

# Vitamin D3 levels in healthy people, including a group aged over 60, in relation to BMI

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## Abstract

Vitamin D plays a role not only in the remodeling of bone, but also in functions involving other organs. Its tissue availability depends on dermal synthesis and/or ingestion from diet, as well as on the amount of adipose tissue binding vitamin D into its cells. This study evaluates vitamin D concentrations in relation to body-mass index (BMI) in healthy people aged over 60 and living in the Subcarpathian Province of southeastern Poland. The study involved 246 participants – 172 women (69.9%), 74 men (31.1%), with an average age of 6.9 ( $\pm 11.9$ ). The mean concentrations of vitamin D, assessed with ECLIA method, was 18 ng/ml, which indicates a marked deficiency in vitamin D. Defined vitamin D deficiency (<20ng/ml) was noted in 62% of participants without any difference between males and females. There was no correlation between BMI and vitamin D deficiency in the studied group. The results suggest the need for vitamin supplementation in healthy people aged over 60 according to the guidelines.

## Key words

vitamin D deficiency, healthy people, supplementation, BMI

## INTRODUCTION

Vitamin D designates a group of fat-soluble steroid compounds with similar chemical structure composed of four rings with a side chain [1]. Most of the demand for this vitamin is satisfied through synthesis carried out in the skin under the impact of b ultraviolet light with a wavelength of 290–315 nm. Vitamin D3 is produced from 7-dehydrocholesterol, mainly by keratinocytes located in the basal and spinous skin layers. The amount of vitamin D produced in skin depends not only on sun exposure, but also on the skin phototype (e.g. the darker skin colour is associated with lower vitamin production), use of sunscreens, air pollution and lifestyle. However, extended exposition of skin to sunlight does not lead to toxic accumulation of vitamin D [2].

Diet is the second important source of vitamin D. When ingested, over 80% is absorbed in the digestive tract, mainly in the jejunum. The presence of salts, bile acid, fatty acids and monoglycerides facilitates its absorption.

Vitamin D, synthesized in skin or acquired from food, is transported to the liver, where it undergoes hydroxylation in the 25<sup>th</sup> position to calcifediol. A chemical compound – 25-hydroxyvitamin (25(OH)D) – is a biologically inactive with a long-half life, and circulating in plasma. Due to this, 25(OH)D is routinely used for the assay of vitamin D concentrations in an organism. The biologically active form of vitamin D – Calcitriol – is synthesized mostly in the kidneys by 1-alpha hydroxylase catalyzing the transformation of calcifediol into 1,25(OH)D. Calcifediol undergoes hydroxylation also in the skin, monocytes, and macrophages [3].

The studies in recent years have increased our understanding of calcitriol's impact on the human organism. Apart from

its main function, which is calcium and bone metabolism, vitamin D is also necessary for the normal function of other organs and systems [4–6]. Calcitriol acts on target cells by binding to a nuclear receptor VDR (vitamin D receptor). Very important was the discovery of this receptor expression not only in bone cells, kidney tubules, and intestinal epithelium, but also in most other tissue and organ cells, including heart muscle, blood vessels, brain, skin, pancreas, adrenal glands, prostate, pituitary gland, and smooth and transverse striated muscles. In the circulation of vitamin D, adipose tissue plays an important role as vitamin D reserve, because in adipocytes this vitamin may be accumulated. The studies showed that a VDR, molecular weight of about 55 kDa, belongs to the superfamily of steroid hormone receptors, together with receptors for glucocorticosteroids, sex steroids, thyroxine, retinoids, fatty acids and eicosanoids [7]. This receptor is a ligand activator in the transcription of over 200 genes, and its highly conservative domain includes zinc fingers and binds to DNA. Moreover, it was found that the biological effects of calcitriol depend of the number of receptors (VDR), their affinity to 1,25 (OH) 2D, heterodimerization of the VDR complex – 1,25(OH)2D with the retinoid receptor X. The affinity of this heterodimer to the responding domains on the level of nuclear DNA and, at least, catabolism of calcitriol, are the subsequent step in calcitriol activity.

