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ORIGINAL ARTICLE

# Two threshold levels of vitamin D and the prevalence of comorbidities in outpatients of a tertiary hospital

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**Abstract**
*Summary* This study evaluated the number of comorbidities between two normal values of 25OHD in outpatients during 1 year of 25OHD measurements. Five hundred twenty-nine outpatients were included, patients with 25OHD ≥ 20 and < 30 ng/mL had the higher number of comorbidities, suggesting that for this specific population, 25OHD ≥ 30 ng/mL would be more appropriate.
*Introduction* This study evaluated the comorbidities between two values of 25OHD in outpatients of a tertiary hospital.
*Methods* This is a cross-sectional study with measures of 25OHD in 1-year period, excluding 25OHD < 20 and > 50 ng/mL, clinical research participants, and liver disease and chronic renal failure patients. Patients were divided into two groups: group 1 (G1), 25OHD ≥ 20 and < 30 ng/mL; and group 2 (G2), 250HD ≥ 30 and ≤ 50 ng/mL. Medical records were reviewed for demographic, laboratory, and comorbidity data.
*Results* From 529 outpatients included, 319 were in G1 (53.3 ± 15.8 years, 85% women), mean 25OHD 24.8 ± 2.8 ng/mL; and 210 outpatients in G2 (56.7 ± 16.0 years, 83% women), mean 25OHD was 36.8 ± 4.8 ng/mL. G1 had the higher number of comorbidities, including altered glycemia, dyslipidemia, hypothyroidism, urinary tract diseases, arthropathy, secondary hyperparathyroidism, anemia, and neurological and psychiatric disorders. Osteoporosis and hypothyroidism were more prevalent in G2. After binary logistic regression, the variables age (OR 0.988, CI 0.97–1.00, $p = 0.048$), osteoporosis (OR 0.54, CI 0.36–0.80, $p = 0.003$), dyslipidemia (OR 1.61, CI 1.10–2.39, $p = 0.015$), arthropathy (OR 2.60, CI 1.40–5.10, $p = 0.003$), anemia (OR 15.41, CI 3.09–280.08, $p = 0.008$), and neurological and psychiatric diseases (OR 3.78, CI 1.98–7.88, $p = 0.001$) maintained significance.
*Conclusion* Patients with serum 25OHD ≥ 20 and < 30 ng/mL had higher prevalence of comorbidities compared to ≥ 30 ng/mL.

**Keywords** Comorbidities · Deficiency · Outpatients · Vitamin D · Vitamin D threshold

## Introduction

Vitamin D has as its main source the cutaneous synthesis through exposure to ultraviolet B rays, or can be obtained from plant sources, ergocalciferol (D2), or from animals, cholecalciferol (D3). Both are used for food fortification or supplementation and undergo the same metabolic process, requiring hepatic and renal hydroxylations to form 25-hydroxyvitamin D (25OHD) and 1,25-dihydroxyvitamin $D_3$ ($1,25OH_2D_3$), respectively. The presence of the vitamin D receptor (VDR) and the 1 alpha hydroxylase enzyme in many tissues gives it a broad spectrum of action. This is associated with the inhibition of cell proliferation, angiogenesis, renin production, and stimulation of insulin production, in addition to being essential, together with the parathyroid hormone (PTH), for calcium metabolism and bone health [1].

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Hypovitaminosis D has an important prevalence in the Brazilian population, in several regions of the country [1], which is a common phenomenon throughout the world, including different populations and countries with a wide range of solar radiation [2, 3]. In Brazil, the prevalence of hypovitaminosis D occurs from north to south, increasing as a function of latitude and reaching 58.5% in cities further south [4].

