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Epidemiology of Vitamin D (EpiVida)—A Study of Vitamin D Status Among Healthy Adults in Brazil

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Abstract

Context: There are few studies of 25-hydroxyvitamin D (25(OH)D) concentrations in healthy adults in Brazil.

Objective: This work aimed to estimate the prevalence of vitamin D status and its association with lifestyle, sociodemographic, and anthropometric data in 3 regions of Brazil.

Methods: A cross-sectional study was conducted among blood donors of both sexes, living in the cities of Salvador, São Paulo, and Curitiba during summer. Blood samples were collected during the procedure. Serum 25(OH)D and parathyroid hormone (PTH) were measured in the same laboratory using chemiluminescence immunoassays. Lifestyle, sociodemographic, and anthropometric data were gathered by an interview with a standardized questionnaire. Vitamin D deficiency and insufficiency was defined as 25(OH)D levels below 20 ng/mL and below 30 ng/mL, respectively.

Results: A total of 1004 healthy adults were evaluated with mean levels of 25(OH)D (28.7 ± 9.27 ng/mL) and PTH (34.4 ± 15.1 pg/mL). The standardized prevalence of vitamin D deficiency and insufficiency was in the study population 15.3% and 50.9%: in Salvador 12.1% and 47.6%, in São Paulo 20.5%, and 52.4% and in Curitiba 12.7% and 52.1%, (P = .0004). PTH levels were negatively correlated with 25(OH)D levels. Greater body mass index (BMI) and higher latitude were significant predictors of vitamin D deficiency, whereas skin color (White), longer duration of sun exposure, and current use of dietary supplement were protective.

Conclusion: This study confirmed the high prevalence of vitamin D deficiency and insufficiency even in the midsummer in a healthy population of Brazil. Vitamin D levels are associated with sun exposure, latitude, BMI, skin color, and use of supplements.

Key Words: vitamin D deficiency, sociodemographic factors, lifestyle, epidemiology, healthy adults, parathyroid hormone

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; CV, coefficient of variation; OR, odds ratio; PTH, parathyroid hormone.

Vitamin D is in fact a "prohormone" given it can be synthesized in the skin from ultraviolet B light on cutaneous sun exposure, and then converted to its active metabolite 1,25-dyhydroxyvitamin D (calcitriol) in the kidney stimulated by parathyroid hormone (PTH). Diet provides low quantities of this "vitamin," and sunlight exposure is its main source. The most abundant circulant form is 25-hydroxyvitamin D (25(OH)D), which is considered the biomarker to evaluate vitamin D status and is classically related to mineral homeostasis and PTH secretion. Low level of 25(OH)D is the most common etiology of secondary hyperparathyroidism (1).

Vitamin D status depends on the population studied, health status, skin color, age, genetic background, geographic characteristics, among other factors, which makes it a considerable challenge to establish their normal levels. Low concentrations of 25(OH)D have been associated with many detrimental health conditions, both skeletal and extraskeletal. Different end points were used to stablish the 25(OH)D ideal levels, including secondary hyperparathyroidism, osteomalacia or osteoporosis, muscle weakness, increased risk of falls or fractures among others, with no definitive consensus so far (2).

The Institute of Medicine defines vitamin D deficiency as 25(OH)D levels lower than 20 ng/mL (< 50 nmol/L) regardless of the population studied (3). Other institutions take into account age, risk factors for vitamin D deficiency, and health status, such as presence of metabolic bone diseases and other chronic diseases to define 30 ng/mL as the preferred level (2, 4, 5).

Vitamin D deficiency is highly prevalent worldwide, with levels below 30 ng/mL (75 nmol/L) being described globally. The lowest levels (< 10 ng/mL or 25 nmol/L) are associated with rickets and osteomalacia and, although more frequent in Asia and the Middle East, can be present all over the world (6). In Brazil, inadequate vitamin D status has been described in all regions. A metanalysis of 72 studies developed throughout the country found an average of 28.16% deficiency

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(25(OH)D < 20 ng/mL) and 45.26% insufficiency (< 30 ng/mL). The southern and southeastern regions had the highest concentration of vitamin D deficiency, while the insufficiency was concentrated in the southeastern and northeastern regions. This metanalysis included studies that used different vitamin D assays, and the majority of the sample size was from the southernmost regions of the country (7). Other studies of the Brazilian population also showed a high frequency of vitamin D deficiency and insufficiency in patients with chronic diseases such as osteoporosis, systemic lupus erythematosus, chronic obstructive pulmonary disease, and others (8-10). Nevertheless, data regarding vitamin D status in a health population of both sexes, with different ages, samples collected at the same time range, measured with the same method, and with sociodemographic information, are lacking for the Brazilian population.