The wide expression of this receptor on different cells determines the multidirectional function of vitamin D, e.g. regulating the effect on hormone secretion, cell proliferation and differentiation. In the immune system, vitamin D inhibits proliferation of Th1 subpopulation of T lymphocytes and production of cytokines typical for these cells (IFN  $\gamma$ , IL-2, TNF). Furthermore, vitamin D stimulates the production of cytokines by Th2 subpopulation of T lymphocytes – IL-4, IL-5, IL-6, IL-9, IL-10 and IL-13. This activity of vitamin D leads to inhibition of the B lymphocytes, similar to the inhibitory effect of Th1 lymphocytes.

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Observations of vitamin D metabolism have also revealed its effect on the function of adipose tissue. The inhibition of leptin production by adipose tissue is one of the regulatory mechanisms. The essential role of leptin is inhibition of the lipogenesis and stimulation of lipolysis which influences lipid metabolism regulated by adipocytes. This regulation by leptin is based on autocrine-paracrine signals. The deficiency of vitamin D increases the release of parathyroid hormone which lead to stimulation of lipogenesis by a higher influx of calcium into the adipocytes. On the other hand, body fat is involved in vitamin D metabolism into the active form of 1,25-dihydroxyvitamin D<sub>3</sub> with the 25-hydroxylase enzyme. Such activity is characteristic for cytochrome enzymes, some of them (3 – CYP2R1, CYP2J2, CYP27A1) located in visceral adipose tissue which takes part in the active degradation, employing enzyme CYP24A1 which is often present in excess (over-expression).

The study of the level of vitamin D level in people with high BMI suggested an inverse relation, i.e. vitamin D deficiency is observed in obese people. This association is more pronounced in young people than in those who are older. There are some options explaining this association, including e.g., lower physical activity resulting in less exposure to sunlight, and vitamin D sequestration in adipocytes, which seems to be most important [8–13].

Vitamin D deficiency in elderly healthy people is an effect of the accumulation of different factors. On the one hand, the ability of skin to synthesize vitamin D decreases with age, similar to the decrease of cholecalciferol absorption in the gut [14]. However, an increase was shown in serum level of 25(OH)D after supplementation in people aged over 80, suggesting secondary causes leading to vitamin D deficiency, e.g. chronic liver or kidney diseases [15]. On the other hand, regulation of the level of vitamin D, including parathormone (PTH) production and release, calcium-vit D feedback and level of D-binding proteins (DBP), may be less efficient than in young people, due to lower release of PTH, increased level of DPH and lower absorption of calcium [15].

The border level for Calcifediol deficiency is 20 ng/ml. Concentrations between deficiency and optimal level are qualified as hypovitaminosis (21–29 ng/ml). Optimal concentrations at 30–80 ng/ml ensure the full effectiveness of vitamin D, whereas concentrations of 25(OH)D above 150 ng/ml are characterized as highly toxic, with a high risk of adverse effects [16].

## OBJECTIVE

The aim of this study was evaluation of the vitamin D level in healthy individuals aged over 60 and living in the Subcarpathian Province of southeastern Poland. The study included BMI, with the intention of finding a relationship between vitamin D levels and BMI values in healthy, elderly people.

## MATERIALS AND METHOD

The study group included 246 healthy people after physical examination and analysis of medical history. Chronic diseases of liver and/or kidneys, use of anticonvulsants, corticosteroids, vitamin D supplementation in the last

month, were the exclusion criteria. The study was performed during early spring.

BMI was estimated according to standard procedure after measurements of body weight and height, following the formula: body weight [kg]/height [m]<sup>2</sup>. The classification of BMI groups was based on BMI value: underweight – BMI <18.5, normal – BMI 18.5–24.9, overweight – BMI 25–29.9, obese – BMI >30. Blood samples were taken from all participants at the same time: in the morning, before breakfast. The serum was obtained by centrifugation and immediately sent to the laboratory. The level of 25(OH)D was determined with the ECLIA method of electrochemiluminescence (Cobas E601, Roche, Switzerland).

Statistical analysis was carried out with STATISTICA including descriptive statistics (mean and standard deviation), chi-square test of independence, Spearman's rank correlation coefficient, Mann-Whitney U test, and Kruskal-Wallis H test. Statistical significance was set at  $p < 0.05$ .

The study was approved by the Bioethics Committee of the Medical University in Lodz, Poland (RNN/177/14/KB).

