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VITAMIN D STATUS IN A CASE SERIES OF ARMENIAN POPULATION: ONE CENTER COHORT DATA

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Abstract

Documenting the current status of vitamin D and its trends is one of goals of nutritional assessment and monitoring for the health agencies.

The purpose of current study was to examine the prevalence of vitamin D insufficiency in a case-series of Armenian population based on one center cohort data, and to reveal its association with season, age and sex. In 2018, 1525 patients were evaluated. Vitamin D insufficiency was defined as a serum 25-OH vitamin D concentration (25-OHD) <20ng/ml. The season was detected as "sunny season" – from May to October inclusively, and "non-sunny" season – from November to April.

All analyses were performed using statistical software (IBM SPSS Statistics for Windows, Version 21.0; IBM Corp., USA). Values of p<0.05 were considered statistically significant. The male/female ratio of investigated patients was 1/2.5, and mean age was 35.14±17.66. No significant difference in vitamin D insufficiency prevalence was found between 3 age groups (p>0.05). The average 25-OH vitamin D level of all investigated patients was 24.11±9.66. The overall prevalence rate of vitamin D insufficiency was 29.3% (n=447), having a significant link with the winter "non-sunny" season (p<0.01), when the sun exposure on the skin is not enough, regardless the sex (p>0.05). No correlation was found between 25-OHD insufficiency and age of patients (p>0.05).

In summary, we conclude that 25-OHD insufficiency is common in Armenian population and is linked with seasonal period. These data indicate that health care providers and public health authorities in Armenia should develop and review country-specific health policies and programs over time.

Keywords: *pandemic, 25-OH vitamin D_3, sunlight exposure, vitamin D deficiency.*

Introduction

Vitamin D is known to regulate the calcium-phosphorus balance in the organism. Over the past decades, studies have been performed to evaluate the impact of vitamin D not only on the skeletal metabolism, but also its important extra-skeletal roles [*Jorde R, Grimnes G, 2011*; *Rosen C et al.*,

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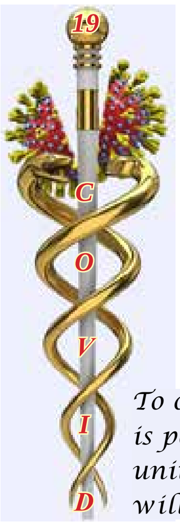
2012]. Increasing evidence suggests that vitamin D deficiency may be associated with some chronic diseases such as cardiovascular disease, type 2 diabetes, obesity, and cancer, with causal factors being the subject for ongoing studies [Seadisomeolia A et al., 2014].The optimal measurable circulating vitamin D in the organism is 25-hydroxyvitamin D (25-OHD), which best describes the total body stores of vitamin D [*Holick M, 2009*].

The populations consist of not only healthy people, but also of people having transient disorders and/or chronic diseases. Thus, the vitamin D status in the general population should be measured not only in "healthy" subjects (as it is done in most case-control studies), but should also include those with chronic or severe disorders, such as diabetes, obesity, viral infections, bronchitis, pneumonia etc. In some populations, such as in the US, it is revealed that even in the same country diverse minority groups showed different prevalence of vitamin D insufficiency, depending on their ethnicity, educational and social status [*Forrest K, Stuhldreher W, 2011*]. Other studies showed the vitamin D deficiency and/or insufficiency in some countries depending on the geographical, age and other parameters [*Rabenberg M et al., 2015; Bettencourt A et al., 2018; Lee M et al., 2019*].

High prevalence of vitamin D insufficiency in populations also is declared to be dependent on some genetic and environmental factors [*Kull M et al., 2009*; *Moran-Auth Y et al., 2013; Clendenen T et al., 2015*; *Jolliffe D et al., 2016*; *Brouwer-Brolsma E et al., 2016*]. Determination of vitamin D status in population has an important implication in general health [*Hovsepian S et al., 2011*]. There is a lack of investigation of vitamin D status in Armenia, and we believe this study can be especially useful in documenting the need for rigorously conducted cross-sectional studies and recognize the limits of that study design. Only recently a study was published indicating the >54% of vitamin D insufficiency in female population of reproductive age in Armenia using the dried blood spot sampling and mass-spectrometric method [*Hutchings N et al., 2021*].



