksiklik oranları 70 yaş üstü kişiler dışında önemli ölçüde farklıydı. Ayrıca Mart ayı vitamin-D seviyeleri Ekim ayı seviyelerine göre önemli ölçüde düşüktü (*p*<0,001).

Sonuç: Klinik uygulamada Serum 25 (OH) vitamin-D seviyelerinin yaşam boyu önemli rolü olup, özellikle çocukluk, ergenlik ve yetişkin dönemlerde serum vitamin-D tayinin periyodik olarak ölçülmesi çok önem taşımaktadır. Bu nedenle yasal olarak zorunlu olarak gıdalara D vitamin takviyesi yapılmasının toplum sağlığı açısından çok büyük önemi vardır.

Anahtar kelimeler: 25-hidroksi vitamin D, yaş grupları, mevsimsel değişim.

INTRODUCTION

Vitamin D is a neurohormone with participates in calcium and phosphorus balance through actions of the intestine, kidney, and bone. The measurement of 25 hydroxy vitamin D (25(OH) vit-D) is accepted as the best indicator to assess vitamin D status of the body, which has a half-life of 2-3 weeks. Since, 1,25-dihydroxy vitamin D (calcitriol) is the active form, cannot represent the vitamin D status due to its short half-life and low circulatory concentration.[1] In recent years, the extra skeletal roles of vitamin D including glucose metabolism, development of tumors and metastasis, and also autoimmune processes have been revealed.[2,3]

Vitamin D deficiency affects people with every age and sex in worldwide, the controlling the blood level of vitamin D is quite complicated in childhood and adolescent periods due to alterations in physical size, organ maturity, differences in metabolism, and immune and hormonal changes.[4] For 25(OH) vit-D deficiency, several cut-off values have been introduced, even no consensus on definition vit-D status.[5,6] However, in this study, the cut-off values of suggested by the Endocrine Society Clinical Practice Guidelines is used which is lower 20 ng/mL for deficiency, 21-29 ng/mL for insufficiency, higher than 30 ng/mL for sufficiency.[6] There are several population studies to evaluate the deficiency and insufficiency rates in childhood, and adults.[7-10]

For this purpose, we aimed to establish reference ranges of 25(OH) vit-D levels in childhood and adult subjects including age-sex-specific partition. Also the seasonal variations of serum 25(OH) vit-D concentrations were evaluated at summer and winter.

MATERIAL AND METHOD

Study Population

The study comprised one hundred eighty-one thousand six hundred sixteen venous blood samples from residual material of the Istanbul Public Health Laboratory workflow (132,443 women, and 49,173 men, median age was 40 and 43 years for women and men, respectively range 0-95 years). The study group was stratified according to age groups; Group 1; 0-2 years, group 2; 3-10 years, group 3; 11-20 years, group 4; 21-50 years group 5; 51-70 years and group 6; over 70 years of age. Of the study group 0.2% were less than 2 years of age; 5.3 % were aged 3-10 years; 12.1% were aged 11-20 years; 48.5% were aged 21-50 years, 25.7% were aged 51-70 years and 8.1% were over 70 years of age. For measuring 25(OH) vit-D, venous blood samples collected into serum separator tubes (SST, Becton Dickinson), centrifuged for 10 minutes at 2000g, and the supernatants were used for measurement of serum 25(OH) vit-D. Fasting was not required for these analyses.

Our study enclosed healthy children and adults who resided in Istanbul at 41° N latitudes. The subjects who have history of acute or chronic illnesses, metabolic disease such as type 1 or type 2 diabetes or renal insufficiency were excluded from the study. In this study, 25(OH) vit-D levels were classified according to the Endocrine Society's guideline recommending cut-off levels of >30 ng/mL, 20-30 ng/mL, and <20 ng/mL, respectively.[6]

This study was approved by the Ethical Committees of Turkish Ministry of Health, Health Directorate of Istanbul, Public Health Laboratory#1 and Istanbul University, Istanbul Faculty of Medicine Faculty (Date:21/02/2020, No:2020/311), and the informed consent was received from the participiants.

Methodology

25(OH) vit-D levels were measured with two-step competitive binding immunoenzymatic assay using Beckman Coulter DXI 800 (Beckman Coulter, USA). The within-run and between day CVs were 4.7% and 8.1% at low (15.5 ng/ml) and 3.5% and 6.5% at high levels (53.0 ng/mL) using manufacturers' low and high level vit-D controls respectively.

