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Vitamin D Deficiency in The General Population

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SUMMARY

Introduction: Vitamin D has been a subject of significant interest among scientists from various scientific fields in recent decades. Its discovery has led to numerous changes in therapy, diagnostics and the treatment of certain diseases. It is believed that almost every cell in the human body possesses receptors for vitamin D. This article examines vitamin D levels from multiple perspectives. The study is based on patient samples collected from individuals undergoing medical treatment. It integrates hygienic, socio-statistical, and epidemiological public health measures to inform readers about the importance of proper adherence to preventive health guidelines in order to maintain adequate vitamin D levels and mitigate the risk of serious diseases. Numerous studies suggest that a slight lack of vitamin D is connected to certain diseases in every organ system.

Aim: The Aim of this study is to provide analysis of vitamin D levels in the blood of 553 patients over a three-year period at a secondary-level healthcare institution, namely Vrbas General Hospital.

Material and Method: A retrospective analysis was conducted on data from patients whose blood samples were collected and tested for vitamin D levels between 2018 to 2020 at Vrbas General Hospital. The analysis identified significant parameters related to vitamin D status. In data processing, the following statistical methods were used to confirm the hypothesis: χ^2 test, two-factor analysis of variance (ANOVA) and regression analysis.

Results: Applying the strictest significance criterion $p<0.001$, a statistically significant difference was observed in the number of respondents across the predefined vitamin D categories, including deficiency and hypervitaminosis.

Conclusion: Our findings clearly show that vitamin D levels among patients at Vrbas General Hospital are significantly lower, in percentage terms, compared to those reported in other countries worldwide. Notably, the prevalence of hypervitaminosis was only 0.72% among of the total sample tested.

Keywords: Vitamin D, Prevention, Vitamin D Deficiency

INTRODUCTION

Vitamin D is a crucial compound involved in numerous biochemical functions in the body. It is often referred to as hormone D, yet its classification remains a subject of debate. In humans, vitamin D is synthesized in the skin and then converted to the total active form, 25(OH)D, in the serum. Only this active form is tipycally monitored in the blood because our laboratories are not developed to develop these two forms. While vitamin D exhibits

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certain hormonal characteristics, this does not inherently qualify it as a hormone. If it were a true hormone, the human body would be capable to synthesize it endogenously through multiple pathways without reliance on external factors such as sunlight. This is precisely in favor of the fact that vitamin D is a vitamin rather than a hormone, as it requires exogenous sources either through sunlight exposure or dietary intake to maintain adequate levels [1]. Vitamin D is found in plant-based foods, though it is primarily found in foods of animal origin [2]. Public health policies worldwide have significantly advanced strategies for preventing vitamin D deficiency, particularly following the onset of the COVID-19 pandemic [3]. Increased emphasis has been placed on research into the role of vitamin D in various organ systems, including the endocrine, cardiovascular, and musculoskeletal systems [4]. Additionally, the discovery of vitamin D receptors in the brain has highlighted their potential association with psychiatric disorders such as depression, anxiety, and even certain forms of psychosis. Long-term vitamin D deficiency may contribute to the development of these conditions if the receptors remain deprived of adequate vitamin D molecules for extended periods. Moreover, research has linked vitamin D deficiency to neurological disorders such as multiple sclerosis, chronic headaches, and certain types of stroke [5]. Vitamin D intake recommendations vary by age group. While the general guideline was previously set at 400 IU per day, recent findings suggest that adults (18 years and older) may require up to 2000 IU daily. However, emphasis remains on physical activity and appropriate sun exposure as primary sources, with supplementation recommended only under expert guidance [6].

AIM

The Aim of this study is to provide analysis of vitamin D levels in the blood of 553 patients over a three-year period at a secondary-level healthcare institution, namely Vrbas General Hospital.

MATERIAL AND METHODS

The academic study was approved by the Ethics Committee of Vrbas General Hospital, Vojvodina, application number: 245/2025.

