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ORIGINAL CONTRIBUTIONS

Prevalence of Vitamin D Depletion, and Associated Factors, among Patients Undergoing Bariatric Surgery in Southern Brazil

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Abstract

Background Hypovitaminosis D is common, before and after gastric bypass surgery. The prevalence of hypovitaminosis D in a large group of candidates for bariatric surgery in Brazil and South America has not been studied.

Objective To evaluate the prevalence of hypovitaminosis D and associated factors in patients undergoing bariatric surgery in Southern Brazil.

Materials and Methods Cross-sectional study involving all patients presenting for bariatric surgery at Hospital de Clínicas de Porto Alegre, from January 2013 to June 2018. Data were extracted from the patients' electronic medical records. Patients who were taking multivitamin supplements or vitamin D supplements, who had renal insufficiency, or had missing data for 25(OH) vitamin D [25(OH)D] levels were excluded.

Results A total of 291 patients were included. Mean subjects' age was 44.9 (SD 10.7) years, and BMI 49.3 (SD 8.3) kg/m^2; 76.6% of the study patients were women, and 87.3% were white. More than half the patients (55.3%) were vitamin D deficient (serum 25(OH)D ≤ 19.9 ng/ml), and 37.1% had insufficient levels (20–29.9 ng/mL). Mean vitamin D level was 19.2 ng/mL (SD 7.6). An inverse correlation was found between 25(OH)D levels and BMI. Vitamin D deficiency was more prevalent in patients with higher BMI [PR 1.02; CI 95% (1.00–1.03)], higher fasting glucose [PR 1.01; CI 95% (1.00–1.01)], in nonwhite patients [PR 1.58; CI 95% (1.30–1.92)] and during autumn/winter season [PR 1.41; CI 95% (1.14–1.75)].

Conclusions Prevalence of vitamin D insufficiency and deficiency is very high among patients presenting for bariatric surgery in Southern Brazil, and the known associated factors are confirmed in this population.

Keywords Bariatric surgery · Vitamin D · Hypovitaminosis D · Brazil

Introduction

Obesity is a growing public health problem. The worldwide rate of obesity nearly tripled since 1975 [1]. In Brazil, 18.9% of adults older than 18 years were obese in 2017 [2]. As a consequence, the numbers of individuals seeking treatment for obesity are also on the rise. The number of bariatric surgeries performed in Brazil increased 46% between 2012 and 2017 [3]. Bariatric surgery is the most effective, and the only available treatment that produces durable long-term weight loss, resulting in improvements in quality of life and obesity-related conditions [4]. However, patients undergoing the procedure are at risk for nutrient deficiencies due to malabsorption, poor eating behavior, food intolerance, and food restriction [5].

Low levels of 25-hydroxyvitamin D [25(OH)D] are common in patients undergoing bariatric surgery. Hypovitaminosis D has been reported in 41 to 98% [6–26] of patients preoperatively, and has been described as an independent risk factor for vitamin D deficiency postoperatively [22]. Vitamin D deficiency and insufficiency are of particular

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concern in patients undergoing gastric bypass since it is well documented that, despite the institution of supplementation after the procedure, serum 25(OH)D often remains below the recommended level of 30 ng/ml [6]. The current recommended repletion strategy for vitamin D postoperatively is vitamin D3 at least 3000 IU/day, up to 6000 IU/day [27].

There is plenty of evidence pointing to untoward implications of low levels of vitamin D. The importance of vitamin D for musculoskeletal health has long been known [28–30]. Studies have demonstrated that bone mineral density after bariatric surgery is significantly lower due to elevated bone turnover and accelerated bone remodeling [31, 32]. In addition, vitamin D deficiency is a common cause of secondary hyperparathyroidism, and could add to bone loss and fracture risk. The correction of vitamin D levels before and after surgery is probably essential to prevent further metabolic bone damage [33]. Furthermore, hypovitaminosis D has been associated with less weight loss after bariatric surgery [23]. More recently, untoward surgical outcomes, higher surgical site and hospital acquired infection rates, and higher in-hospital and 1-year mortality have also been associated with lower preoperative vitamin D levels [23, 34–36].