Vitamin D deficiency is diagnosed through the measurement of 25OHD, its main circulating form and the best indicator for monitoring vitamin D status, which has a half-life in circulation of 2 to 3 weeks [1]. However, there is divergence about the ideal level of vitamin D. The Institute of Medicine (IOM) considers levels equal to or greater than 20 ng/mL appropriate for most individuals [5], while the Endocrine Society deems levels equivalent to or higher than 30 ng/mL to be sufficient. In addition, the Endocrine Society considers levels of 25OHD between 21 and 29 ng/mL as insufficient and levels below 20 ng/mL as deficient [6].

Considering the existence of controversy about the recommended level of vitamin D, the present study aims to evaluate whether there is a difference in the number and type of comorbidities in an outpatient population of the Hospital de Clínicas da Universidade Federal do Paraná (HC-UFPR), comparing two thresholds of normality for vitamin D.

## Subjects and methods

This observational, analytical, and cross-sectional study used the results of vitamin D measures of outpatients treated at the HC-UFPR during a 1-year period.

All 25OHD samples analyzed by the laboratory of the HC-UFPR for outpatients from January to December of 2012 were selected, excluding those performed as part of clinical studies or research protocols or those coming from inpatients, patients with chronic renal or hepatic failure, or patients with levels of 25OHD lower than 20 or higher than 50 ng/mL. Samples were separated into two groups: group 1 (G1), 25OHD $\geq 20$ and $< 30$ ng/mL; and group 2 (G2), 25OHD $\geq 30$ and $\leq 50$ ng/mL. Only the first measurement in the study period for the same patient was selected for the study. There was no contact between researcher and patients. Calcium and parathyroid hormone (PTH) were measured in the same serum sample collected for vitamin D, by prior centrifugation at 4.200 rpm for 10 min. The dosage of vitamin D was performed by the chemiluminescence method in an automated analyzer, LIAISON®, DiaSorin, with an inter-assay variation of 20%, sensitivity of 99.5%, and specificity of 100%.

The medical records were reviewed searching for demographic data, presence of comorbidities, and laboratory tests performed closest to the 25OHD sample. The data regarding the use of supplements were poor and not considered for analysis.

Calcium (normal value (NV) = 8.4–10.2 mg/mL) and PTH (NV = 15–68.3 pg/mL) were analyzed by Arzenazo III colorimetric and chemiluminescence, respectively, on the ARCHITECT ci8200® Analyzer, Abbott.

To make the analysis more feasible, some comorbidities described in the medical records were grouped as follows: pneumopathy (chronic obstructive pulmonary disease, asthma); cardiopathy (coronary artery disease, congestive heart failure, arrhythmias, valvular diseases); altered glycemia (diabetes, impaired fasting glucose, insulin resistance, glucose intolerance); diseases of the gastrointestinal tract (peptic disease, haepatopathy, cholelithiasis, cholecystitis, malabsorptive syndromes, inflammatory intestinal disease); diseases of the urinary tract (chronic renal failure, nephropathy, lithiasis, cystitis, urinary tract infection); arthropathies (rheumatoid arthritis, osteoarthritis); other rheumatopathies (fibromyalgia, lupus, carpal tunnel syndrome, plantar fasciitis, bursitis, tendinitis, gout, Behçet's disease, dermatomyositis, myositis); thyroid (nodules, goiter, thyroid dysfunction, multinodular goiter, thyroidectomy, hyperthyroidism); anemias (iron deficiency, megaloblastic, aplastic, hereditary); neoplasia (breast, thyroid, uterus, fibroid, pituitary, parathyroid, bone marrow transplantation); and neurological and psychiatric disorders (mood disorders—depression, bipolar, anxiety—myasthenia gravis, multiple/systemic sclerosis, neuritis, trigeminal neuralgia, neuropathy, epilepsy), in addition to history of bariatric surgery and the diagnoses of obesity, high blood pressure, osteoporosis, dyslipidemia, psoriasis, hypothyroidism, and secondary hyperparathyroidism. Diseases found at low frequency were grouped as "other comorbidities."