All patients included in the study were aged 18 and older. The findings based on the collected data, highlight that preventive measures play a crucial role in preventing hypovitaminosis and vitamin D deficiency. Vitamin D levels are reported in the accepted and globally adopted SI system only. The methods are based on standard routine methods for the detection of vitamin D, and the units of measurement are: (70-250nmol/l)- optimal vitamin D levels, (25-70nmol/l)-hypovitaminosis, (<25nmol/l)-deficiency, (>250nmol/l)-hypervitaminosis. These parameters were used to assess vitamin D levels extracted from blood samples collected in 2018, 2019 and 2020. Since the COVID-19 was recorded in Serbia only at the beginning of March 2020. It is clear that this study does not focus on COVID-19-19 patients, but rather on the general population, as indicated by the title. The study emphasizes a biochemical perspective and reviews preventive actions and supplementation strategies. Vrbas General Hospital used the Architect 25-OH Vitamin D test, a microparticle chemiluminescent immunoassay for the quantitative determination of 25-OH hydroxyvitamin D in human serum and plasma.

Various statistical methods were applied, including the non-parametric $\chi 2$ test, binomial logistic regression and two-factor analysis of variance (ANOVA). The study tested the following hypotheses: The first hypothesis assumes that there will be statistically significant differences in the distribution of patients across categories based on vitamin D levels in the blood as well as in the direction of change (hypovitaminosis and vitamin D deficiency). The second hypothesis assumes that there will be statistically significant differences in the lack of vitamin D between men and women with women expected to have lower vitamin D levels than men. The third hypothesis suggests that there will be a higher percentage of respondents who have vitamin D deficiency in relation to the percentage of respondents who have hypervitaminosis. The fourth hypothesis assumes that there will be statistically significant differences in vitamin D deficiency in women in 2020 compared to 2019 and 2018 due to the emergence of the Sars cov 2 viral pandemic. The fifth hypothesis assumes that there will be an interaction effect between gender and year of blood sampling predicting that women who had blood samples taken in 2020 will exhibit the greatest vitamin D deficiency compared to all other gender-year interac-

tions.

RESULTS

For the first hypothesis, a non-parametric test confirmed a statistically significant difference in the number of respondents across the established categories of vitamin D levels ($\chi 2=439.31$, $p<0.001$). The majority of respondents (N=291, 52.62%) were classified as having hypovitaminosis, followed by those with optimal vitamin D levels (N=31, 5.60%), Awhile smallest group consisted of those with hypervitaminosis (N=4, 0.72%). The presentation of these data can be seen in

Table 1. Differences in the percentage of patients belonging to a certain category of vitamin D levels. Table shows the gradation of vitamin D levels determined in the given subjects.

Categorization of vitamin D in a given population	Number of respondents in procents
deficiency	5,60%
Hypovitaminosis	52,62%
optimal level	41,04%
hypervitaminosis	0,72%
total number of respondents	100%

Table 2a. The percentage of subjects tested for vitamin D in relation to gender and age are shown in the table below

Gender and age of vitamin D sampling	Number of respondents
M 2018	0,54%
M 2019	4,33%
M 2020	5,24%
F 2018	10,84%
F 2019	52,80%
F 2020	26,22%
Total	100%

Table 1. For the second hypothesis, two statistical methods were applied, leading to the conclusion that there were no statistically significant differences in the distribution of men and women across the categories of vitamin D deficiency, that is, hypovitaminosis and deficiency ($\chi 2=0.005$, $p=0.942$). However, gender differences were found ($\chi 2=213.18$, $p<0.001$), in relation to total vitamin D deficiency both hypovitaminosis and deficiency combined. The third hypothesis was tested using the χ^2 test, which confirmed that there was a statistically significant difference in the number of respondents across the established categories of vitamin D levels, specifically deficiency and hypervitaminosis ($\chi 2=20.829$, $p<0.001$). A larger number of respondents (N=31) had vitamin D deficiency, compared to those with hypervitaminosis (N=4). For the fourth hypothesis, the χ^2 test indicated that there were no statistically significant differences in vitamin D levels in relation to gender and year of blood sampling ($\chi 2=15.197$, $p=0.437$). These results are presented in Tables 2a and 2b. The last fifth hypothesis was tested using a two-factor ANOVA, with gender and the year of blood sampling as independent variables and vitamin D levels as dependent variable. The results showed no main effects of gender ($F=0.937$, $p=0.333$, $\eta 2=0.002$), or year of blood sampling ($F=0.436$, $p=0.647$, $\eta 2=0.002$), nor any interaction effects ($F=0.113$, $p=0.893$, $\eta 2=0.000$). This confirms that neither gender nor the year of blood sampling have no statistically significant impact on vitamin D levels. also from table 2A and 2B, it can be clearly concluded that the increase in the extraction of vitamin D was not statistically significant in 2020, which would be expected due to the emergence of the COVID-19 pandemic. This table can clearly show that the sampling of vitamin D from the blood was the most common in 2019, which can clearly show that even if the COVID-19 pandemic did not exist in Serbia in 2019, the preventive measures of the hospital here were at a much higher level in order to prevent health impairment from SARS CoV-2 virus. And it was prevented by timely substitution.

