DOI: https://doi.org/10.2298/SARH241123012K
UDC: 613.2:577.161.2; 616-084

CURRENT TOPIC / АКТУЕЛНА ТЕМА

Public health aspects of vitamin D

Marko Koprivica[1,2], Ana Miljković[1,3]

[1]University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia;
[2]Institute of Public Health of Vojvodina, Novi Sad, Serbia;
[3]Health Center of Novi Sad, Novi Sad, Serbia

SUMMARY
In recent decades, the prevalence of known but insufficiently treated diseases and disorders has increased significantly. However, there is the manifestation of disorders whose causes were already known but were not sufficiently controlled. Public health problems are becoming more frequent and more current. Among the current public health problems, many symptoms and diseases are linked to certain vitamins, unhealthy lifestyles, and other contributing factors. Vitamin D is one of the current public health topics that has recently attracted increasing scientific attention. A biologically essential compound, vitamin D affects many functions in the human body, and the deficiency of this vitamin is widespread throughout the world. Vitamin D can be found in the form of dietary supplements, but it is also recognized as a registered medication in some contexts.
Keywords: disease prevention; public health; vitamin D

INTRODUCTION

The COVID-19 pandemic has highlighted numerous public health issues and significantly increased interest in preventive health measures, both at the personal and global level. This pandemic has prompted people to think about the importance of preventive measures in the occurrence of diseases [1]. One of the leading public health problems was vitamin D deficiency. It is a liposoluble, hydrophobic compound that can be found in two main forms: vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol). The most common source of vitamin D is food of animal origin such as tuna, sardines, cod, and turkey. It is also found in plants, but it is scarcely bioavailable in these foods. We should not omit the fact that a large part of vitamin D is created endogenously through exposure to sunlight [2]. Vitamin D affects numerous organ systems, but lately its anti-cancer role and its great influence on the immune system have been highlighted. It also affects the cardiovascular, endocrine, and immune system, but it affects other organ systems as well, leading to a wide range of diseases. Moreover, numerous inflammatory bowel diseases, and some liver and lung diseases can also lead to a decrease in levels of vitamin D (Table 1) [3].

Table 1. General guidelines for preventing vitamin D deficiency and recommended daily intake [5]

Age (years)	Vitamin D recommended daily intake (IU)
< 1	≤ 400
1–18	≤ 1000
18–75	≤ 2000
> 75	≤ 4000

PUBLIC HEALTH REVIEW AND PUBLIC HEALTH PLANS AND RECOMMENDATIONS

Obesity is another condition associated with vitamin D deficiency, as shown by meta-analytical studies that included over 24,000 participants under the age of 18 [4]. These studies clearly indicate that deficiency in obese individuals is greater than in those who are optimally nourished [4]. The depot of vitamin D is mainly located in the liver, but it can also be stored in adipose tissue. This has critical implications, as achieving optimal vitamin D levels is more challenging in obese individuals due to its sequestration in fat stores [3]. It is important to point out that vitamin D_2 can be found in mushrooms, some plants, and yeast, while vitamin D_3 can be found in foods of animal origin and also via sun exposure [5]. All recommendations are based on a patient's age and vitamin D levels. The primary route of vitamin D elimination is via feces, along with loss through skin shedding [5]. When it was first reported that over 95% of children with rickets received vitamin D exclusively through breast milk, the American Pediatric Scientific Council recommended supplementation with vitamin D for newborns, infants, and children. Vitamin D has receptors in all cells in the body, but its best-known role is in the prevention of rickets [6]. (Sentence restructured below.) Dental caries represent an important public health problem. Studies have shown that insufficient vitamin D intake via breast milk, coupled with inadequate supplementation, can lead to degenerative changes in tooth enamel and other dental defects in children [8]. In a randomized controlled study conducted on school children,

Received • Примљено: November 23, 2024
Revised • Ревизија: January 31, 2025
Accepted • Прихваћено: February 2, 2025
Online first: February 4, 2025