### Statistical analysis

Quantitative variables were described by mean and standard deviation statistics. The qualitative variables were described by frequencies and percentages. To evaluate the homogeneity of distributions, the Chi-square test and Fisher's exact test were considered. The Mann-Whitney test was used to evaluate the influence of quantitative variables; the Spearman correlation was used for the other qualitative and quantitative variables in association with the level of 25OHD and the Kruskal-Wallis test for the seasons. Multivariate analysis was performed through binary logistic regression. $p$ values lower than 0.05 indicated statistical significance. The software R (R Core Team, 2015 and R Development Core Team, 2016) version 3.2.3 was used for the analysis of data (R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, URL (https://www.R-project.org/).

## Results

Of the 1265 vitamin D dosages in 2012, 736 met the exclusion criteria (132 samples due to diverse reasons and 604 samples had 25OHD levels lower than 20 or higher than 50 ng/mL). Of the remaining 529 tests, 319 (28.1%) presented 25OHD ≥ 20 and < 30 ng/mL and 210 (18.5%) presented 25OHD ≤ 30 and ≤ 50 ng/mL All these 529 results of 25OHD would be considered sufficient by the IOM and only 39.7% by the Endocrine Society. Of the 529 25OHD dosages that were included in the study, 319 belonged to G1 (53.3 ± 15.8 years, 85% women) and 210 to G2 (56.7 ± 16.0 years, 83% women). Age was higher in G2 ($p = 0.007$) and BMI higher in G1 ($p < 0.001$). Blood samples were collected predominantly in the summer and fall in both groups. Figure 1 shows the distribution of 25OHD levels of each group according to age. The mean of 25OHD was 24.8 ± 2.8 and 36.8 ± 4.8 ng/mL in G1 and G2, respectively ($p < 0.001$). Demographic and laboratory data referring to the date closest to the blood collection for 25OHD are shown in Table 1.

The mean number of comorbidities per patient was higher in G1 (4.17 ± 2.2) compared to G2 (3.4 ± 1.6) ($p < 0.001$). Among the comorbidities found, the most prevalent in G1 were high blood pressure (56%), obesity (45%), dyslipidemia (45%), altered glycemia (34%), osteoporosis (34%), and hypothyroidism, and in G2 were high blood pressure (55%), osteoporosis (50%), obesity (36%), dyslipidemia (36%), hypothyroidism (34%), and altered glycemia (26%). The individual analysis of each group did not show an association between vitamin D level and laboratory tests, or number or type of comorbidities, except for a lower level of 25OHD in patients with urinary tract disease ($p < 0.002$) in G1 (Table 2). The laboratory tests evaluated were similar between groups (Table 1).

Comparative analysis between the groups showed a higher mean age ($p = 0.007$) in G2, as well as higher number of patients with osteoporosis ($p < 0.001$) and hypothyroidism ($p = 0.036$). Several comorbidities were more prevalent in G1 such as secondary hyperparathyroidism ($p < 0.001$), neurological and psychiatric diseases ($p < 0.001$), anemia ($p < 0.001$), arthropathy ($p = 0.006$), urinary tract disease ($p = 0.029$), dyslipidemia ($p = 0.031$), and heart disease ($p = 0.053$), and obesity ($p = 0.054$) also showed a trend towards higher prevalence in this group. These results are summarized in Table 2. Figure 1 shows the percentage of positive patients per comorbidity and the difference between both thresholds.