DISCUSSIONS

Hypovitaminosis as well as vitamin D deficiency, can cause various bone diseases, including osteoporosis, osteopenia, and in chil-

Table 2b. The percentage of men and women classified by category of vitamin D level and by age of blood sampling

Vitamin D levels	Gender and age					
	M 2018	M 2018	M 2018	M 2018	M 2018	M 2018
Deficiency	0%	0%	10,34%	3,33%	7,53%	2,75%
Hypovitaminosis	100%	54,16%	37,93%	60%	52,73%	51,03%
Optimal level	0%	45,83%	51,72%	36,66%	38,69%	45,51%
Hypervitaminosis	0%	0%	0%	0%	1,02%	0,68%
Total	100%	100%	100%	100%	100%	100%

dren rickets as well as severe osteomalacia in older adults. The fortification of milk and other products with vitamin D, introduced several decades ago, has proven effective in reducing the incidence of rickets worldwide. However, despite these measures, subclinical signs of vitamin D deficiency remain prevalent in both developed and developing countries, with an estimated global prevalence affecting up to 1 billion people [7]. One of the crucial public health challenges in recent years, particularly since the end of 2019, has been the COVID-19 pandemic, caused by the SARS-CoV-2 RNA virus. Vitamin D itself played a significant role in modulating cytokine activity, and as this study shows, its therapeutic use contributed to clinical improvement in COVID-19 patients [8]. Research has also explored the relationship between vitamin D on endometriosis, revealing a correlation between specific vitamin D levels and its therapeutic effects on endometriosis. Vitamin D receptors play a key role in this process [9]. When vitamin D receptors interact with vitamin D, they highly influence certain gene transcription. It is well established that over two hundred genes can be activated by vitamin D [10]. Furthermore, vitamin D deficiency is associated with the reduces transcription of certain genes involved in the synthesis of insulin, thereby contributing to the development of type 2 diabetes, and gestational diabetes [11]. Meta-analytic studies indicate that vitamin D reduces the incidence of hip fractures in two ways. First, optimal vitamin D levels support proper mineralization. Second, by acting on vitamin D receptors in the brain, it helps maintain postural stability and balance, reducing the risk of falls [12]. Another meta-analysis study, comparing vitamin D supplementation with found that therapeutic doses improved symptoms of allergic rhinitis, even in the absence of corticosteroid therapy, although combined therapy with corticosteroids did not produce significantly better results than vitamin D alone [13]. A randomized controlled study of 124 patients provided strong statistical evidence supporting the beneficial effects of combined therapy with vitamin B12 and vitamin D. Combined therapy with vitamin B12 and vitamin D can significantly improve the health of the bone, immune and neurological systems [14]. A large meta-analysis incorporating 13 studies and 515,406 patients examined the link between vitamin D levels and suicidal ideation. The results of this extensive meta-analytic study showed that vitamin D levels are lower in patients with suicidal ideation. These results underscore the preventive role of vitamin D in suicide risk reduction, particularly among high-risk populations with severe vitamin D deficiency [15]. In a double-blind controlled study that investigated the effect of vitamin D on a subtype of vertigo. The results were more than fascinating, even over 85% of the subjects who received therapeutic doses of vitamin D had a lower recurrence rate of this type of vertigo than the control group of subjects [16]. Also, meta-analytical research that was carried out along certain hospitals showed that the results have a very high significance in vitamin D therapy in therapeutic doses, but the studies determined that the therapeutic dose of vitamin D taken in an adequate dose and in a certain period of time can lead to a reduction of symptoms of the entire spectrum of depression [17]. A randomized controlled trial concluded that supplementation with 2000 IU to 4000 IU in pregnant women reduced the risk of infection, with promising outcomes for premature infants [18]. Vitamin also D3 plays a key role in brain function as a neurosteroid and regulator of nerve cells, especially in the context of glucocorticoid-induced neurotoxicity. Chronic administration of the synthetic glucocorticoid prednisolone has been shown to cause significant neurological changes, including oxidative stress, decreased synaptic plasticity, and changes in hippocampal structure, which can lead to cognitive and emotional disorders. Vitamin D3 supplementation has shown a protective effect, reducing oxidative stress, improving synaptic function, and alleviating depressive symptoms in experimental animals. Vitamin D3 also acted as a modulator of inflammatory processes in the brain, reducing activation of the NF-κB signaling pathway, which is associated with neuroinflammation and neurodegeneration. These findings suggest that maintaining optimal vitamin D3 levels may be essential for protecting the brain from the negative effects of stress and neurotoxic substances [19]. Preventive and timely measures in monitoring vitamin D levels significantly reduce the prevalence deficiency of this vitamin [20].