The rates of vitamin D deficiency and insufficiency in patients seeking bariatric surgery has been well studied in North America, Europe, and Middle East. However, to our knowledge, in South America, only very few studies with modest sample sizes were carried out [37–39]. Current guidelines recommend that circulating levels of vitamin D are determined and that any deficiency (i.e., levels below 20 ng/ml) is treated in order to maintain a 25(OH)D level above 30 ng/ml. Preoperative treatment of vitamin D insufficiency (i.e., levels 20.0–29.9 ng/mL) is not consensus, but supplementation is commonly advised [27, 28, 40, 41].

The Brazilian population is highly miscigenated. In the deep South of Brazil, the ingestion of oily fish and other sources of vitamin D precursors is very low [42]. Also, the number of sunny days is lower than in the North of Brazil and, because the rates of skin cancer are high in the region, the majority of the population avoids unprotected sunlight exposure [43]. Given these regional characteristics, one could expect that vitamin D insufficiency/deficiency is highly prevalent. If the prevalence is indeed very high, screening strategies may be unnecessary, and vitamin replacement could be instituted immediately. The number of patients being evaluated for bariatric surgery in our state is in the range of several thousands. If a very large number of laboratory determinations is saved, precious (and, in our case, scarce) resources would be saved. A systematic vitamin D supplementation policy could probably be implemented, helping more patients achieve normal levels in a shorter time, making the postoperative management easier.

Therefore, the purpose of this study was to evaluate the prevalence of hypovitaminosis D in patients presenting for bariatric surgery in Southern Brazil. Secondarily, we aimed to identify factors that might be associated with deficiency of vitamin D in this population.

Material and Methods

We conducted a cross-sectional observational study involving all consecutive patients presenting for bariatric surgery at Hospital de Clínicas de Porto Alegre (HCPA) from January 2013 to June 2018. HCPA is a University Hospital, teaching, and secondary-tertiary care facility. The exclusion criteria were missing data for 25(OH)D levels, intake of multivitamin or vitamin D supplements until 3 months prior to serum 25-OH vitamin D determination, and renal insufficiency (creatinine > 1.5 mg/dL). The study was approved by the HCPA Research Ethics Committee (no. 18-0074).

Prior to surgery, as part of standard care and preoperative assessment protocol, patients were evaluated in the Bariatric Surgery and Endocrinology outpatient units of HCPA. The electronic medical records of 536 patients were reviewed. General clinical data were collected on demographic characteristics (age, gender, auto-declared skin color, educational level), medical history, and current medications. Anthropomorphic assessments (height, weight, and waist circumference) were performed in accordance with the recommendations of the Brazilian Ministry of Health's Food and Dietary Surveillance System.

Biological data collected included hemoglobin, albumin, parathyroid hormone (PTH), serum-corrected calcium, lipid profile, insulin, fasting glucose, glycated hemoglobin, and vitamin B12 level. Laboratory results and clinical data were only considered if collected no more than 6 months before the collection of the sample for 25(OH)D level. The Homeostatic Model Assessment of Insulin Resistance score (HOMA-IR score) was calculated.

Serum 25(OH)D levels were measured by chemiluminescence (ARCHITECT 25-OH VITAMIN D® microparticle immunoassay, Abbott Diagnostics, Lake Forest, IL, USA). Vitamin D status was defined according to the Endocrine Society's latest guidelines for vitamin D levels (deficiency 19.9 ng/ml; insufficiency 20–29.9 ng/mL; sufficiency ≥ 30 ng/mL) [29], and PTH levels above 72 pg/mL were considered to represent hyperparathyroidism. Reference ranges of normal levels were 211–946 pg/mL for vitamin B12 and 8.6–10 mg/dL for serum-corrected calcium. Blood sampling season was defined as spring/summer (October–March) or autumn/winter (April–September).