Correspondence to:
Marko KOPRIVICA
Banatska 6A
21000 Novi Sad, Serbia
markokoprivica@uns.ac.rs

which lasted three years in Mongolia, the results clearly showed that supplementation with vitamin D in an adequate dose was effective in patients with a deficiency of this vitamin, but not effective in overall physical development of children [9]. A study conducted in China showed that vitamin D deficiency was more common in girls than in boys. However, the study included a pediatric population aged from birth to four years [10]. While vitamin D hypervitaminosis is rare, it is often caused by improper and inadequate use of this vitamin. In the United States, about three percent of people take more than the optimal dose of vitamin D, and it has been proven that there can be numerous consequences, namely the following: increased excretion of calcium in the urine, which can lead to nephrolithiasis, headache, nausea, and ataxia [11]. Some studies emphasize numerous advantages of supplementation with vitamin D_3 compared to vitamin D_2, as D_3 is more effective in achieving optimal serum levels and elicits a stronger biological response, which is obtained exclusively from dietary sources [12]. Vitamin D_3 is synthesized in the skin with sun exposure and has greater potency in activating vitamin D receptors [13]. A significant risk factor for the development of vitamin D deficiency is darker pigmentation of the skin, which filters sunlight and reduces the efficiency of vitamin D precursors in the skin [14]. Systematic meta-analytical studies support this, showing that children in Africa exhibit pronounced vitamin D deficiency and, consequently, a greater tendency to respiratory diseases such as asthma [15].

VITAMIN D DEFICIENCY AND INFECTIOUS DISEASES

Hospital-acquired infections caused by *Clostridioides difficile* have attracted the attention of the scientific public, especially in recent decades. It is known that only three antibiotics are effective against this bacterium. Recently, a new antibiotic from the group of macrolides, fidaxomicin, has demonstrated high efficacy. Retrospective four-year studies clearly show the severity of this infection in patients with comorbidities [16]. A randomized controlled trial further corroborates earlier findings, revealing that patients who received parenteral vitamin D_3 experienced significantly faster recovery. This outcome is attributed to cholecalciferol's dual role in modulating the immune system and positively influencing the intestinal microbiota [17]. The Epstein–Barr virus, which is a known and proven cause of sarcoma and cancer, also causes a major public health problem [18]. Vitamin D deficiency, as well as selenium deficiency, have a significant indirect effect on the occurrence of autoimmune diseases with comorbid Epstein–Barr virus infection [19]. Also, one of the most pressing public health problems in the last five years was the infection caused by the SARS-CoV-2 virus. An important role was played by liposoluble vitamins and their influence on cytokines, and a special role in an adequate immune response was played by vitamin D and vitamin E [20]. Vitamin E is the name for a group of compounds known as tocopherols. The most important biological function is played by alpha-tocopherol, which is responsible for preventing an exaggerated immune response [21].

INTERACTION OF VITAMIN D AND DRUGS

Vitamin D and its analogs have a strong synergistic effect with azacitidine and other anticancer drugs. Studies have shown that these compounds significantly enhance the efficacy of certain anticancer treatments compared to the effects of the drugs used independently [22]. Some drugs used in epilepsy, such as phenytoin, can induce cytochrome P450 and thereby accelerate the breakdown of vitamin D, and if used long-term can lead to severe deficiency of this vitamin. Therefore, patients should be closely monitored through regular check-ups to prevent the consequences of these effects [23]. Phenobarbital, carbamazepine, and primidone have a similar effect on vitamin D – these antiepileptic drugs also contribute to a decrease in vitamin D [24]. One of the strongest vitamin D antagonists that lowers serum vitamin D levels are corticosteroids. They impair vitamin D absorption in the intestines and stimulate the activity of hydroxylase enzymes, leading to a significant reduction in serum vitamin D levels [25].