The aim of this study was to evaluate 25(OH)D and parathyroid hormone (PTH) levels in healthy adults from urban areas of Brazil, according to age group, sex, and latitude of residence.

Materials and Methods

Study Design

This was a cross-sectional, multicenter study among adults in Brazil, conducted over a period of 3 consecutive months, from December 14, 2020 to March 29, 2021, at 3 blood banks (Hospital Santo Antônio, Salvador, Bahia; Associação Beneficente de Coleta de Sangue–COLSAN, São Bernardo do Campo, São Paulo; and Instituto Paranaense de Hemoterapia e Hematologia–Hemobanco, Curitiba, Paraná). São Bernardo do Campo is an industrial city considered part of the megalopolis São Paulo; for this reason it will be considered as São Paulo. These sites were selected based on an objective review of site capacity to enroll enough participants, and on their location at different latitudes. Weekly study-site visits, enrollment reports, and data audits were conducted to ensure standardized procedures at all study sites.

Study Population

All individuals volunteering for blood donation at the 3 blood banks were screened. Inclusion criteria were being aged 18 years or older and eligible to donate blood (good health, no communicable diseases or illegal drug use, and weigh ≥ 50 kg). Individuals were excluded if they did not live in one of the cities where the study sites were located, reported current use of vitamin D supplements in the last 30 days, or were blood donors who have recovered from COVID-19 in 2019 (plasma convalescent donors). Eligible individuals were recruited following a quota system set up so that the final sample would be equally stratified by sex (male and female), and by 3 age groups (18-29 years, 30-44 years, and > 45 years). Considering a prevalence of vitamin D deficiency of 20% to 35% in the study regions, with a CI of 95% and error of 5%, the sample size was estimated at 334 individuals for each city, thus a total of 1004 participants were enrolled. The study protocol was approved by an ethical review board (approval No. 3.797.104), and all participants provided written informed consent prior to enrollment.

Data Collection

A structured questionnaire was administered in person by trained and certified interviewers. A team of study interviewers was hired and trained by one of the investigators (E.D.M.) in each participating center. They were given an orientation on the protocol and specific details concerning participation in the study. Prior to study commencement, they all carried out practice sessions with authenticated respondents. These preliminary interviews were observed and critiqued by the investigators.

The questionnaire included information on socioeconomic and lifestyle characteristics, such as age, sex, race/ethnicity, education, monthly income, sunlight exposure time (average number of minutes per day), smoking status, physical activity, and current use of multivitamin and dietary supplements with no more than 10 µg per day of vitamin D. Daily sunlight exposure was also quantified based on the interview, frequency and length of outdoor activities, location of work and/or daily routine, and usual outdoor clothing. The self-reported values for weight and height were used to compute body mass index (BMI) as the weight in kilograms divided by height in meters squared. Participants were divided into categories based on their BMI according to the following criteria: underweight (BMI < 18.5), normal weight (BMI ≥ 18.5-25), overweight (BMI ≥ 25-30), obesity class I (BMI ≥ 30-35), obesity class II (BMI ≥ 35-40), and obesity class III (BMI ≥ 40). Smoking status was defined by 3 categories: never smokers, former smokers, and current smokers.

The skin phototype defined by sunburn and tanning history was classified from I to VI as proposed by Fitzpatrick (11): I) the skin burns easily and never tans; II) the skin burns easily and tans minimally with difficulty; III) the skin burns moderately and tans moderately and uniformly; IV) the skin burns minimally and tans moderately and easily; V) the skin rarely burns and tans profusely; and VI) the skin never burns and tans profusely).