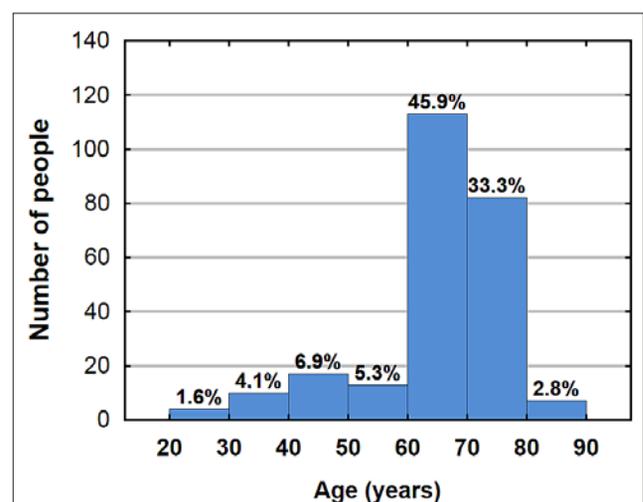
## RESULTS

246 individuals – 172 females (69.9%) and 74 males (31.1%) – participated in the study. Mean age of  $65.9 \pm 11.8$  years was a higher value for men ( $68.6 \pm 12.5$  years) than for females ( $64.7 \pm 9.5$  years) (Tab. 1).

**Table 1.** Mean age of study females and males

| Features    | Gender |    |      |     |      |      |     |     |    |    |
|-------------|--------|----|------|-----|------|------|-----|-----|----|----|
|             | Female |    |      |     | Male |      |     |     |    |    |
|             | Me     | S  | min  | max | Me   | s    | min | max |    |    |
| Age (years) | 64,7   | 68 | 12,5 | 22  | 82   | 68,6 | 70  | 9,5 | 37 | 84 |

The graphical distribution of the studied population in the age groups was shown in Fig. 1.



**Figure 1.** Number and percent of participants in given age groups

The mean value of BMI in all participants was  $25.9 \pm 4$ . The number of overweight participants and those with normal BMI value were similar. Obese and underweight participants constituted a minority (Fig. 2).

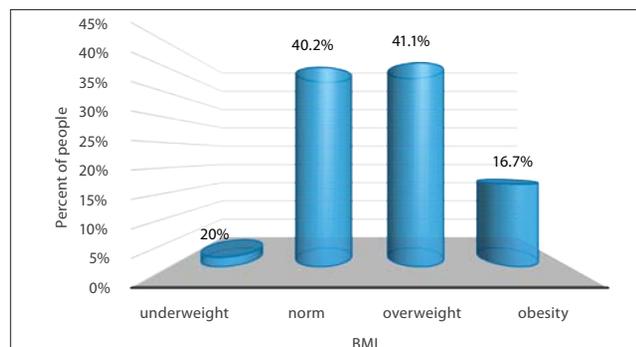


Figure 2. BMI distribution within the studied group

Mean level of vitamin D3 in the studied group was 18±8.7ng/ml with lower median (17 ng/ml) (Tab. 2).

Table 2. Level of vitamin D3 in the studied group

| Level of vitamin D3 (ng/ml) | Me   | s  | c <sub>25</sub> | c <sub>75</sub> | min | max |    |
|-----------------------------|------|----|-----------------|-----------------|-----|-----|----|
|                             | 18.0 | 17 | 8.7             | 12              | 23  | 3   | 54 |

Classification of vitamin D3 levels was based on following criteria:

- <20 ng/ml – deficiency;
- 20–30 ng/ml – suboptimal concentration;
- 30–50 ng/ml – optimal concentration;
- 50–100 ng/ml – high concentration;
- >100 ng/ml – potentially toxic concentration.

Vitamin D3 deficiency was identified in 61.8% (152 participants), in the remaining 27.2% (67 participants) the level of vitamin D3 was suboptimal. Optimal level and high concentration was noted in a minority of studied people (Fig. 3).