CONSEQUENCES OF SELF-INITIATED VITAMIN D SUPPLEMENTATION

Limits for vitamin D deficiency (< 20 ng/ml) and insufficiency (20–30 ng/ml) to adequate levels of serum (30–80 ng/ml) are not completely scientifically based [26]. A randomized cohort study showed that taking vitamin D can result in severe hypercalcemia, but also that the optimal dose can prevent the occurrence of certain cancers [27]. Dexamethasone, a corticosteroid commonly used in various treatments, is a well-documented example of a drug that negatively impacts vitamin D metabolism [28]. Self-initiated intake of supplements and medicines, including vitamin D, can lead to serious health consequences if undertaken without consulting a healthcare professional. Both the dose and the duration of vitamin D supplementation can lead to serious consequences. A patient who used the prescribed therapy for an inadequate period of time subsequently developed severe complications, including vomiting, disorientation, and drowsiness. Laboratory analyses revealed hypercalcemia and acute kidney injury as a result of improper use [28].

Consequences of vitamin D hypovitaminosis

Apart from the key impact of vitamin D deficiency on the bone system, which results in osteopenia and osteoporosis, vitamin D has also been linked with diseases of nervous tissue, muscle, kidney, immune, and other organ systems [29]. Therefore, vitamin D deficiency is associated with the onset of malignant neoplasms of various types, hypertension, autoimmune diseases, type 2 diabetes, depression, and other diseases. The duration of vitamin D deficiency

also influences the disease course and impairment of health. A certain degree of deficiency and its duration are necessary for a disease to develop [30].

CONCLUSION

Preventing vitamin D deficiency requires a combination of proper dietary habits and proactive healthcare practices. Routine and timely visits to a physician are essential for early detection and prevention of hypovitaminosis. Routine medical check-ups can help identify symptoms of diseases associated with impaired vitamin D absorption, prompting targeted laboratory tests to assess serum vitamin D levels. Preventive and corrective measures for vitamin D deficiency can significantly reduce the risk of numerous associated diseases. Furthermore, it is crucial to consider the potential interactions between medications and vitamin D metabolism, as certain drugs can interfere with its absorption and function. Careful monitoring and adherence to professional guidance are vital to ensuring safe and effective vitamin D supplementation.

Ethics: This article was written in accordance with the ethical standards of the institutions and the journal.

Conflict of interest: None declared.