Statistical Analysis

The data were analyzed using SPSS 21 (SPSS, Chicago, IL, USA). The results were expressed as mean±SD. The normality of the data distribution was evaluated by the Kolmogorov-Smirnov test. The chi-square (χ^2), Kruskal–Wallis variance analysis and a post-hoc analysis using Mann–Whitney U-test were performed for unequal variances. Correlation analyses were carried out by the Spearman test. Statistical significance was defined as $p<0.05$.

RESULTS

Figure 1 presents 25(OH) vit-D levels in different age groups of study group. The mean 25(OH) vit-D concentration of all study group was 21.7±13.3 ng/mL being significantly lower in women compared with men (21.35±13.52 ng/mL vs 22.54±12.5 ng/mL, $p=0.008$ respectively). In entire group, the average vit-D level was 31.48±13.81 ng/mL in 0-2 years group, dropped to 20.7 ng/mL in 3-10 years age group, and the lowest concentration was obtained in 11-20 years age group. In adult period, higher 20 years of age, mean 25(OH) vit-D levels ranged between 20.1 to 24.3 ng/mL, the higher levels were found in 70 years and over.

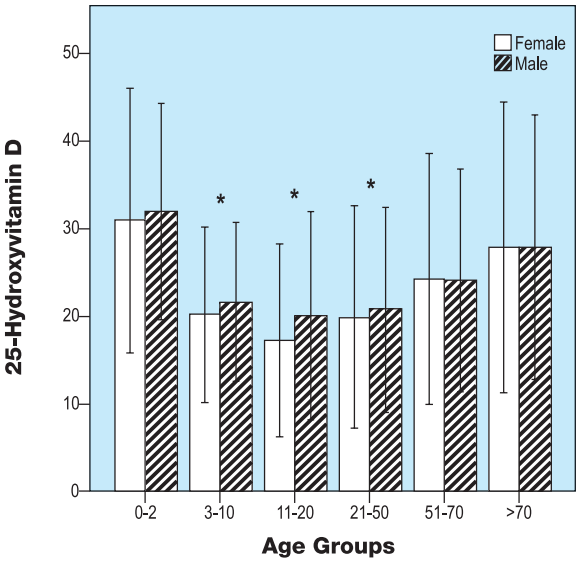

Figure 1. 25(OH) vit-D levels of females and males in different age groups. Each value represents the mean ± SD.
*p<0.05 significantly different than women.

In entire group, the deficiency rate was 43.8%, and 44.0%, the insufficiency rate was 29.4% and 34.8%, and severe deficiency rate was 11.4% and 4.9% for women and men respectively, and approximately 16.0% of the population had sufficient level of vitamin D (Table). The severe deficiency rate, insufficiency and sufficiency rates were significantly different between females and males ($p=0.001$ for all). When we investigated the deficiency rates in age groups; the lowest deficiency rate was seen in 0-2 age group, as 25.2%, and 14.6% in girls and boys, and the highest deficiency in 11-20 year age group (57.2% and 54.4%), the insufficiency rate in 3-10 age group (41.0%, 34.9%) for boys and girls, respectively. The insufficiency rates of 50-70 year and over 70 years age groups were lower than 36.1% for both sexes, respectively. The different deficiency rates have found between both genders except the subjects over 70 years. The significantly different insufficiency rates were observed in all age groups of females and males except 0-2 years age group.

Table. The prevalances of 25-(OH) vitamin D deficiency in different age groups in Turkish population.

Age Groups (years)	Prevalances of 25-(OH) vitamin D			
	Severe Deficiency (%)	Deficiency (%)	Insufficency (%)	Sufficiency (%)
0-2	1.7	20.0	29.5	48.8
3-10	3.9	48.0	38.1	10.1
11-20	12.2	56.1	24.9	6.8
21-50	12.4	47.2	28.4	12.0
51-70	5.8	36.5	35.8	21.9
>70	5.1	26.2	34.5	34.2
Total	**9.6**	**43.8**	**30.9**	**15.7**