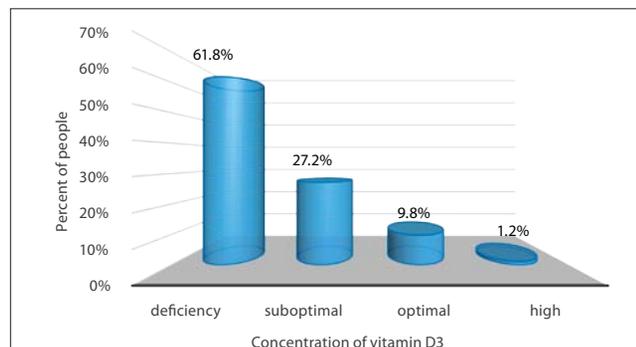


Figure 3. Distribution of vitamin D concentrations

Analysis of the relationship between vitamin D3 deficiency and gender in the studied group of people did not show statistical differences between males and females (p=0.3092). (Tab. 3).

Table 3. Vitamin D concentrations in relation to gender of participants

| Gender | Level vit. D3 (ng/ml) |      |     |     | P  |        |
|--------|-----------------------|------|-----|-----|----|--------|
|        | Me                    | s    | min | max |    |        |
| Female | 18.5                  | 17.0 | 8.7 | 5   | 54 | 0.3092 |
| Male   | 16.8                  | 17.0 | 8.7 | 3   | 52 |        |

p – probability calculated using Mann-Whitney test

Analysis of the vitamin D level, from deficiency to high level, did not show differences between the percentage of people in particular groups (Tab. 4).

Table 4. Distribution of vitamin concentrations in females and males

| Vitamin D3 level | Female      | Male       | Total |
|------------------|-------------|------------|-------|
| Deficiency       | 105 (61.0%) | 47 (63.5%) | 152   |
| Suboptimal       | 45 (26.2%)  | 22 (29.7%) | 67    |
| Optimal          | 20 (11.6%)  | 4 (5.4%)   | 24    |
| High             | 2 (1.2%)    | 1 (1.4%)   | 3     |
| Total            | 172         | 74         | 246   |

Analysis of participants’ age in relation to vitamin D3 levels showed a lower level in the older subgroup, but the correlation was weak (R = -0.11). Moreover, it was not statistically significant, only close to statistical significance (p < 0.10) (Fig. 4).

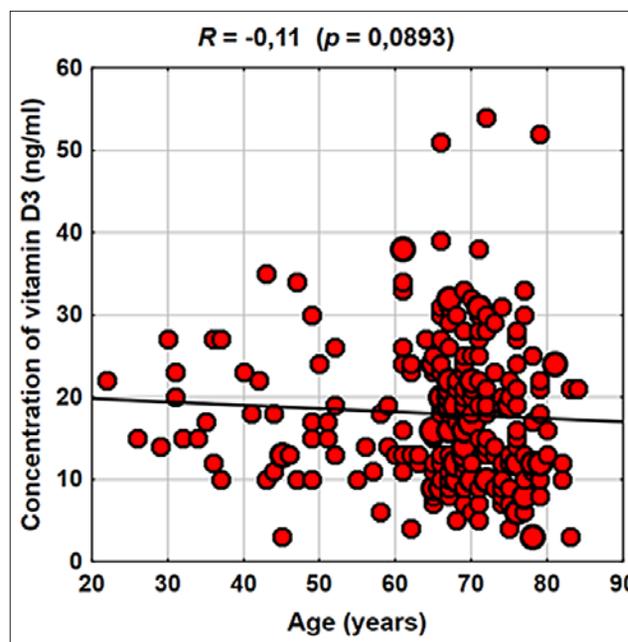


Figure 4. Vitamin D concentration in groups below and above the age of 60

These data were in agreement with other observations that with age the possibility of vitamin D3 deficiency increases. However, a reasonable number of the elderly showed an optimal level of vitamin D3.

A similarly weak correlation was noted when the relationship between BMI and vitamin D3 level was assayed (Fig. 5). Statistical significance was on the border line (p=0.0535).

However, in division with respect to BMI, the average value concentration of vitamin D3 was on similar level. Furthermore, there was no statistically significant difference between these groups and vitamin D3 concentration. Higher BMI was associated with a downward trend, but this dependence also lacked statistical significance (Tab. 3).

Comparing the frequency of vitamin deficit in relation to BMI classification it was noted that among obese participants the risk of vitamin D3 deficiency was above 80%, while for those with BMI within the norm the risk was 50%. The difference between the groups was statistically significant (p < 0.05) (Fig. 6).