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 20.0® (Cary, EUA). Descriptive data were expressed as frequencies (%) for categorical data, means and standard deviations (SD) for continuous data with normal distribution,. and median and interquartile range (IQ) for continuous data without normal distribution. When appropriate, comparisons between groups were performed using Student's *t* test or Mann-Whitney's test, for continuous variables, and chi-square test or Fisher's exact test for the categorical variables. Correlations were done with Pearson's test for data with normal distribution and Spearman's test for data without normal distribution. The analysis of factors associated with vitamin D deficiency was performed by univariate and multivariate robust Poisson Regression. The multivariate model was built through a backward stepwise selection. Age, because it is clinically associated with vitamin D deficiency, and variables with a p value < 0.05 were included in the multivariate analysis. Statistical significance was accepted at $p < 0.05$.

Results

A total of 291 patients met the inclusion criteria and were enrolled for data analysis (Fig. 1). Their characteristics are summarized in Table 1. The excluded patients did not differ from the included patients in terms of age, gender, skin color, and BMI (data not shown). In our sample, mean age was 44.9 (10.7) years; 76.6% were female; 87.3% were white. The mean weight of participants was 132 (25.3) kg and mean BMI was 49.3 (8.3) kg/m^2. Ten percent of subjects had class II obesity and 90% had class III obesity. Comorbidities were highly prevalent: 78% had hypertension; 43% had diabetes mellitus; 36.8% had dyslipidemia, and 57.7% had multiple comorbidities. Multiple comorbidities were more common in class II than in class III obesity (79.3% vs 55.3%, $p = 0.013$). Regarding nutritional deficiencies, 2.6% was vitamin B12 deficient; 92.4% had hypovitaminosis D (37.1% insufficiency; 55.3% deficiency), being 19.2 (7.6) ng/mL the mean 25(OH)D level. Severe vitamin D deficiency (< 10 ng/mL) was present in 10.3% of patients. Vitamin D distribution for the entire study group was normal. White patients had statistically significant higher hemoglobin levels and lower prevalence of vitamin D insufficiency and deficiency (Table 1).

Parathyroid hormone levels were elevated in 37% of patients, and a statistically significant, negative correlation was found between PTH and vitamin D ($r = -0.370$, $p = 0.006$). Calcium level was normal in 85.7% of subjects, low in 10.2%, and elevated in 4.1%. No correlation was seen between calcium and vitamin D levels ($r = 0.026$, $p = 0.803$), nor between waist circumference and vitamin D ($r = -0.170$, $p = 0.104$). A significant inverse correlation was found between vitamin D levels and BMI (Fig. 2; $r = -0.257$, $p < 0.001$); and between vitamin D levels and HOMA-IR ($r = -0.445$, $p = 0.005$).

The mean 25(OH)D levels measured in spring/summer were significantly higher than those measured in the autumn/winter [spring/summer 20.9 (7.8) ng/mL vs autumn/winter 17.6 (7.1) ng/mL; $p < 0.001$]. The highest 25(OH)D mean level occurred in February [25.3 (6.8) ng/mL], and the lowest mean level occurred in August [15.8 (6.0) ng/mL].

On univariate analysis (Table 2), vitamin D deficiency was associated with higher BMI, being nonwhite, having type 2 diabetes mellitus, blood sampling in autumn/winter, use of calcium channel blockers, and higher fasting glucose or glycated hemoglobin. After multivariate adjustment, higher BMI, being nonwhite, autumn/winter blood sampling season and higher fasting glucose remained independently associated with vitamin D deficiency (Table 3).