REFERENCES

1. Holt-Lunstad J. Social Connection as a Public Health Issue: The Evidence and a Systemic Framework for Prioritizing the "Social" in Social Determinants of Health. Annu Rev Public Health. 2022;43:193–213. [DOI: 10.1146/annurev-publhealth-052020-110732] [PMID: 35021021]
2. Koprivica M, Bjelanović J. Vitamin D u ishrani i njegova dejstva na nervni sistem. Medicinski časopis. 2022;56(4):158–60. [DOI: 10.5937/mckg56-40957]
3. Koprivica M, Kašiković Lečić S. Uzroci, posledice i lečenje nedostatka vitamina D kod ljudi. Medicinski časopis. 2023;57(3):119–24. [DOI: 10.5937/mckg57-43860]
4. Fiamenghi VI, Mello ED. Vitamin D deficiency in children and adolescents with obesity: a meta-analysis. J Pediatr (Rio J). 2021;97(3):273–9. [DOI: 10.1016/j.jped.2020.08.006] [PMID: 33022267]
5. Płudowski P, Kos-Kudła B, Walczak M, Fal A, Zozulińska-Ziółkiewicz D, Sieroszewski P, et al. Guidelines for Preventing and Treating Vitamin D Deficiency: A 2023 Update in Poland. Nutrients. 2023;15(3):695. [DOI: 10.3390/nu15030695] [PMID: 36771403]
6. Chang SW, Lee HC. Vitamin D and health – The missing vitamin in humans. Pediatr Neonatol. 2019;60(3):237–44. [DOI: 10.1016/j.pedneo.2019.04.007] [PMID: 31101452]
7. Mansur JL, Oliveri B, Giacoia E, Fusaro D, Costanzo PR. Vitamin D: Before, during and after Pregnancy: Effect on Neonates and Children. Nutrients. 2022;14(9):1900. [DOI: 10.3390/nu14091900] [PMID: 35565867]
8. Durá-Travé T, Gallinas-Victoriano F. Dental caries in children and vitamin D deficiency: a narrative review. Eur J Pediatr. 2024;183(2):523–8. [DOI: 10.1007/s00431-023-05331-3] [PMID: 37966493]
9. Ganmaa D, Bromage S, Khudyakov P, Erdenenbaatar S, Delgererekh B, Martineau AR. Influence of Vitamin D Supplementation on Growth, Body Composition, and Pubertal Development Among School-aged Children. JAMA Pediatr. 2023;177(1):32–41. [DOI: 10.1001/jamapediatrics.2022.4581] [PMID: 36441522]
10. Liu Z, Huang S, Yuan X, Wang Y, Liu Y, Zhou J. The role of vitamin D deficiency in the development of paediatric diseases. Ann Med. 2023;55(1):127–35. [DOI: 10.1080/07853890.2022.2154381] [PMID: 36452736]
11. Bouillon R, Manousaki D, Rosen C, Trajanoska K, Rivadeneira F, Richards JB. The health effects of vitamin D supplementation: evidence from human studies. Nat Rev Endocrinol. 2022;18(2):96–110. [DOI: 10.1038/s41574-021-00593-z] [PMID: 34815552]
12. Pludowski P, Takacs I, Boyanov M, Belaya Z, Diaconu CC, Mokhort T, et al. Clinical Practice in the Prevention, Diagnosis and Treatment of Vitamin D Deficiency: A Central and Eastern European Expert Consensus Statement. Nutrients. 2022;14(7):1483. [DOI: 10.3390/nu14071483] [PMID: 35406098]
13. Chan HN, Zhang XJ, Ling XT, Bui CH, Wang YM, Ip P, et al. Vitamin D and Ocular Diseases: A Systematic Review. Int J Mol Sci. 2022;23(8):4226. [DOI: 10.3390/ijms23084226] [PMID: 35457041]
14. Vitamin D. In: Drugs and Lactation Database (LactMed®). Bethesda (MD): National Institute of Child Health and Human Development; 2024.
15. Chanie ES, Zhang G, Le Souef P. The serum level of vitamin D and prevalence of vitamin D deficiency among children with asthma in Asia and Africa: a systematic review and meta-analysis. Arch Public Health. 2024;82(1):103. [DOI: 10.1186/s13690-024-01321-5] [PMID: 38970116]
16. Koprivica M, Đekić Malbaša J. Epidemiological characteristics of infections caused by bacteria *Clostridioides difficile* toxins. Srpski arhiv za celokupno lekarstvo. 2024;152(9–10):505–8. [DOI: 10.2298/SARH240625077K]
17. Lee SH, Park HK, Kang CD, Choi DH, Park SC, Park JM, et al. High Dose Intramuscular Vitamin D3 Supplementation Impacts the Gut Microbiota of Patients With Clostridioides Difficile Infection. Front Cell Infect Microbiol. 2022;12:904987. [DOI: 10.3389/fcimb.2022.904987] [PMID: 35774395]
18. Koprivica M. Epstein-Barr virus – uzroci, posledice, dijagnostika i lečenje Epstein-Barr virusa kod ljudi. Sanamed. 2024;19(1):87–91. [DOI: 10.5937/sanamed0-48644]
19. Cyna W, Wojciechowska A, Szybiak-Skora W, Lacka K. The Impact of Environmental Factors on the Development of Autoimmune Thyroiditis–Review. Biomedicines. 2024;12(8):1788. [DOI: 10.3390/biomedicines12081788] [PMID: 39200253]
20. Shakoor H, Feehan J, Al Dhaheri AS, Ali HI, Platat C, Ismail LC, et al. Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19?. Maturitas. 2021;143:1–9. [DOI: 10.1016/j.maturitas.2020.08.003] [PMID: 33308613]
21. Koprivica M, Miljković A. Uticaj vitamina E na različite organske sisteme. Sanamed. 2024;19(2):215–9. [DOI: 10.5937/sanamed0-49398]
22. Kulling PM, Olson KC, Olson TL, Feith DJ, Loughran TP Jr. Vitamin D in hematological disorders and malignancies. Eur J Haematol. 2017;98(3):187–97. [DOI: 10.1111/ejh.12818] [PMID: 27743385]
23. Fan HC, Lee HS, Chang KP, Lee YY, Lai HC, Hung PL, et al. The Impact of Anti-Epileptic Drugs on Growth and Bone Metabolism. Int J Mol Sci. 2016;17(8):1242. [DOI: 10.3390/ijms17081242] [PMID: 27490534]
24. Arora E, Singh H, Gupta YK. Impact of antiepileptic drugs on bone health: Need for monitoring, treatment, and prevention strategies. J Family Med Prim Care. 2016;5(2):248–53. [DOI: 10.4103/2249-4863.192338] [PMID: 27843822]
25. Dhawan P, Christakos S. Novel regulation of 25-hydroxyvitamin D3 24-hydroxylase (24(OH)ase) transcription by glucocorticoids: cooperative effects of the glucocorticoid receptor, C/EBP beta, and the Vitamin D receptor. J Cell Biochem. 2010;110(6):1314–23. [DOI: 10.1002/jcb.22645] [PMID: 20564225]
26. Haines ST, Park SK. Vitamin D supplementation: what's known, what to do, and what's needed. Pharmacotherapy. 2012;32(4):354–82. [DOI: 10.1002/phar.1037] [PMID: 22461123]