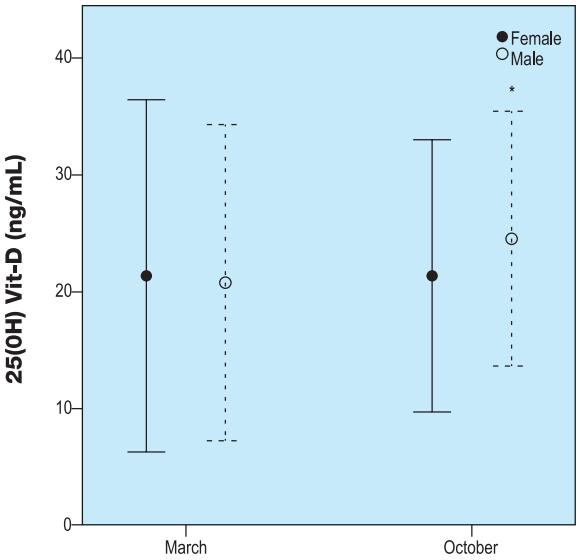

Figure 2. Seasonal changes in 25-(OH) vit-D levels in men and women bars represents standart deviation.
*p<0.05 significantly different 25-(OH) vit-D levels were found in March compared to October for men.

The 25(OH) vit-D levels varied significantly across different seasons (Figure 2). In entire group, the mean 25(OH) vit-D levels of March was significantly lower than those of October (21.2±14.7 vs 22.2±14.7 ng/mL, p=0.000). While 25(OH) vit-D levels of women remained unchanged for the March and October (21.35±15.1 and 21.35±1.7), the decreased 25(OH) vit-D levels were found in March compared to October for men (p<0.001). When the deficiency rates were evaluated, severe deficiency, insufficiency rates were also significantly different between two seasons (11.2% vs 8.0%, and 26.5% vs 35.6%).

DISCUSSION

In this study, the 25(OH) vit-D levels have been evaluated through childhood and adults in 181,616 subjects, so that this is one of the largest comprehensive population-based study which is done in Turkey. The highest 25(OH) vit-D concentrations were found in 0-2 years of girls and boys. The 25(OH) vit-D levels declined through the years until to about 50 years of age, then showed elevation in subjects older than 50 years. In utero, the requirement of vit-D is met from the mother through the placenta, and if the mother has a sufficient level of vit-D, the infant has born with a sufficient level of vitamin D due the 2-3 weeks of half-life of 25(OH) vitamin D.[6] Depending our findings, the lower vit-D deficiency rate obtained in the 0-2 age group, the low rate of vit-D deficiency can be explained that the regular follow-up of babies in the first year and the routine usage of vit-D supplements for breast-fed babies in the 0-2 age group. However, in a meta-analysis, vit-D deficiency was reported between 2-58% for neonates and 30-76% for mothers.[11] The mean 25(OH) vit-D concentration was the lowest in 11-20 years age group for girls and boys. Additionally, 25(OH) vit-D levels of females in all age groups were lower than those of males (p=0.001, for all groups) in good agreement with the other studies except 0-2 year age group.[12-14] However, the studies conducted in different regions of the Turkey, have reported lower vit-D levels compared to our results.[15,16] Even though, Lippi *et al* reported the lower deficiency and severe deficiency rates in Caucasian, and Italian children and adolescents.[17,18] compared to our results, there are studies to report similar or higher 25(OH) vit-D results in children and adolescent periods.[9,15,19,20] The reasons for the prevalence of vit-D deficiency in children and adolescents are the acceleration of growth, skeletal development, a significant increase in calcium and phosphorus need, as well as changing nutritional factors during childhood. Moore *et al*. also noted the differences of vit-D intake in girls and boys during adolescence period, therefore, girls get less vitamin D than boys at the same age group, and only 32% of girls get enough vitamin D from the diet.[21]

The Institute of Medicine (IOM) report points out the circulatory 25(OH) vit-D levels should be higher than 20 ng/mL in order to provide skeletal health.[22] However, depending our findings, 25(OH) vit-D levels of the subjects between 20-50 years of age, were 19.9 ng/mL, and 20.8 ng/mL for females and males respectively. According to the results of the NHANES study, 25(OH) vit-D deficiency of 20-59 age group was 24%, and it was significantly lower than our deficiency rate, which was about 44%, however, severe deficiency was almost similar compared to our results.[23,24] The previous studies conducted in different regions of Turkey, similar or higher deficiency rates were reported in adults.[25-27] In our previous cross-sectional study conducted 20-85 years of subjects from urban and rural parts of Turkey, we reported higher vit-D deficiency rates compared to the current study because of difference of the sampling method of two studies. TURDEP-II was performed with samples from rural and urban parts of Turkey, whereas, the samples of current study comprised the subjects from different parts of Istanbul.[28]