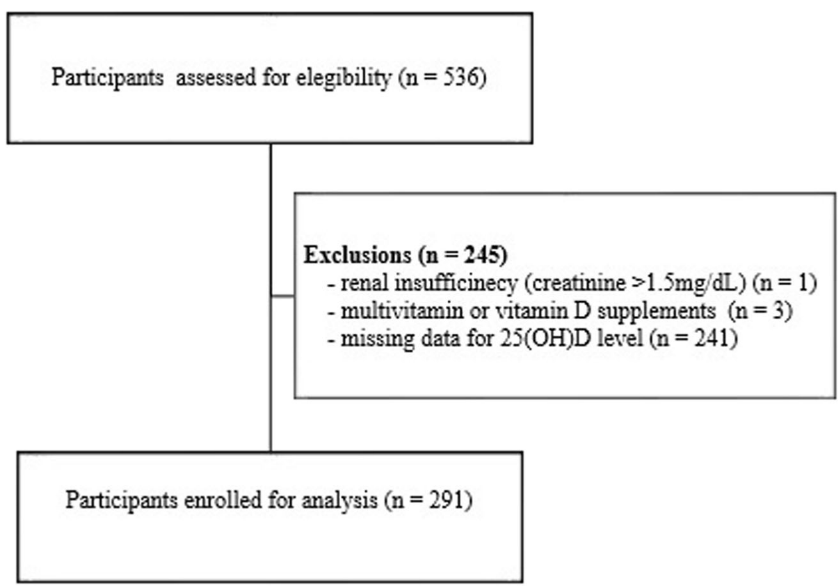

Fig. 1 Inclusion and exclusion flow chart

Table 1 Characteristics of bariatric surgery candidates

Characteristic	Total	White $n = 254$	Nonwhite $n = 37$	*p* value
Demographics				
Age (years)	44.9 (10.7)	44.9 (10.8)	44.7 (10)	0.931[a]
Gender				
Female	223 (76.6)	191 (75.2)	32 (86.5)	0.149[c]
Educational level				0.059[c]
No education	114 (39.2)	100 (39.4)	14 (37.8)	
Elementary School	78 (26.8)	62 (24.4)	16 (43.2)	
High school	92 (31.6)	86 (33.9)	6 (16.3)	
University degree (complete or incomplete)	7 (2.4)	6 (2.3)	1 (2.7)	
Season				0.385[c]
Spring/summer	138 (47.4)	123 (48.4)	15 (40.5)	
Autumn/winter	153 (52.6)	131 (51.6)	22 (59.5)	
Anthropometric assessment				
Weight (kg)	132 (25.3)	132.1 (25.5)	131.5 (24)	0.901[a]
Height (m)	1.64 (0.1)	1.64 (0.1)	1.61 (0.1)	0.067[a]
Body Mass Index (kg/m^2)	49.3 (8.3)	49.1 (8.3)	50.7 (8)	0.272[a]
Waist circumference (cm)	135.4 (17.1)	135.7 (17)	133.1 (18.8)	0.691[a]
Comorbidities				
Hypertension	227 (78)	198 (78)	29 (78.4)	1.000[c]
Diabetes mellitus type 2	125 (43)	110 (43.3)	15 (40.5)	0.859[c]
Dyslipidemia	107 (36.8)	96 (37.8)	11 (29.7)	0.368[c]
Thyroid disease				0.150[c]
Hyperthyroidism	2 (0.7)	2 (0.8)	0 (0)	
Hypothyroidism	45 (15.5)	43 (16.9)	2 (5.4)	
Multiple comorbidities	168 (57.7)	151 (59.4)	17 (45.9)	0.154[c]
Laboratorial findings				
Insulin (uU/mL)	25.5 (18)	25.6 (18)	24.5 (23.2)	–[d]
Glycated hemoglobina (%)	6 (1.7)	6 (1.7)	6.3 (1.7)	0.414[b]
Fasting glucose (mg/dL)	105 (36.3)	104.5 (38.8)	113 (34.5)	0.890[b]
PTH (pg/L)	67.5 (37.8)	67.5 (37.2)	67.2 (51.1)	–[d]
Serum-corrected calcium (mg/dL)	9.0 (0.8)	9.0 (0.8)	9.2 (0.6)	0.532[a]
Hemoglobin (g/dL)	13.3 (1.4)	13.4 (1.4)	12.5 (1.2)	0.001[a]
Albumin (g/dL)	4.25 (0.4)	4.3 (0.4)	4.3 (0.1)	–[d]
Vitamin B12 (pg/mL)	412.9 (213)	415.6 (214)	409.4 (217)	0.927[b]
25(OH)D (ng/mL)	19.2 (7.6)	19.9 (7.6)	14.4 (5.5)	0.000[a]
Nutricional deficiencies				
Vitamin D status				0.008[c]
Insufficiency	108 (37.1)	100 (39.4)	8 (21.6)	
Deficiency	161 (55.3)	132 (52)	29 (78.4)	
Sufficiency	22 (7.6)	22 (8.6)	0 (0)	
Vitamin B12 deficiency	5 (2.6)	5 (2.0)	0 (0)	1.000[c]