Armenia is a mountainous middle-low income country in the south Caucasus, which has a great diversity of climates based on altitude. The capital city Yerevan, where the "Muratsan" hospital is located, has a semi desert and dry climate with an average sun of 2700 *h/year*, equivalent to south Italy based on its latitude. The summers are sunny and the winters are cold and wetter with temperatures below freezing in the mid-winter months. Springs are sunny enough, but the temperature and rainfalls are obstacles for the skin exposure. Months with the lowest ultraviolet index are January and December, with an average maximum index of 2, which represents a low health risk from the exposure to the sun's ultraviolet rays. The highest ultraviolet index is revealed in July near to 11. Armenians belong to the Europoid and Armenoid race types with white or light olive skin color. The religion of the overwhelming majority of Armenians (97%) is Christianity and the dress wearing is similar to Christians in European countries, having no cultural and religious influence on sex-related eating and dress wearing habits and behaviours, that can restrict skin exposure.

In the current work we investigated the case-series of the vitamin D status in people, who visited "Muratsan" hospital complex, which has primary care units, outpatient and inpatient clinics.

The purpose of current study was to examine the prevalence of vitamin D insufficiency in a case-series of patient population based on one center cohort data, as well as to investigate the possible association with season, age and sex.

Materials and methods

In 2018, 1525 patients in "Muratsan" laboratory diagnostics were evaluated, in whom the serum 25-OHD level was measured. For all patients the following data was gathered: age, sex and the season of blood sampling. The season was detected as sunny season – from May to October inclusively, when the skin sunlight exposure is sufficient and not sunny season – from November and April. Participants with renal and liver insufficiency, known bone diseases, fractures, heart failure, and rheumatoid arthritis were excluded.Venous blood samples were collected in the morning after an 8-hours fasting. The measurement was done immediately after the blood sampling and only in one patch. The 25-OHD was measured by immunoassay method using Cobas 411 analyzer (Switzerland, 2013). Vitamin D insufficiency was defined as serum 25-OHD concentrations <20*ng/ml* [*Washington D, 2011; Giustina A et al., 2018*]. Serum total 25-OHD is the sum of the concentrations of serum 25-OHD3 (cholecalciferol) and serum 25-OHD2 (ergocalciferol), which are considered to be of equal biological value. The laboratory does not participate in any external quality assessment scheme, so the 25-OHD values are not standardized and cannot be compared with other international study results.

All statistical analyses were performed using statistical software (IBM SPSS Statistics for Windows, Version 21.0; IBM Corp., USA). The chi-square test, student t-test, and the Pearson correlation coefficient were used for the data analysis. Values of $p<0.05$ were considered statistically significant.

TABLE 1.

Main characteristics' comparison between three age groups of investigated people.

Age groups Main variables	years of age <18 (N=342)	19-49 (N=775)	>50 (N=408)
Sex			
Male (N)	107	216	108
Female (N)	235	559	300
Female to male ratio	2.2	2.59	2.78
Seasonal variation of 25-OHD measurement			
Sunny season (N)	173	388	213
Non-sunny season (N)	169	387	195
Sunny to non-sunny season ratio	1.02	1.00	1.09
Vitamin D insufficiency prevalence depending on the season of the year			
Sunny season (%)	25.4	17.8	21.5
Non-sunny season (%)	39.1	25.8	34.9
Sunny to non-sunny season ratio	0.65	0.69	0.62
Mean 25-OHD (*ng/ml*)	25.61±8.8	23.22±9.4	23.5±10.8
Average 25-OHD (*ng/ml*) depending on season			
Sunny season	28.1±8.9	27.1±8.7	25.98±7.9
Non-sunny season	23.12±6.8	19.34±5.6	21.02±6.4
Sunny to non-sunny season ratio	1.22	1.40	1.24