Depending our results, over the age of 50 years, the prevalence of 25(OH) vit-D deficiency decreased from 50% to 27% for those aged 70 and over, whereas, the insufficiency rate increased in older people compared to young adults. Atli *et*

al reported 35% of deficiency rate was in geriatric patients for both genders.[26] However, the surveys in worldwide have been shown that the insufficiency rate was higher especially in elderly people, varying in different countries. The studies from North America reported the lower rates of 25(OH) vit-D deficiency and insufficiency in the middle-aged population compared to our findings, while studies performed in European elderly revealed the lower vit-D concentrations compared to their American peers.[29-31]

In geriatric subjects, the studies have also pointed out that the significance of the living conditions on the plasma concentration of vitamin D. The people who lives in a nursing homes have been exhibited the lower 25(OH) vit-D and higher deficiency rates due to indoor life, insufficient sun exposure, and inadequate intake of vit-D from diet. However, the results of studies on vitamin D deficiency in the geriatric population are not consistent. While in a multi-center study, the prevalence of vit-D deficiency was reported as 80% in 80-year old women who live in nursing home in another study from Ireland, the deficiency rate was reported as 40% in same age group.[26,32,33]

When the 25(OH) vit-D levels have been investigated according to the seasons, the increased 25(OH) vit-D levels were observed in October compared with March in men, but, these differences were not observed for women. There are studies to show the lower 25(OH) vit-D levels in the months of winter and autumn and higher levels especially at the end of the summer.[34-36] We also demonstrated the significant differences between men and women in March and October, similar to the findings of Kunt *et al*.[34] When the deficiency rates were evaluated, the deficiency rates were 47.5% and 40.0%, and insufficiency rates 26.5% and 35.6%, and severe deficiency rate was 11.2% and 8.0% for females and males at the end of the winter. In a study conducted in Turkey, Erol *et al* reported much higher deficiency rate at the end of winter, but, the insufficiency rate was almost similar to our findings.16 Nevertheless, several studies have revealed the increased 25(OH) vit-D deficiency in winter time compared to summer.[24,37,38] In a study conducted in French people older than 60 years of age, the deficiency rate was reported as 31%, being the highest at central and Northern part of France and the lowest at southern part depending on the differences of the sun exposure and latitudes at different regions of France.[39] The variability in 25(OH) vit-D levels through the seasons can be explained by the changes in sunlight across the months. Sunlight is the primary source of vitamin D synthesis, and reduced UV presence has been shown in the northern hemisphere in winter.[40] Some European countries which are situated above 37° North have insufficient sunlight due to the reduced amount of solar UV that arrives the earth during winter time, leading to reduced dermal vit-D synthesis.[41] Therefore, the synthesis of vitamin D is also actually zero in people who reside in Istanbul during autumn and winter times, so that the dietary sources of vitamin D gain priority in synthesis of vitamin D.

All these reasons bring to the agenda the importance of fortification of foods with vitamin D in terms of public health, especially for countries where UV intake is insufficient due to geographical reasons or for countries where dietary habits or socio-economic conditions are insufficient. However, the fortification policies can change across the countries, while in some countries vit-D supplementation is mandatory, in some countries, fortification with vit-D is voluntary, or only allowed for some kind of foods.[42,43] Although there have been several randomized controlled studies showing the effects of vitamin D supplementation on reducing cardiovascular complications, respiratory tract infections, pregnancy complications and mortality, still we need future studies to explore the effect of vitamin D fortification and dose-response relations.[44]

This study has some limitations and strengths. The strengths of our study are its large sample size with almost equal numbers of both sexes in all age groups. Nevertheless, the lack of detailed information about subjects including the body mass index, and nutritional habits, and comorbidities are the most important limitations of the study.

CONCLUSION

The results of this study are important in that the measurement of serum 25 (OH) vit-D levels contribute greatly to clinical practice throughout the lifetime. In order to prevent deficiencies of this vitamin and to prevent its adverse effects on general health, serum vit-D determination should be measured periodically especially in childhood, adolescence and adulthood, and legally mandatory food supplementation may meet a great contribution for public health.

*The authors declare that there are no conflicts of interest.