Based on the questionnaires, 2 distinct variables on physical activity were considered: work/routine daily activity and leisure time activity. Participants were asked to classify themselves into 1 of 3 groups of work/routine activity: 1) mainly sedentary, 2) predominantly walking without heavy lifting, or 3) mainly walking including climbing stairs or lifting heavy objects. Likewise, they were asked to classify themselves in 1 of 4 groups of leisure time activity: 1) mainly sedentary, 2) light to moderate activity comprising walking and/or riding a bicycle, 3) regular sports and exercise or heavy gardening, or 4) athletic training (12). The latitude, longitude, and altitude of each city were as follows 12°58′ S, 38°28′ W, and 12 m (Salvador); 23°41′ S, 46°33′ W, and 762 m (São Bernardo do Campo); and 25°26′ S, 49°16′ W, and 925 m (Curitiba), respectively (obtained from http://maps.google.es/). To make use of these data, latitudes were added to the database as numeric variables with 2 decimals (ie, Salvador = 12.98).

Measurements of 25-Hydroxyvitamin D and Parathyroid Hormone

All participants provided a single, nonfasting venous blood sample of 10 mL. Blood samples were collected during blood donation and were kept under refrigeration until centrifugation in refrigerated centrifuges, the serum separated into at least 2 aliquots, and immediately frozen and stored at −20 °C until analysis, which took place less than a week after sampling in a certified laboratory by DEQAS for 25(OH)D measurement. Serum 25(OH)D levels were measured by competitive electrochemiluminescence immunoassays using the Elecsys 2010 system (Roche Diagnostics) with an intra-assay coefficient of variation (CV) of 4%, and an interassay CV of

8%. Serum PTH was measured by an electrochemiluminescence immunoassay (Roche Diagnostics GmbH), reference range = 10 to 65 pg/mL, with an intra-assay CV of 2.8% and an interassay CV of 3.0% to 3.6%.

Based on serum 25(OH)D level, participants were grouped into 4 categories: vitamin D sufficiency = 25(OH)D greater than or equal to 30 ng/mL; vitamin D insufficiency = 25(OH)D greater than or equal to 20 and less than 30 ng/mL; vitamin D deficiency = 25(OH)D less than 20 ng/mL; and severe vitamin D deficiency = 25(OH)D less than 10 ng/mL (4).

Statistical Analysis

Results are presented as the means (±SD), and categorical data are summarized as percentages. With respect to the participants' vitamin D status and characteristics, *t* test for independent samples and one-way analysis of variance were used for continuous data, and the chi-square test was used to compare frequencies.

Age-specific prevalence of vitamin D deficiency was calculated for men and women. Since the age structure of our sample was predefined by a quota system, age-standardized prevalence of vitamin D deficiency for men and women was calculated overall and in each city studied. The direct standardization method using the age distribution of Brazil's estimated population for 2020 as a standard was used to calculate the age-standardized rates.

Linear associations between predictor variables and serum 25(OH)D concentrations were assessed by simple and stepwise multiple linear regression analyses. Logistic regression was also performed to determine independent predictors of 25(OH)D concentration below 20 ng/mL (13). Adjusted odds ratios (ORs) and respective 95% CIs were estimated by multivariate-adjusted logistic regression analyses to calculate the association between predictor variables, adjusted for all other predictor variables including age, sex, race/ethnicity, education levels, month of recruitment, income, BMI groups, smoking history, physical activity at work and at leisure activities, Fitzpatrick skin phototype, daily sun exposure time, outdoor attire, outdoors work/daily routine and leisure activities, type of housing, latitude, and multivitamin and diet supplement use. Univariate analysis was performed to arrive at a final model that included statistically significant ($P < .2$) independent variables in the adjusted logistic regression analysis. Sociodemographic variables (eg, age and sex) were forced into the model. Linear trends (dose-response ratio) across ordered categories were tested by scoring the categories and modeling the variables as continuous variables in the statistical models. *P* values of likelihood ratio tests were used to test for statistical significance in all logistic regression analyses. All regression analyses were performed separately for men, women, and overall. Differences were considered statistically significant at *P* less than .05. All the statistical analyses were performed using STATA statistical software (version 12) (StataCorp).