The multivariate analysis was considered as dependent variables the two groups of reference intervals for vitamin D (G1 and G2), and as independent, the variables with a significant difference between the two groups. After binary logistic regression, the variables age ($p = 0.019$), osteoporosis ($p < 0.001$), higher number of comorbidities ($p < 0.001$), arthropathy ($p = 0.042$), anemia ($p = 0.016$), and neurological and psychiatric diseases ($p = 0.003$) maintained significance (Table 3). Patients younger without osteoporosis but with higher number of comorbidities, arthropathy, anemia, or neurological and psychiatric diseases were more likely to be in G1. Patients with higher number of comorbidities, the

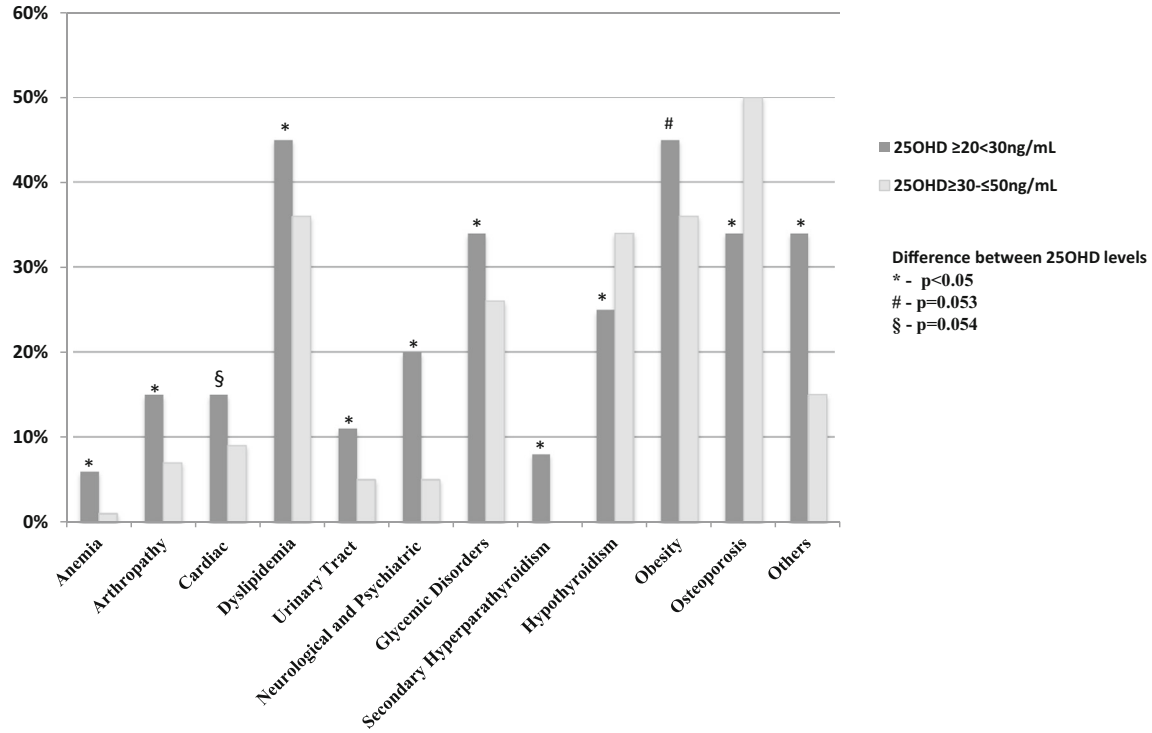


**Fig. 1** Comparison of the percentage of positive patients per comorbidity in each threshold of vitamin D (25OHD)

**Table 1** Descriptive analysis and laboratory results of the groups studied

| Characteristics | G1<br>20 ≤ 25OHD < 30 ng/mL | G2<br>30 ≤ 25OHD ≤ 50 ng/mL | *p* |
|---|---|---|---|
| Gender (%) | | | |
| Female | 271 (85%) | 174 (83%) | 0.519 |
| Male | 48 (15%) | 36 (17%) | |
| Season (%) | | | |
| Spring/Winter | 11 (3%) | 10 (5%) | 0.590 |
| Summer/Fall | 308 (97%) | 200 (95%) | |
| Age | | | |
| | 53.3 ± 15.8 | 56.7 ± 16.1 | *0.007* |
| Laboratory | | | |
| Vitamin D (ng/mL) | 24.8 ± 2.8 | 36.8 ± 4.8 | *< 0.001* |
| Calcium (mg/dL) | 9.2 ± 0.5 | 9.2 ± 0.5 | 0.868 |
| PTH (pg/mL) | 69.0 ± 57.9 | 60.8 ± 31.2 | 0.275 |
| Glycemia (mg/dL) | 108.1 ± 43.7 | 102.8 ± 37.0 | 0.408 |
| Creatinin (mg/dL) | 0.8 ± 0.7 | 0.8 ± 0.2 | 0.561 |
| Total cholesterol (mg/dL) | 183.3 ± 36.3 | 182.0 ± 39.7 | 0.733 |
| HDL (mg/dL) | 45.6 ± 13.3 | 47.0 ± 12.4 | 0.102 |
| LDL (mg/dL) | 114.7 ± 35.1 | 108.5 ± 37.4 | 0.164 |
| Tryglicerídes (mg/dL) | 125.7 ± 76.3 | 116.5 ± 58.1 | 0.451 |
| TGO (U/L) | 21.7 ± 13.2 | 22.1 ± 12.9 | 0.423 |
| TGP (U/L) | 21.5 ± 17.9 | 21.5 ± 13.3 | 0.909 |
| Body mass index | | | |
| | 30.9 ± 7.3 | 28.6 ± 6.4 | *< 0.001* |
| Total number of comorbidities | | | |
| | 4.18 ± 2.2 | 3.39 ± 1.6 | *< 0.001* |

Italic refers to significant values $p<0.005$