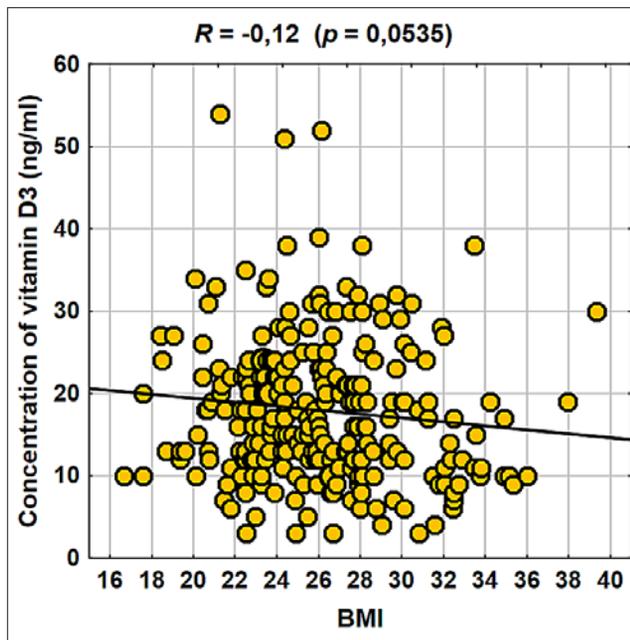


Figure 5. Vitamin D concentrations and BMI

Table 3. Vitamin D concentration in relation to body weight

| Classification acc. BMI | Vitamin D3 (ng/ml) |      |     |     | p      |
|-------------------------|--------------------|------|-----|-----|--------|
|                         | Me                 | s    | min | max |        |
| underweight             | 18,2               | 20,0 | 7,9 | 10  | 0,1042 |
| normal                  | 18,8               | 18,0 | 8,9 | 3   |        |
| overweight              | 18,2               | 16,0 | 8,7 | 3   |        |
| obese                   | 15,4               | 12,0 | 8,1 | 3   |        |

p – probability calculated using Kruskal-Wallis test

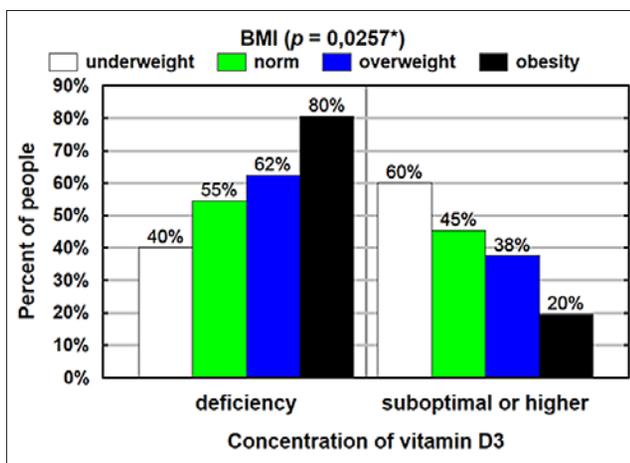


Figure 6. Comparison of the frequency of vitamin D deficit in relation to BMI

Statistical analysis of vitamin D3 concentrations was performed in relation to selected variables using chi-square test of independence, Spearman's rank correlation coefficient, Mann-Whitney test, and Kruskal-Wallis test. The association between obesity and vitamin D3 deficiency was expected, according to general knowledge. However, the observation that within the group with normal BMI, the risk of vitamin D3 deficiency was about 50%, suggested the involvement of other than adipose tissue effects on vitamin D3 level.

## DISCUSSION

The deficiency of vitamin D is common and is often obvious in countries with a low standard of living and shortage of food. It is estimated that this deficiency is noted in over 1 billion people worldwide (<30ng/ml) [17]. Furthermore, this vitamin D shortage is considered as one of the major health problems among children and the elderly. Moreover, in countries like the USA, the deficiency of vitamin D (level below 20 ng/ml) has been noted in 36% of healthy young people (18–29 years of age) and 41% of adults (49–83 years of age) [18]. Epidemiological studies in Europe showed an even larger scale of vitamin D deficiency [19–22].