RESULTS AND DISCUSSION

In 2018, approximately 8600 patients performed laboratory analyses in the Laboratory Diagnostics of "Muratsan" University Hospital, from which a total of 1525 patients (each 6-th patient) included in the study, regardless the sex, age and vitamin D supplementation intake. The male/female ratio of investigated patients was as 1/2.5 (28.3%/71.7%), and the mean age was 35.14±17.66. From the investigated patients 342 (22.4%) were under 18 years of age, 698 (50.8%) – from 19-49 years of age (the reproductive age), and 408 (26.8%) – >50 years of age. Significant differences in vitamin D insufficiency prevalence, mean 25-OHD levels, female/male ratio, as well as seasonal variation were not found between these 3 age groups, as it is shown in table ($p>0.05$).

As it is shown in the table, there is not significant difference between the age groups about the average vitamin D insufficiency, but it is obviously seen, that in three groups separately there is a dependence of vitamin D insufficiency from the season in each of the age groups ($p<0.01$).

From all investigated patients, 40% (n=610) had no known diseases and were included as so called "healthy" people. The rest 60% had different chronic or acute diseases, such as pneumonia, bronchitis, diabetes mellitus type 1 and type 2, gastritis etc. No difference was found in vitamin D insufficiency in the group of "healthy" people, comparing to patients with some diseases ($p>0.05$), mean 25-OHD was 23.7±6.4 and 22.8±4.5, respectively, indicating that even so-called "healthy" population has near the same prevalence of vitamin D insufficiency.

The average 25-OHD level of all investigated patients was 24.11±9.66 (Fig. 1). The overall prevalence rate of vitamin D insufficiency was 29.3% (n=447), showing a significant link with the winter season ($p<0.05$), when the sun exposure on the skin is not enough. In comparison with the neighbor country Iran, the prevalence of vitamin D deficiency was reported as 9.5%-severe, 57.6%-moderate and 14.2-mild deficiencies respectively, which showed no connection with the sun exposure duration [*Hashemipour S et al., 2004*]. At the same time, in European countries, a vitamin D deficiency is found

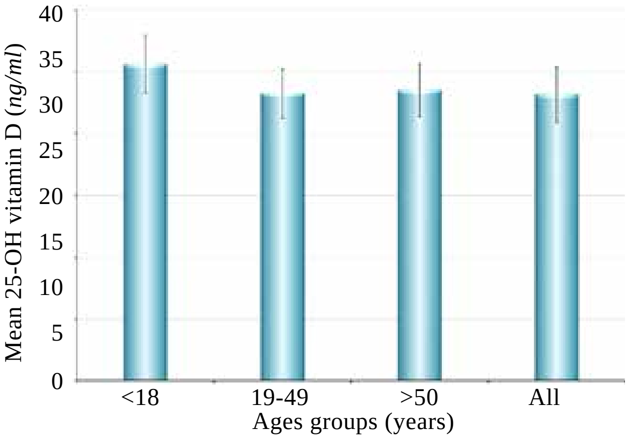


FIGURE 1. The average 25-oH vitamin D level in three age groups of Armenian population.
NOTE: Mean level of Vitamin D for each of the three age groups and for the entire study population, with error bars indicating the plus/minus standard deviation

in 13% of population, where the risk was several times higher among ethnic minorities [*Kiely M, Cashman K, 2018*]. It is expected, that vitamin D declines with age; still there is lack of knowledge about differences in modern lifestyle and dietary behaviour that can influence the vitamin D outcomes. In the recently published paper, Borecka O. and co-authors (2021) showed that in contrast to common presumptions, older adults had a significantly higher daily dietary intake of vitamin D (4.0 μg) than young adults (2.4 μg), as well as higher 25-OHD (56.9 *nmol/L*) than young adults (43.2 *nmol/L*), indicating at least as good vitamin D status as that of younger adults. Interestingly in our study we did not find any age relation of vitamin status, which can be explained with more common food and lifestyle behaviour of the population, which predominantly consists of Armenians.