REFERENCES

1. Saggese G, Vierucci F, Prodam F, et al. Vitamin D in pediatric age: consensus of the Italian Pediatric Society and the Italian Society of Preventive and Social Pediatrics, jointly with the Italian Federation of Pediatricians. Italian J Pediatrics 2018; 44: 51 https://doi.org/10.1186/s13052-018-0488-7.
2. Jeon SM, Shin EA. Exploring vitamin D metabolism and function in cancer. Exp Mol Med 2018; 50: 20. doi: 10.1038/s12276-018-0038-9
3. Bikle DD. Extraskeletal actions of vitamin D. Ann NY Acad Sci 2016; 1376: 29-52.
4. Jung B, Adeli K. Clinical laboratory reference intervals in pediatrics: the CALIPER initiative. Clin Biochem 2009; 42: 1589-1595.
5. Canadian Paediatric Society. Vitamin D supplementation: recommendations for Canadian mothers and infants. Paediatr Child Health 2007; 12: 583-598.
6. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an European Society Clinical Practice guideline. J Clin Endocrinol Metab 2011; 96: 1911-1930.
7. Higgins V, Truong D, White-Al Habeeb NMA, et al. Pediatric reference intervals for 1,25-dihydroxyvitamin D using the DiaSorin LIAISON XL assay in the healthy CALIPER cohort. Clin Chem Lab Med 2018; 56: 964-972.
8. Vierucci F, Del Pistoia M, Fanos M, et al. Vitamin D status and predictors of hypovitaminosis D in Italian children and adolescents: a cross-sectional study. Eur J Pediatr 2013; 172: 1607-1617.
9. Satman I, Colak Ozbey N, Boztepe H, et al. Prevalance and of vitamin D deficiency and associated factors in Turkey. Endocrine Abstracts 2013; 32: 135 DOI: 10.1530/endoabs.32.P135
10. Kumar J, Muntner P, Kaskel FJ, Hailpern SM, Melamed ML. Prevalance and associations of 25-hydroxy vitamin D deficiency in US children: NHANES 2001-2004. Pediatrics 2009; 1214: 362-370.
11. Alpdemir M, Alpdemir MF. Vitamin D deficiency status in Turkey: A meta-analysis Int J Med Biochem 2019; 2: 118-131.
12. Du X, Greenfiels H, Fraser DR, et al. Vitamin D deficiency and associated factors in adolescent girls in Beijing. Am J Clin Nutr 2001; 74: 494-500.
13. Harkness LS, Cromer BA. Vitamin D deficiency in adolescent females. J Adolesc Health 2005; 37: 75.
14. Mansbach JM, Ginde AA, Camargo AC. Serum 25-Hydroxyvitamin D Levels Among US Children Aged 1 to 11 Years: Do Children Need More Vitamin D? Pediatrics 2009; 124: 1404–1410.
15. Bozkurt S, Alkan BM, Yıldız F, et al. Age, sex, and seasonal variations in the serum Vitamin D3 levels in a local Turkish Population. Arch Rheumatol 2014; 29: 14-19.
16. Erol M, Yigit O, Kucuk SH, Gayret OB. Vitamin D Deficiency in children and adolescents in Bagcilar, Istanbul. J Clin Res Pediatr Endocrinol 2015; 7: 134-139.
17. Lippi G, Montagnana M, Targher G. Vitamin D deficiency Italian children CMAJ 2007; 177: 1529-1530.
18. Lippi G, Montagnana M, Meschi T, Borghi L. Vitamin D concentration and deficiency across different ages and genders. Aging Clin Exp Res 2012; 24: 453-461.
19. Marrone G, Rosso I, Moretti R, Valent F, Romanello C. Is vitamin D status known among children living in Northern Italy? Eur J Nutr 2011; 51: 143-149.
20. Gonzalez-Gross M, Valtuena J, Breidenassel C, Moreno LA, HELENA Study group. Vitamin D status among adolescents in Europe: the Healthy life style in Europe by Nutrition in Adolescence study. Br J Nutr 2012; 107: 755-764.
21. Moore C, Murphy M, Keast D, Holick MF. Vitamin D intake in the United States. J Am Diet Assoc 2004; 104: 980-983.
22. IOM (Institute of Medicine) 2011 Dietary reference intakes for calcium and vitamin D. Washington DC: The National Academies Press.
23. Ginde AA, Liu MC, Camargo CA. Demographic differences and trends of vitamin D insufficiency in the US population, 1988-2004. Arch Intern Med 2009; 169: 626-632.
24. Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum hydroxyvitamin D status of adolecents and adults in two seasonal subpopulations from NHANES III. Bone 2002; 30: 771-777.
25. Hekimsoy Z, Dinc G, Kafesciler S, et al. Vitamin D status among adults in the Aegean region of Turkey. BMC Public Health 2010; 10: 782.
26. Atli T, Gullu S, Uysal AR, Erdogan G. The prevalance of vitamin D deficiency and effects of ultraviolet light on vitamin D levels in elderly Turkish population. Arch Gerontol Geriatr 2005; 40: 53-60.
27. Alagol F, Shihadeh Y, Boztepe H, et al. Sunlight exposure and vitamin D deficiency. J Endocrinol Invest 2000; 23; 173-177.
28. Satman I, Omer B, Tutuncu Y, et al. TURDEP-II Study Group. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013; 28: 169-180.
29. Hyppönen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. Am J Clin Nutr 2007; 85: 860-868.
30. Rucker D, Allan JA, Fick GH, Hanley DA. Vitamin D insufficiency in a population of healthy Western Canadians. CMAJ 2002; 166: 1517-1524.
31. Mosekilde L. Vitamin D and the elderly. Clin Endocrinol (Oxf) 2005; 62: 265-281.
32. Bruyere O, Decock C, Delhez M, et al. Highest prevalence of Vitamin D inadequacy in institutionalized women compared with non-institutionalized women: a case-control study. Womens Health (London Engl) 2009; 5: 49-54.
33. Cashman KD, Muldowney S, McNulty B, et al. Vitamin D status of Irish adults: findings from National adult Nutrition Survey. Br J Nutr 2012; 109: 1248-1256.
34. Kull M, Kallikorm R, Tamm A, Lember M. Seasonal variance of 25-(OH) vitamin D in the general population of Estonia, a Northern European country. BMC Public Health 2009; 9: 22 doi:10.1186/1471-2458-9-22.
35. Elizondo-Montemayor L, Castillo EC, Rodríguez-López C, et al. Seasonal Variation in Vitamin D in Association with Age, Inflammatory Cytokines, Anthropometric Parameters, and Lifestyle Factors in Older Adults. Mediators of Inflammation 2017; 5719461, https://doi.org/10.1155/2017/5719461.
36. Okan S, Okan F, Demir O. Relationship Between the Vitamin D Status and the Season, Place of Living, Age, Gender, and Chronic Disease. Erciyes Med J 2020; 42: 78–83. DOI: 10.14744/etd.2019.45577
37. Andersen R, Brot C, Jakobsen J, et al. Seasonal changes in vitamin D status among Danish Adolescent girls and elderly women: the influence of sun exposure and vitamin D intake. Eur J Clin Nutr 2013; 67: 270-274.
38. Guillemant J, Le HT, Maria A, et al. Wintertime vitamin D deficiency in male adolescents: effect of parathyroid function and response to Vitamin D3 supplements. Osteoporosis Int 2001; 12: 875-879.
39. Chapuy MC, Preziosi P, Maamer M, et al. Prevalence of Vitamin D Insufficiency in an Adult Normal Population. Osteoporos Int 1997; 7: 439–443.
40. O'Neill CM, Kazantzidis A, Ryan MJ, et al. Seasonal Changes in Vitamin D-Effective UVB Availability in Europe and Associations with Population Serum 25-Hydroxyvitamin D. Nutritients 2016; 8: 533
41. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers and cardiovascular disease. Am J Clin Nutr 2004; 80: 1678S-1688S.
42. Jääskeläinen T, Itkonen ST, Lundqvist A, et al. The positive impact of general vitamin D food fortification policy on vitamin D status in a representative adult Finnish population: evidence from an 11-y follow-up based on standardized 25-hydroxyvitamin D data. Am J Clin Nutr 2017; 105: 1512–1520.
43. Black LJ, Walton J, Flynn A, Cashman KD, Kiely M. Small increments in vitamin D intake by Irish adults over a decade show that strategic initiatives to fortify the food supply are needed. J Nutr 2015; 145: 969–976.
44. Autier P, Mullie P, Macacu A, et al. Effect of vitamin D supplementation on non-skeletal disorders: a systematic review of meta-analyses and randomized trials. Lancet Diabetes Endocrinol 2017; 5: 986–1004.