Results

In total, 1004 of 1029 eligible individuals invited to participate in the study were enrolled for a response rate of 97.6%. Participant characteristics by study site and sex varied among cities as shown in Table 1, except for age and BMI.

The overall mean serum 25(OH)D level was 28.7 ± 9.27 ng/mL. The standardized prevalence of vitamin D deficiency and insufficiency in the whole study population was 15.3% and 50.9%, in Salvador was 12.1% and 47.6%, in São Paulo was 20.5% and 52.4% and in Curitiba 12.7% and 52.1%, respectively ($P = .0004$).

The vitamin D status of all study participants according to selected characteristics is summarized in Table 2. Compared to men, women exhibited a significantly lower mean 25(OH)D level ($P = .002$), with a higher prevalence of vitamin D deficiency ($P = .004$). Neither the mean serum concentrations nor the prevalence of vitamin D deficiency were significantly different by age strata, whereas there was a significant difference both in the mean level of 25OHD ($P < .0001$) and prevalence of vitamin D deficiency ($P < .001$) according to the city of study site.

Obese and overweight individuals presented with lower mean serum 25(OH)D concentrations ($P < 10^{-10}$) and higher percentages of vitamin D deficiency ($P < 10^{-9}$). Participants who worked mostly indoors, had low work/daily routine activity, or low leisure time with lower physical activity levels were more likely to have a higher percentage of vitamin D deficiency and lower 25(OH)D concentrations (all $P < .05$). Moreover, individuals with more time of daily sun exposure, with larger body surface exposed to the sun, who engage in outdoor leisure activities more often, and are current users of multivitamin or dietary supplement were more likely to have higher 25(OH)D concentrations and a lower percentage of vitamin D deficiency (all $P < .05$). Race/ethnicity, educational level, income, smoking history, and type of housing had no effect on vitamin D levels or status.

Associations between predictor variables and 25(OH)D concentrations analyzed by linear regression are depicted in Table 3. Among the variables retained in the stepwise multiple linear regression, all except age and sex were associated with 25(OH)D concentrations. In this adjusted model, there was a stronger association between BMI and 25(OH)D levels and a weaker association between body surface area exposed to sun and 25(OH)D.

Adjusted ORs for low serum 25(OH)D concentration with a cutoff value of less than 20 ng/mL according to levels of predictors variables in men and women are shown in Table 4. Multiple logistic regression analysis revealed that greater BMI and higher latitude were significant predictors of vitamin D deficiency, whereas skin color (white), longer duration of sun exposure, and current use of dietary supplements were protective both in men and women. When both sexes were combined, the associations detected in the sex-specific analyses remained, but sex was not significantly associated with vitamin D deficiency.

PTH mean levels were 34.4 ± 15.1 ng/mL and elevated in only 3.5% of the study population. It was negatively correlated with serum 25(OH)D levels ($r = -0.292$; $P < 10^{-7}$), and was different between vitamin D categories ($P < 10^{-8}$) (Fig. 1). The number of patients by age strata did not allow for an evaluation of PTH by age; age distribution was not different by site.

Discussion

This is the first representative study that investigated in a healthy population in Brazil the 25(OH)D and PTH levels in 3 urban Brazilian cities with different latitudes during midsummer and found that most participants had vitamin D deficiency (15.3%) or insufficiency (50.7%). We further showed