In our study in the non-sunny season period the mean level of 25-OHD was 23.04±10.07 versus to the sunny period (from May to October), where it was 25.23±9.13 ($p<0.0001$). It should be mentioned that in 751 patients (49.2%) blood sampling was done in non-sunny season versus to the 774 (50.8%) – in sunny period of the year. In the figure 2 the seasonal prevalence of vitamin D insufficiency in the study population is described.

No sex difference was found based on 25-OHD level and age ($p>0.05$). The correlation study was conducted to reveal the connection between 25-OHD level and age of patients, and no correlation was found ($p>0.05$).

Vitamin D deficiency is widespread throughout the world, with some associations being cited as diet, lifestyle, age, sun exposure, and climate. This work brings further documentation about the vitamin D insufficiency, particularly in Armenian population, because there is a lack of data about. An earlier evidence in about this population vitamin D status showed lower average 25-OHD for female population in comparison to our data. However, it should be mentioned that, in contrast to our materials, they used another method of 25-OHD measurements, did not include male population, and included pregnant women, in whom they found a markedly high prevalence of vitamin D deficiency [*Hutchings N et al., 2021*]. Authors showed a difference of mean 25-OHD value between age groups but not clinically significant, in our work we also did not find age-specific differences. Although we did not include children in the current work, it can reasonably be assumed that diet and lifestyle are largely similar to those of adults, allowing us to extend these results to the pediatric population as well. There is no national program of vitamin D supplementation to the general population, only infants until two years old are supplemented with vitamin D via protocols. This issue needs to be overcome with the creation and adaptation of a national program of public health intervention, for which the current results could be helpful, indicating the seasonal requirements of vitamin D in our country.

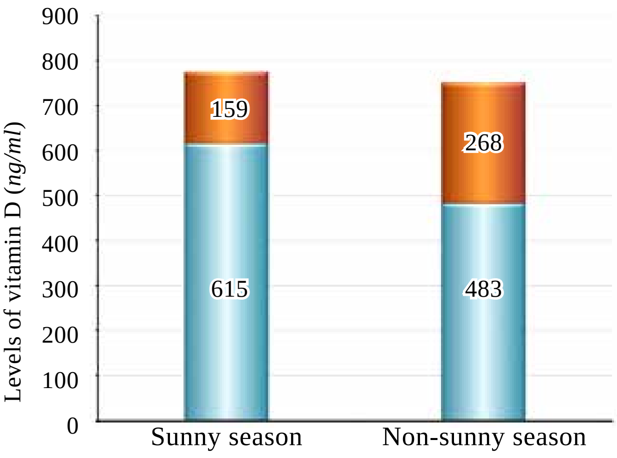


FIGURE 2. The seasonal variation of vitamin D status in the case-series population in Armenia. Levels of Vitamin D insufficiency (brown columns), sufficient status (turquoise columns).

The main weakness of current work is the study design, which represents case-series reports of patient population not chosen by precise statistical sampling methods, as well as the restricted information on other analyses and biochemical findings of patients. Another weakness is the evaluation mainly of an urban population living in the capital city of Armenia, which cannot perfectly represent the population of the whole country, particularly with regard to rural communities. A major strength is the representation of large cohort case-series of Armenian population for vitamin D status evaluation, which can serve as baseline-data and essential information for the Government Health Agencies to perform further representative cross-sectional standardized studies and to conduct country-specific guidelines.

CONCLUSION

There is a high prevalence of vitamin D insufficiency in Armenian population, although Armenia is known to be a "sunny" country and has at least half of a year sunny months with enough sun exposure. A significant link was found between sunny and non-sunny seasonal periods and vitamin D insufficiency prevalence. The current study provides data that can be used to inform public health directives. It is important, that health care providers and government health agencies in Armenia are aware of this prevalence of vitamin D insufficiency and develop and re-evaluate over time the country-specific health policy and programs. An effective educational and interventional strategy should be implemented in our population to prevent and to treat the vitamin D insufficiency, taking into account the revealed seasonal variations of vitamin D status.

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