*25OHD* 25hydroxyvitamin D, *G1* group 1, *G2* group 2

diagnosis of arthropathy, anemia, or neurological and psychiatric diseases presented a 1.28, 1.98, 12.05, and 2.84 times greater risk, respectively, to belong to G1.

## Discussion

This study examined the presence of comorbidities in two normal vitamin D thresholds in an outpatient population of a tertiary care hospital, showing a higher number of comorbidities in patients with vitamin D ≥ 20 and < 30 ng/mL. The controversy about the appropriate level of vitamin D is important to the diagnosis and treatment decision of vitamin D deficiency, seeing that in this sample, only 39.7% of patients would be considered sufficient by both criteria and that the impact to the general health is unknown. A recent paper by Schramm S. et al. [7] showed amplitude of the prevalence rates from 6 to 92% of 25OHD deficiency, reliant on the guideline applied. Deficiency (25OHD < 20 ng/mL) and vitamin D insufficiency (< 30 ng/mL) are highly prevalent, ranging from 20 to 60% and 90%, respectively, of individuals between 18 and 85 years old [8], reaching 71% in this age group in out- and inpatients [9].

This study did not show a direct association between the presence of comorbidities, with the exception of urinary disease, and the two levels of vitamin D evaluated separately. This finding contradicts the literature that describes in several studies the association of low levels of vitamin D with comorbidities [6, 10, 11]. The limitation of studying only the range in which there is a discussion about normality may have excluded the individuals most affected by the comorbidities, or may suggest that the morbidities occur at levels below 20 ng/mL, where there is no doubt about the harm of vitamin D deficiency. Another explanation is the low variability of vitamin D levels inside either group, with a mean of 24.8 ± 2.8 ng/mL in G1 and 36.8 ± 4.8 ng/mL in G2, making them somewhat more homogeneous. The results of this study are complementary to the literature in that they offer more data about patients with insufficient (intermediate) vitamin D levels.