Data expressed as the mean (standard deviation), median (interquartile range), or *n* (prevalence). [a] *T* test. [b] Mann-Whitney *U* test. [c] chi-squared test. [d] Variables with less than five nonwhite patients with available data

Discussion

The present study showed that among patients awaiting bariatric surgery in Southern Brazil, vitamin D depletion is highly prevalent. In addition, we found that higher BMI, being nonwhite, autumn/winter season, and higher fasting glucose are independent risk factors for vitamin D deficiency preoperatively.

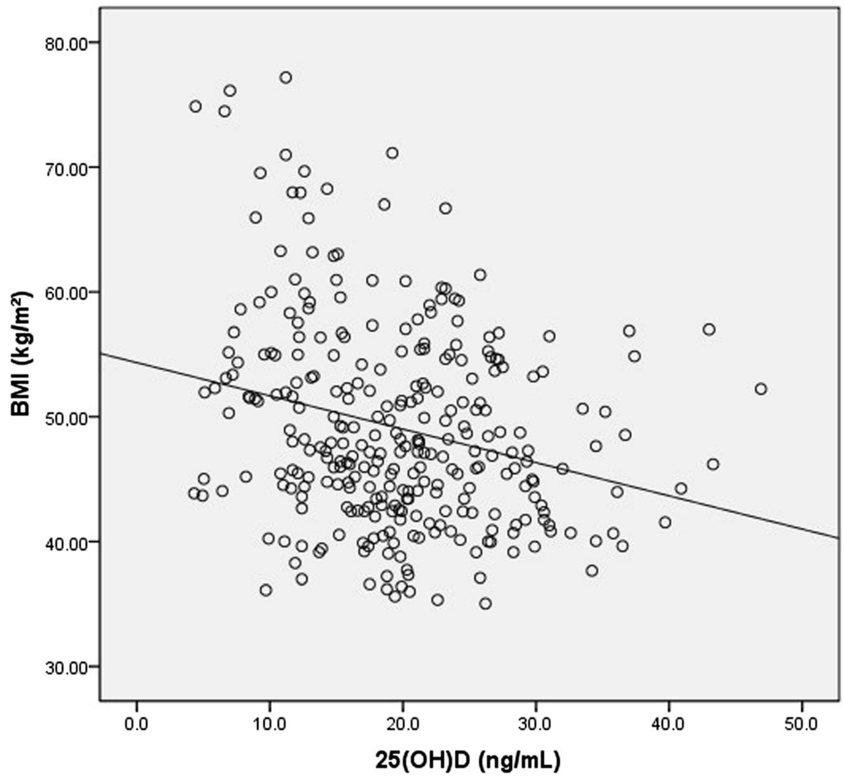

Fig. 2 Pearson's correlation coefficient (*r*) between 25(OH)D levels and body mass index (BMI): a significant weak inverse correlation was found ($r = -0.257$)

A retrospective study on bariatric surgery patients of the Metropolitan area of Porto Alegre has reported that 85% of bariatric surgery patients are female with mean age of 41.3 (10.2) years, similar to this study [76.6% female; 44.9 (10.7) years] [44]. The skin color distribution of our sample is alike the distribution in the general population of Southern Brazil [45]. The higher rate of multiple comorbidities in class II patients in comparison to class III patients found in our sample is probably due to the current Brazilian guidelines for bariatric surgery: once patients with a BMI between 35 and 40 kg/m^2 must have at least one obesity-related co morbidity to be considered potentially eligible for bariatric surgery [46, 47].