CONCLUSION

A hygienic, epidemiological, and socio-sta-

tistical review of vitamin D serves as a comprehensive synthesis of public health analyses addressing the widespread issue of vitamin D deficiency. Beyond its numerous direct effects on organ systems, vitamin D also influences gene expression, activation, and transcription. Vitamin D deficiency remains a serious global problem. Data from Vrbas General Hospital show that a significant percentage of adults have hypovitaminosis or vitamin D deficiency. These results are in line with global trends, where it is estimated that more than a billion people worldwide have inadequate levels of vitamin D. Preventive measures, including education, proper nutrition, and exposure to sunlight, are essential for addressing this deficiency. Recommendations for vitamin D intake should be adapted to different population groups, taking into account individual risk factors. Further research is necessary to better understand its optimal levels and therapeutic potential in various medical conditions.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Nedostatak vitamina D u opštoj populaciji

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KRATAK SADRŽAJ

Uvod: Vitamin D je poslednjih decenija bio predmet značajnog interesovanja naučnika iz različitih naučnih oblasti. Njegovo otkriće dovelo je do brojnih promena u terapiji, dijagnostici i lečenju određenih bolesti. Veruje se da skoro svaka ćelija u ljudskom telu poseduje receptore za vitamin D. Ovaj članak ispituje nivoe vitamina D iz više perspektiva. Studija se zasniva na uzorcima pacijenata prikupljenim od osoba koje se podvrgavaju medicinskom lečenju. Ovaj članak integriše higijenske, socio-statističke i epidemiološke mere javnog zdravlja kako bi informisao čitaoce o važnosti pravilnog pridržavanja preventivnih zdravstvenih smernica kako bi se održali adekvatni nivoi vitamina D i ublažio rizik od ozbiljnih bolesti. Brojne studije sugerišu kako je blagi nedostatak vitamina D upravo povezan sa oboljevanjem svakog sistema organa od određenih bolesti.
Cilj: Cilj ove studije je da se obezbedi analizu nivoa vitamina D u krvi kod 553 pacijenta tokom trogodišnjeg perioda u zdravstvenoj ustanovi sekundarnog nivoa, naime u Opštoj bolnici u Vrbasu.
Materijal i metode: Sprovedena je retrospektivna analiza podataka pacijenata čiji su uzorci krvi prikupljeni i testirani na nivoe vitamina D između 2018. i 2020. godine u Opštoj bolnici Vrbas. Analizom su identifikovani značajni parametri vezani za status vitamina D. U obradi podataka korišćene su sledeće statističke metode za potvrdu hipoteze: χ^2 test, dvofaktorska analiza varijanse (ANOVA) i regresiona analiza.
Rezultati: Primenom najstrožeg kriterijuma značajnosti $p<0,001$, primećena je statistički značajna razlika u broju ispitanika u okviru unapred definisanih kategorija vitamina D, uključujući nedostatak i hipervitaminozu.
Zaključak: Naši nalazi jasno pokazuju da su nivoi vitamina D među pacijentima u Opštoj bolnici Vrbas značajno niži, u procentualnom smislu, u poređenju sa onima prijavljenim u drugim zemljama širom sveta. Primetno je da je prevalencija hipervitaminoze bila samo 0,72% među ukupnim testiranim uzorkom.

Ključne reči: vitamin D, prevencija, nedostatak vitamina D

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