The most prevalent comorbidities in the two groups were high blood pressure, obesity, dyslipidemia, altered glycemia, osteoporosis, and hypothyroidism, which were also the diseases most commonly diagnosed in a study performed in

**Table 2** Presence or absence of comorbidities per group and the difference between groups

| Comorbidities | Vitamin D levels | | | | | | |
|---|---|---|---|---|---|---|---|
| | G1: 25OHD ≥ 20 and < 30 ng/mL | | | G2: 250HD ≥ 30 and ≤ 50 ng/mL | | | |
| | Absent | Present | $p^1$ | Absent | Present | $p^2$ | $p$ |
| Anemia | 299 (94%) | 20 (6%) | 0.914 | 209 (99%) | 1 (1%) | 0.255 | *< 0.001* |
| Arthropathy | 271 (85%) | 48 (15%) | 0.822 | 195 (93%) | 15 (7%) | 0.914 | *0.006* |
| Cardiac disorder | 272 (85%) | 47 (15%) | 0.608 | 191 (91%) | 19 (9%) | 0.293 | 0.053 |
| Dyslipidemia | 175 (55%) | 144 (45%) | 0.556 | 135 (64%) | 75 (36%) | 0.886 | *0.031* |
| Urinary tract disease | 285 (89%) | 34 (11%) | *0.023* | 199 (95%) | 11 (5%) | 0.178 | *0.029* |
| Gastrointestinal tract diseases | 272 (85%) | 47 (15%) | 0.199 | 183 (87%) | 27 (13%) | 0.978 | 0.543 |
| Neurological and psychiatric disorder | 255 (80%) | 64 (20%) | 0.681 | 199 (95%) | 11 (5%) | 0.438 | *< 0.001* |
| Glycemic disorder | 209 (66%) | 109 (34%) | 0.871 | 156 (74%) | 54 (26%) | 0.663 | *0.037* |
| High blood pressure | 139 (44%) | 180 (56%) | 0.577 | 94 (45%) | 116 (55%) | 0.345 | 0.788 |
| Secondary hyperparathyroidism | 295 (92%) | 24 (8%) | 0.431 | 210 (100%) | 0 | NC | *< 0.001* |
| Hypothyroidism | 238 (75%) | 81 (25%) | 0.999 | 139 (66%) | 71 (34%) | 0.358 | *0.036* |
| Bariatric surgery | 275 (86%) | 44 (14%) | 0.416 | 181 (86%) | 29 (14%) | 0.945 | 0.996 |
| Past fractures | 300 (94%) | 18 (6%) | 0.260 | 197 (94%) | 13 (6%) | 0.546 | 0.800 |
| Neoplasia | 286 (90%) | 33 (10%) | 0.335 | 188 (90%) | 22 (10%) | 0.698 | 0.961 |
| Obesity | 177 (55%) | 142 (45%) | 0.232 | 125 (64%) | 70 (36%) | 0.911 | 0.054 |
| Osteoporosis | 209 (66%) | 110 (34%) | 0.846 | 105 (50%) | 105 (50%) | 0.990 | *< 0.001* |
| Rheumathopathy | 281 (88%) | 38 (12%) | 0.373 | 192 (91%) | 18 (9%) | 0.775 | 0.222 |
| Pneumopathy | 300 (94%) | 19 (6%) | 0.064 | 200 (95%) | 10 (5%) | 0.519 | 0.697 |
| Psoríasis | 314 (98%) | 5 (2%) | 0.649 | 207 (99%) | 3 (1%) | 0.327 | 1.000 |
| Tobacco use | 293 (92%) | 25 (8%) | 0.912 | 192 (91%) | 18 (9%) | 0.580 | 0.770 |
| Thyroid disease | 282 (88%) | 37 (12%) | 0.644 | 186 (89%) | 24 (11%) | 0.273 | 0.952 |
| Others | 212 (66%) | 107 (34%) | 0.545 | 179 (85%) | 31 (15%) | 0.599 | *< 0.001* |

Italic refers to significant values $p<0.005$

*25OHD* 25hydroxyvitamin D, *G1* group 1, *G2* group 2

$p^1$ values for the comparison between the presence and absence of comorbidity in G1

$p^2$ values for the comparison between presence and absence of comorbidity in G2

Austria that analyzed only patients with suboptimal 25OHD levels (< 30 and < 20 ng/mL) [9]. Vitamin D deficiency has been associated in other studies with an increased risk of chronic disorders such as cardiovascular disease, multiple sclerosis, rheumatoid arthritis, type 1 and 2 diabetes mellitus, cancer, autoimmune diseases, Crohn's disease, infectious diseases, and mental health disorders [6, 10, 11]. Suboptimal vitamin D values also contributed to bone conditions such as osteoporosis, falls, and fractures [12].