Deficiency of vitamin D has also been shown in studies performed in Europe within a project including women diagnosed with osteopenia and osteoporosis. Within the examined group of 8,532 women aged over 65 (mean value – 74.2 years), 79.6% suffered from hypovitaminosis (vitamin D – 32ng/ml), while 32.1% of the women showed a level at the border line of vitamin D3 deficiency (20 ng/ml). A studied group of people below 65-years-of- age, showed a vitamin D level of around 30 ng/ml in 86%, while 45% showed a level at the border line of vitamin D deficiency. The geographical distribution of hypovitaminosis and vitamin deficiency revealed the lowest frequency in France, while in Spain this frequency was the highest [23].

In an important study, Gaugris et al. carried out a meta-analysis, a 10-year observation of women after menopause, and vitamin D3 deficiency. A vitamin D level below 20 ng/ml was noted in a wide range of studies and varied, depending on a group, from 1.6 – 86%. In a selected group with the diagnosis of osteoporosis, this deficiency (level below 12 ng/ml) was observed in 12.5–76%. The explanation for such differences in results are associated with dietary supplements, regular supplementation with vitamin D and, among other factors – sun exposure [24]. Merelo et al., in a study which included 776 patients, noted vitamin D deficiency (level < 20 ng/ml) in 45.1% of the participants, while severe deficiency (level < 10 ng/ml) was identified in only 9.8% of the group. In summary, a level of vitamin D below the recommended value of 30 ng/ml was observed in 88.9% of participants [25].

In Polish studies performed in group of postmenopausal women (mean 69.1 ± 5.7 years), vitamin D mean value was 13.6 ng/ml; the level above 30 ng/ml was observed only in 4% of the women. The hypovitaminosis (20–30ng/ml vitamin D) was found in 12.8% of the group. Deficiency, defined as levels below 20 ng/ml, was observed in 83.2% of the examined women [26]. In the presented study involving a group of 246 persons, deficiency of vitamin D (mean level 18ng/ml) was noted in 152 people (61% of women and 63.5% of men). The mean level of vitamin D 20–30ng/ml was observed in only 67 of the participants (44%). These data are comparable to other studied performed in different European countries. However, the season (spring) of assay is important for the results of this study, as sun exposure during that season is limited to only 3 hours a day, which limits the synthesis of vitamin D [27].

The relation of vitamin D synthesis with the season and sun exposure (UVB radiation) has important clinical consequences. The fluctuations in vitamin D levels are associated with sun exposure, which depends on the hours of sunshine during certain months and the whole year. This should be taken into account when the results of vitamin D

assays are analyzed [28]. This association is important not only for Europe but for tropical countries as well.

Studies in the United Arab Emirates showed the lowest levels of vitamin D in winter, as opposed to results obtained in summer. The low level in winter correlated with a higher frequency of bone fractures incidence. However, the difference in vitamin D level between women wearing traditional Arab clothing, and women wearing European-style clothing did not reach statistical significance, although the level of vitamin D was lower in women dressed in Arab-style clothing [29].

Independently from vitamin D synthesis or supplementation, its concentrations also depend on the values of BMI. Among obese persons, the risk of vitamin D3 deficiency is as high as 80% of the population, while in the group with appropriate BMI, this risk is much lower (statistically significant difference) [28]. Moreover, the metabolism of vitamin D correlates better with the total amount of body fat than with BMI, which underlies the possibility of accumulation of the vitamin in fat tissue [31]. Similar results were obtained from a study of obese individuals who required a 40% higher consumption of vitamin D than people of normal body weight to reach an equal level of 25(OH) vitamin D ( $p < 0,03$ ) [32].

The multifactorial causes of vitamin D deficiency associated with obesity include poor sun exposure due to the habits of those who are deficient in the vitamin, e.g. staying indoors, covering the skin to mask obesity, and unsuitable diet. It was shown that skin synthesis of vitamin D may be impaired in obese people. Exposure to UVB radiation increased the level of vitamin D, lower (57%) than in healthy people with normal body weight [33].

## CONCLUSIONS

The obtained results showed vitamin D deficiency in people aged over 60, which indicates the need for regular supplementation of vitamin D, according to recommendations.

The statistically significant relationship between vitamin D deficiency and increased BMI value suggests the need for the regular supplementation of vitamin D sufficient for obtaining the optimal level.

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