Table 1. Descriptive characteristics of study population

Variables	Salvador			São Paulo			Curitiba			Total			*P*
	Men (168)	Women (168)	Total (336)	Men (167)	Women (167)	Total (334)	Men (167)	Women (167)	Total (334)	Men (502)	Women (502)	Total (1004)	
Age, median	37	36	36	38	35	38	38	36	37	38	36	37	.944
(interquartile range), y	(26-49)	(28-47)	(28-48)	(27-48)	(26-49)	(27-48)	(27-48)	(26-47)	(27-48)	(27-48)	(27-48)	(27-48)	
Race or ethnic group													$< 10^{-5}$
White	20.8	20.2	20.5	42.5	44.9	43.7	74.3	74.3	74.3	45.8	46.4	46.1	
Mixed	50.6	46.4	48.5	41.3	38.9	40.1	18.0	15.6	16.8	36.7	33.7	35.2	
Black	26.2	31.5	28.9	13.2	13.2	13.2	4.8	6.6	5.7	14.7	17.1	15.9	
Other	2.4	1.8	2.1	3.0	3.0	3.0	3.0	3.6	3.3	2.8	2.8	2.8	
Fitzpatrick skin type[a]													$< 10^{-4}$
Type I, 0-6	6.5	7.9	7.2	8.4	10.2	9.3	9.6	10.2	9.9	8.2	9.4	8.8	
Type II, 7-12	10.1	17.6	13.8	24.0	22.8	23.4	31.7	29.9	30.8	21.9	23.4	22.7	
Type III, 13-18	34.5	28.5	31.5	32.9	40.7	36.8	35.9	37.7	36.8	34.5	35.7	35.1	
Type IV, 19-24	39.3	32.1	35.7	26.3	19.2	22.8	18.6	18.0	18.3	28.1	23.0	25.6	
Type V, 25-30	7.7	12.1	9.9	7.2	5.4	6.3	3.6	4.2	3.9	6.2	7.2	6.7	
Type VI, 31+	1.8	1.8	1.8	1.2	1.8	1.5	0.6	0.0	0.3	1.2	1.2	1.2	
BMI													.353
Underweight, 17.0-18.4	0.0	1.8	0.9	0.6	0.6	0.6	1.2	1.2	1.2	0.6	1.2	0.9	
Normal, 18.5-24.9	35.1	34.5	34.8	28.7	34.1	31.4	31.7	43.1	37.4	31.9	37.3	34.6	
Overweight, 25.0-29.9	38.7	42.3	40.5	46.1	41.3	43.7	40.7	27.5	34.1	41.8	37.1	39.4	
Obesity I, 30.0-34.9	23.2	12.5	17.9	15.6	15.6	15.6	21.6	17.4	19.5	20.1	15.1	17.6	
Obesity II, 35.0-39.9	1.8	5.4	3.6	6.0	6.6	6.3	4.8	7.2	6.0	4.2	6.4	5.3	
Obesity III, ≥ 40.0	1.2	3.6	2.4	3.0	1.8	2.4	0.0	3.6	1.8	1.4	3.0	2.2	
Blood donation, ≥ 2×/y	12.5	14.3	13.4	50.3	44.9	47.6	68.3	67.7	68.0	43.6	42.2	42.9	10^{-5}
Cigarette smoking													$< 10^{-4}$
Never smoker	83.3	93.5	88.4	67.7	72.5	70.1	88.6	91.6	90.1	79.8	85.9	82.9	
Former smoker	10.7	4.2	7.4	25.7	19.8	22.8	7.2	6.0	6.6	14.6	10.0	12.3	
Current smoker	6.0	2.4	4.2	6.6	7.8	7.2	4.2	2.4	3.3	5.6	4.2	4.9	

Abbreviation: BMI, body mass index.
[a]Type I (0-6): pale white skin; always burns, never tans; type II (7-12): white skin; almost always burn, rarely tans; type III (13-18): light brown skin; burns moderately, tans uniformly; type IV (19-24): moderate brown skin; burns minimally, tans easily; type V (25-30): dark brown skin; rarely burns, tans easily; type VI (31+): dark brown to black skin; never burns. Bold = statistically significant.

Table 2. Unadjusted mean serum 25-hydroxyvitamin D level and prevalence of vitamin D deficiency (< 20 ng/mL) by selected characteristics