The comparison between the two groups showed a higher total number of comorbidities per patient, and a higher prevalence of several comorbidities in G1 when compared to G2.

**Table 3** Multiple linear regression of comorbidities and vitamin D levels

| Comorbidities (reference G1) | Estimate | OR | 2.5% | 97.5% | $p$ |
|---|---|---|---|---|---|
| Age | − 0.014 | 0.986 | 0.973 | 0.997 | 0.019 |
| Osteoporosis | − 0.884 | 0.432 | 0.292 | 0.655 | < 0.001 |
| Number of comorbidities | 0.247 | 1.281 | 1.142 | 1.440 | < 0.001 |
| Arthropathy | 0.683 | 1.981 | 1.042 | 3.930 | 0.042 |
| Anemias | 2.489 | 12.057 | 2.427 | 218.78 | 0.016 |
| Neurologic and psychiatric diseases | 1.045 | 2.843 | 1.451 | 6.017 | 0.003 |

Binary logistic regression with G1 and G2 as dependent variables; *G1* group 1 (250HD ≥ 20 and < 30 ng/mL); *G2* group 2 (25OHD ≥ 30 and ≤ 50 ng/mL)

The data were similar to those observed in a study with obese children, in which 38% had vitamin D levels between 20 and 30 ng/mL associated with the total number of comorbidities found [13]. However, in this study, patients in G2 (vitamin D ≥ 30 and < 50 ng/mL) were older and had more osteoporosis compared to G1, and had less secondary hyperparathyroidism, suggesting that these higher risk patients were probably being treated with vitamin D, as has already been described in another study, which may indicate more supplementation [9]; unfortunately, we do not have information about supplementation in these patients.

The prevalence of pneumopathies and smoking was not different between the groups, although the literature reports reduced concentrations of 25OHD in smokers [1], as well as the association of lower levels of 25OHD with lower lung function and worse asthma control [14]. Actually, it was not possible to associate the level of 25OHD with the presence or absence of chronic obstructive pulmonary disease in another study [1].

This study showed a higher prevalence of secondary hyperparathyroidism in G1, suggesting that the vitamin D level was still inadequate for some patients, inducing secondary hyperparathyroidism. The IOM suggests that the serum level of 20 ng/mL of 25OHD would protect 97.5% of the population against adverse bone events, in the same way that the Dachverband Osteologie guideline suggests concentrations > 20 ng/mL for osteoporosis prevention [15]. According to the International Osteoporosis Foundation, the level should be > 30 ng/mL, while the American Society for Bone and Mineral Research allows physicians to decide about the lower limit they consider normal [9]. Published studies with Brazilian populations have shown that 30 ng/mL is needed to avoid secondary hyperparathyroidism and higher risk of fractures [1, 16].

There was no correlation in the present study between the level of 25OHD and fractures, although elderly patients who received calcium and vitamin D had fewer fractures [17]. Possibly, our findings are the results of the exclusion of patients with lower levels of 25OHD; besides, fractures were captured in the medical records.

We observed a trend towards a higher prevalence of heart disease in G1, consistent with many studies that have shown an inverse association between 25OHD levels and hypertension, coronary artery calcification, and heart diseases such as myocardial infarction [18–20]. High blood pressure was the most prevalent comorbidity in this study in both groups; however, there was no correlation with the level of 25OHD. Although, such association has already been described [18], the higher probability to develop high blood pressure in patients with 25OHD ≤ 30 ng/mL [21] and the higher prevalence of cardiovascular risk factors were observed in the lower quartile of 25OHD [22].