In this study, an inverse correlation between body mass index (BMI) and serum 25(OH)D concentration was found. Previous studies have reported this correlation as well and qualified obesity as a risk factor for vitamin D deficiency [48–53]. Although association between reduced 25(OH)D concentrations and obesity is well-established, the mechanisms behind this relationship are unclear. These could include lower dietary intake, impaired skin synthesis, lower sunlight exposure, sequestration of 25(OH)D in the adipose tissue, distribution of 25(OH)D into a larger whole body tissue volume, alterations in protein binding, or faster metabolic clearance [54].

There is limited data on the preoperative vitamin D status in patients undergoing bariatric surgery in Brazil. In our study, we found higher rates of hypovitaminosis D and lower mean levels of 25(OH)D in comparison to the available published data. This difference might be attributed to the fact that the two previous studies were carried out in coastal cities, where the inhabitants are more prone to sun exposure [37, 38]. A very small study ($n = 22$) performed in an inner city of Brazil has found similar rates of hypovitaminosis D in bariatric patients prior to surgery (92%), but the cutoff values used were not reported by the authors [39]. A community-based study in Southeast Brazil has found hypovitaminosis D in 70.7% of a large sample of the general population [55].

The major sources of vitamin D are sun exposure, and, to a lesser extent, dietary intake. Natural diets that most humans consume contain a small amount of vitamin D, unless they are rich in oily fish and cod liver oil [56]. It is worth noting that, although Brazil is sunnier and placed in a smaller latitude than Europe and North America, the prevalence of hypovitaminosis D in bariatric surgery candidates is similar to—or even higher than—the one found in studies carried out in these places [7, 9, 11, 13, 22–24, 26]. In Brazil, there is no food fortification policy, and the dietary intake of vitamin D is almost universally below the daily recommendation [42, 57–59], being occasional sun exposure the major source of 25(OH)D. Once sunlight is plentiful even in the winter months, this finding is more likely due to behavioral habits. However, the existent literature concerning the role of latitude in vitamin D levels is controversial [60–62].

Table 2 Univarite analysis: variables and prevalence of vitamin D deficiency

Variables	25(OH)D < 20 ng/mL $n = 161$	25(OH)D ≥ 20 ng/ml $n = 130$	PR (95% CI)	*p* value
Age (years)[a]	45.2 (10.8)	44.5 (10.7)	1.01 (0.99–1.01)	0.575
Gender [c]				
Female	123 (55.1)	100 (44.9)	0.99 (0.77–1.25)	0.916
Male	38 (55.9)	30 (44.1)	1	
Skin color [c]				
Nonwhite	29 (78.4)	8 (21.6)	1.51 (1.23–1.85)	0.000
White	132 (52)	122 (48)	1	
BMI (Kg/m^2)[a]	50.7 (9.1)	47.6 (6.8)	1.02 (1.01–1.03)	0.000
Season[c]				
Autumn/winter	96 (62.7)	57 (37.3)	1.33 (1.08–1.65)	0.009
Spring/summer	65 (47.1)	73 (52.9)	1	
Multiple comorbidities[c]				
Yes	94 (56)	74 (44)	1.03 (0.83–1.27)	0.802
No	67 (54.5)	56 (45.5)	1	
Diabetes mellitus 2[c]				
Yes	78 (62.4)	47 (37.6)	1.25 (1.02–1.53)	0.033
No	83 (50)	83 (50)	1	
Hypertension[c]				
Yes	126 (55.5)	101 (44.5)	1.02 (0.79–1.31)	0.908
No	35 (54.7)	29 (45.3)	1	
Statin[c]				
Yes	30 (50.8)	29 (49.2)	1	
No	131 (56.5)	101 (43.5)	1.11 (0.84–1.46)	0.455
Thiazides[c]				
Yes	70 (57.4)	52 (42.6)	1.07 (0.87–1.31)	0.548
No	91 (53.8)	78 (46.2)	1	
Calcium blocker[c]				
Yes	29 (70.7)	12 (29.3)	1.34 (1.07–1.69)	0.012
No	132 (52.8)	118 (47.2)	1	
Glycated Hemoglobin (%)[b]	6.2 (2.1)	5.8 (1.1)	1.07 (1.01–1.12)	0.014
Fasting glucose (mg/dL)[b]	108 (48)	100.5 (28.5)	1.01 (1.0–1.01)	0.003