	25(OH)D, ng/mL			Vitamin D deficiency, < 20 ng/mL		
	No.	Mean ± SD	*P*	N (%)	95% CI	*P*
Sex			**.002**			**.004**
Male	502	29.6 ± 10.3		65 (12.9)	6.8-23.2	
Female	502	27.8 ± 8.1		87 (17.3)	10.8-26.6	
Age, y			.354			.685
18-29	336	29.4 ± 9.1		43 (12.8)	5.8-25.9	
30-39	236	28.1 ± 8.6		42 (17.8)	9.1-31.9	
40-49	217	28.2 ± 9.1		31 (14.3)	6.0-30.5	
50-59	166	28.4 ± 8.3		29 (17.5)	7.8-34.8	
60-69	49	29.8 ± 15.3		7 (14.3)	2.6-51.3	
City			**$< 10^{-4}$**			**$< 10^{-3}$**
Salvador	336	30.2 ± 10.4		39 (11.6)	4.8-25.2	
São Paulo	334	27.1 ± 8.3		69 (20.7)	12.8-31.7	
Curitiba	334	28.8 ± 8.8		44 (13.2)	6.1-26.2	
Race			.317			.329
White	463	29.3 ± 8.9		58 (12.5)	6.3-23.4	
Mixed	353	28.1 ± 9.2		64 (18.1)	10.6-29.2	
Black	160	28.4 ± 10.6		27 (16.9)	7.2-34.9	
Other	28	27.8 ± 7.2		3 (10.7)	0.8-64.8	
BMI						**$< 10^{-9}$**
Normal or underweight	356	30.9 ± 10.1	**$< 10^{-10}$**	38 (10.7)	4.3-24.3	
Overweight	396	28.5 ± 9.0		56 (14.1)	7.3-25.5	
Obesity class I	177	26.5 ± 7.8		33 (18.6)	8.9-34.9	
Obesity class II/III	75	24.2 ± 6.3		25 (33.3)	18.2-52.9	
Smoking			0.111			0.377
Never smoker	831	28.8 ± 8.9		123 (14.8)	9.6-22.1	
Former smoker	123	27.3 ± 8.5		22 (17.9)	7.1-38.2	
Current smoker	49	30.4 ± 15.6		7 (14.3)	2.6-51.3	
Fitzpatrick score[a]			.785			.925
Type I, 0-6	88	29.6 ± 9.4		10 (11.4)	2.2-42.0	
Type II, 7-12	227	28.8 ± 9.3		34 (15.0)	6.6-30.5	
Type III, 13-18	351	28.4 ± 8.4		52 (14.8)	7.6-26.8	
Type IV, 19-24	256	28.4 ± 8.9		43 (16.8)	8.5-30.6	
Type V, 25-30	67	29.6 ± 13.7		11 (16.4)	4.4-45.8	
Type VI, 31+	12	27.2 ± 7.4		2 (16.7)	1.3-75.9	
Multivitamins			**$< 10^{-9}$**			**$< 10^{-5}$**
No/past	791	27.8 ± 8.1		131 (16.6)	11.2-23.9	
Current	209	32.1 ± 12.1		21 (10.0)	2.9-29.5	
Use of supplements			**$< 10^{-5}$**			**$< 10^{-5}$**
No/past	909	28.0 ± 8.7		147 (16.2)	11.1-23.0	
Current	92	31.8 ± 11.2		5 (5.4)	0.3-49.2	

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index.
[a]Type I (0-6): pale white skin; always burns, never tans; type II (7-12): white skin; almost always burn, rarely tans; type III (13-18): light brown skin; burns moderately, tans uniformly; type IV (19-24): moderate brown skin; burns minimally, tans easily; type V (25-30): dark brown skin; rarely burns, tans easily; type VI (31+): dark brown to black skin; never burns. Bold = statistically significant.

that, greater BMI and higher latitude were significant predictors of vitamin D deficiency.

The high prevalence of vitamin D deficiency observed during summer in healthy individuals indicates Brazil is a risky area for vitamin D deficiency, with a prevalence close to European countries (14). It affects an alarming number of healthy individuals; as an example, São Paulo, with a population of almost 12 million people, would have 20% of adults with vitamin D deficiency during summer. Indeed, these numbers could be even worse during the winter, when an expected drop in vitamin D levels of approximately 30% is expected, as shown before in São Paulo (15).