In this study, a higher prevalence of dyslipidemia ($p = 0.031$) and glucose disorders ($p = 0.037$) was seen in G1 patients, as already described by others [23–25]. Higher prevalence of diabetes in a tertiary care center was observed with vitamin D lower than 20 ng/mL [26], and the supplementation of calcium with vitamin D in patients with altered fasting glucose decreased the insulin resistance and prevent the glycemic worsening compared to placebo [27], and in adults at risk of type 2 diabetes, cholecalciferol improved β cell function [28].

The presence of higher BMI in G1, associated with a trend towards a higher prevalence of obesity in this group ($p = 0.054$), agrees with the literature that showed lower baseline vitamin D levels in obese individuals and lower vitamin D production after exposure to ultraviolet radiation (UVB) [29]. Weight loss, instead, increased the circulating concentration of 25OHD in obese or overweight postmenopausal patients [30]. However, in an elderly population, the elevation of 25OHD by vitamin D supplementation was not influenced by adipose tissue mass [31].

Anemia was more prevalent in G1 ($p < 0.001$), consistent with a higher risk for anemia (hemoglobin < 11 g/dL) in patients with vitamin D levels below 30 ng/mL compared with normal levels (49 vs. 36%) [32].

The prevalence of hypothyroidism in the present study was higher in G2, which differs from another study showing that hypothyroid patients had lower levels of 25OHD (14.79 ± 2.11 ng/mL) compared to healthy individuals (44.53 ± 14.91 ng/mL) [33].

Neurological and psychiatric disorders were more prevalent in patients with 25OHD ≥ 20 and < 30 ng/mL compared to those with 25OHD ≥ 30 and ≤ 50 ng/mL ($p < 0.001$), data already described in a meta-analysis that showed higher risk of depression (OR 1.3) in the lower vitamin D category [34]. Despite the association of the diagnosis of depression and anxiety with low levels of vitamin D [35], the supplementation of high doses of vitamin D had no effect on depressive symptoms compared to placebo [36].

Other abnormalities, such as alterations of the urinary tract and arthropathies, had greater prevalence in G1, results corroborated by the literature [11, 37].

This study, probably due to the number of patients involved, did not show any difference in the prevalence of cancer and gastrointestinal tract disease, although both diseases were associated previously with low vitamin D levels [6, 9].

Despite the higher prevalence of comorbidities in the group considered insufficient by national and international endocrinology societies, it is not recommended to measure 25OHD for the general population, but only on the suspicion of deficiency for individuals belonging to populations at risk or in those whose clinical situation is relevant [38]. Whether a low vitamin D level alone is a marker of ill health is a matter to be clarified in the future [39]. Interventions to raise the level of vitamin D present conflicting data on the reduction of mortality, myocardial infarction, stroke, lipid fractions, glucose, and

blood pressure, according to consensus endorsed by the Endocrine Society. It is recommended to prescribe vitamin D supplementation for the prevention of falls and bone disease, but not for the purpose of preventing cardiovascular disease or death, or improving quality of life [6].

The limitations of this study are that the sample consists of outpatients of a tertiary hospital, and therefore with higher prevalence of comorbidities; also, the indications for 25OHD dosage and vitamin supplementation were not known, as well as information on race and sun exposure. The absence of this information in clinical charts shows that there is generally a greater interest in measuring serum vitamin D levels before investigating the classical risk factors for deficiency/insufficiency.

## Conclusion

Outpatients of a tertiary hospital with 25OHD ≥ 20 and < 30 ng/mL had higher prevalence of comorbidities compared to those with levels ≥ 30 and ≤ 50 ng/mL, suggesting that for this specific population 25OHD within the latter range would be more appropriate.

**Compliance with ethical standards** The study was approved by the research ethics committee (CEP-HC-UFPR), 46017715.0.3001.0096.

**Conflict of interest** None.

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