27. Tobias DK, Luttmann-Gibson H, Mora S, Danik J, Bubes V, Copeland T, et al. Association of Body Weight With Response to Vitamin D Supplementation and Metabolism. JAMA Netw Open. 2023;6(1):e2250681. [DOI: 10.1001/jamanetworkopen.2022.50681] [PMID: 36648947]
28. Bhat JR, Geelani SA, Khan AA, Roshan R, Rathod SG. Vitamin D toxicity due to self-prescription: A case report. J Family Med Prim Care. 2022;11(4):1561–3. [DOI: 10.4103/jfmpc.jfmpc_1525_21] [PMID: 35516667]
29. Grant WB, Wimalawansa SJ, Pludowski P, Cheng RZ. Vitamin D: Evidence-Based Health Benefits and Recommendations for Population Guidelines. Nutrients. 2025;17(2):277. [DOI: 10.3390/nu17020277] [PMID: 39861407]
30. Giustina A, Bilezikian JP, Adler RA, Banfi G, Bikle DD, Binkley NC, et al. Consensus Statement on Vitamin D Status Assessment and Supplementation: Whys, Whens, and Hows. Endocr Rev. 2024;45(5):625–54. [DOI: 10.1210/endrev/bnae009] [PMID: 38676447]

Јавноздравствени аспекти витамина Д

Марко Копривица[1,2], Ана Миљковић[1,3]

[1]Универзитет у Новом Саду, Медицински факултет, Нови Сад, Србија;
[2]Институт за јавно здравље Војводине, Нови Сад, Србија;
[3]Дом здравља „Нови Сад", Нови Сад, Србија

САЖЕТАК

Последњих деценија све чешће се јављају познате али недовољно лечене болести и поремећаји. Такође, долази и до испољавања поремећаја чији су узроци одранније познати, али нису били довољно контролисани. Јавноздравствени проблеми постају све чешћи и значајнији. Међу њима, многи симптоми и болести повезани су са недостатком витамина, нездравим начином живота и другим узрочницима.

Витамин Д је једна од актуелних јавноздравствених тема која у последње време привлачи све већу научну пажњу. Ово биолошки важно једињење утиче на бројне функције у људском организму, а његов недостатак је чест у многим деловима света. Витамин Д се може наћи у облику суплемената, али може бити регистрован и као лек.

Кључне речи: превенција болести; јавно здравље; витамин Д