[a] Data are expressed as mean (standard deviation), [b] median (interquartile range), [c] *n* (prevalence) or prevalence ratio (confidence interval)

In this study, low levels of 25(OH)D were particularly prevalent among nonwhite patients. None of the nonwhite subjects had adequate 25(OH)D levels compared to 8.6% of white subjects. Vitamin D deficiency was present in 78.4% of nonwhite patients, while only 52% of white subjects were vitamin D deficient. These findings are in accordance with several previous studies [9, 15, 22, 63, 64], and are explained by the fact that melanin absorbs ultraviolet photons in competition with 7-dehydrocholesterol, the precursor molecule that is photoconverted in previtamin D. Thus, the more melanin in human skin, the longer exposure to or higher intensity of UV radiation is required to maximize previtamin D3 formation [65].

This study had limitations. First, data were collected retrospectively, resulting in a significant number of excluded patients (45.7%) due to incomplete data, which can have led to selection bias. Additionally, information on sun exposure and dietary intake were not analyzed, and a comparison with non-obese controls was not performed.

There is growing evidence that vitamin D sufficiency is needed for optimal health. Recently, studies have shown that vitamin D might play a role in muscle function and in the risks of colon cancer, cardiovascular disease, diabetes, and multiple sclerosis [66–75]. In addition, the well-known importance of vitamin D for bone and mineral metabolism makes hypovitaminosis D particularly

Table 3 Multivariate analysis for risk factors of vitamin D deficiency

Variables	Adjusted PR (95% CI)	*p* value
Age	1.00 (0.99–1.01)	0.858
Skin color		< 0.001
Nonwhite	1.58 (1.30–1.92)	
White	1	
Body mass index	1.02 (1.00–1.03)	0.003
Season		
Autumn/winter	1.41 (1.14–1.75)	0.002
Spring/summer	1	
Fasting glucose	1.01 (1.00–1.01)	0.002

Data expressed as prevalence ratio (confidence interval)

concerning among bariatric surgery candidates since, as shown in this study, this population is essentially composed of perimenopausal women, who are intrinsically at higher risk for bone loss by virtue of estrogen deficiency. Even though weight loss is the main objective of gastric bypass, minimizing the untoward effects of the surgery, and to ensure long-term quality of life is equally relevant. Based on this, it seems evident the importance of vitamin D for the maintenance of the global health of patients undergoing gastric bypass.

In conclusion, considering the very high prevalence of vitamin D deficiency and insufficiency among bariatric surgery candidates living in Southern Brazil, treatment for hypovitaminosis D might routinely be considered in this population, especially in those with characteristics identified as vitamin D deficiency independent risk factors, such as higher BMI and, mainly, nonwhite skin color. For these patients, measuring blood levels of 25(OH)D could probably be unnecessary prior to the institution of replacement. This could save scarce resources for the national health service. Notwithstanding, long-term interventional studies are required to assess the advantages and side effects of systematic vitamin D supplementation in this population, as well as to define the optimal dose of vitamin D supplementation therapy.

Author Contribution The manuscript has been read and approved by all authors.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in this study were in accordance with the ethical standards of the HCPA Research Ethics Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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