Table 3. Association between variables and serum 25-hydroxyvitamin D concentration (ng/mL) analyzed by stepwise multiple linear regression analyses[a]

Variables	Men β (95% CI)	P	Women β (95% CI)	P	Total Regression coefficient β (95% CI)	P
Female sex	–	–	–	–	–	
Age, y	0.027 (−0.042 to 0.096)	.444	−0.023 (−0.080 to 0.034)	.431	−0.969 (−2.130 to 0.191)	.102
Race or ethnic group, White vs other	0.982 (−0.908 to 2.872)	.308	2.791 (1.310 to 4.273)	.011	−0.002 (−0.047 to 0.043)	.933
Body mass index	−0.496 (−0.686 to −0.306)	$< 10^{-6}$	−0.260 (−0.393 to −0.128)	$< 10^{-3}$	1.856 (0.651 to 3.062)	$< 10^{-3}$
Latitude	−0.221 (−0.380 to −0.063)	.006	−0.140 (−0.284 to 0.004)	.056	−0.357 (−0.472 to −0.243)	$< 10^{-8}$
Average time under sun on weekday, min	0.008 (−0.003 to 0.019)	.151	0.021 (0.008 to 0.034)	.002	−0.096 (−0.284 to −0.044)	.007
Part of body exposed to sun					0.012 (0.003 to 0.020)	.006
Whole body (with bathing suit) vs less	2.390 (−1.190 to 4.969)	.069	2.426 (0.203 to 4.649)	.033	2.243 (0.524 to 3.962)	.011
Leisure time physical activity						
Regular sports and exercise/athletic training vs less	3.950 (2.191 to 5.710)	$< 10^{-4}$	0.586 (−0.801 to 1.974)	.407	2.292 (1.163 to 3.422)	$< 10^{-4}$
Regular use of dietary supplements						
(current vs no/past)	0.672 (−1.554 to 2.899)	.553	4.761 (2.698 to 6.824)	$< 10^{-5}$	2.393 (0.861 to 3.925)	.002

β, regression coefficient β.
[a]Predictors included in the model were sex, age, race/ethnicity, BMI, latitude, time of sun exposure, part of body exposed to the sun, leisure time physical activity, and regular use of dietary supplements. No significant effects of education levels, income, work location, skin phototype, leisure outdoor, physical activity at work, or house type were found in the adjusted models. Bold = statistically significant.

Brazil is known as a tropical country; however, it has continental dimensions with substantial latitude differences between regions. In addition, there are other variables such as genetics, socioeconomic, lifestyle, and cultural habits in the population that make the extrapolation of any data about vitamin D levels difficult. As expected, the highest prevalence of vitamin D deficiency occurred in the cities with higher latitude (São Paulo and Curitiba). However, Salvador, a city located in the northeast of Brazil, had a percentage of vitamin D deficiency or insufficiency very close to Curitiba in the south region. This was demonstrated before in other tropical cities of the north and northeast of Brazil in specific populations of postmenopausal women and older individuals, but for the first time in a healthy population (16, 17). Although Salvador has a higher percentage of dark-skinned individuals than Curitiba, these cities had averages of 25(OH)D that were not different from each other. These findings suggest that the greater abundance of solar radiation existing in Salvador due to its greater proximity to the equator may overcome the melanin barrier to produce vitamin D in the skin. So, dark skin would be a risk factor for vitamin D deficiency only in regions with limited solar radiation.

The higher prevalence of vitamin D deficiency in São Paulo, the largest city of the country with 20.4 million inhabitants, may be due to lifestyle characteristics, less leisure time spent outside, or the fact that it is an industrialized city with higher levels of pollutants, which could interfere with sun exposure. Even though we excluded individuals taking vitamin D supplements in the past 2 months, another possibility is that more people could have taken multivitamins and supplements during the past winter in Curitiba to avoid COVID infection. The demographic variables were different between cities, but they were not significant at the multivariate analysis, excluding a possible effect on vitamin D levels. Although less likely, misinformation could have occurred when answering the questionnaire and interfered with data.

A sex difference was observed with lower 25(OH)D and a higher prevalence of vitamin D deficiency in women compared to men, but it did not persist in multivariable analysis, like the findings of other studies (18, 19). 25(OH)D levels were similar in the age strata, which differs from the literature showing a decrease in vitamin D with aging (19), although another study also did not show a difference in vitamin D by age (20). The age limit to be a blood donor restricted the inclusion of individuals older than 69 years and could explain these results.

The lifestyle habits confirmed the importance of duration and area of body surface exposed to the sun, as well as the amount of outside physical activity, all directly related to higher levels of vitamin D as seen in different studies (21-23). On the other hand, other factors such as skin type or education or income level were not associated with 25(OH)D levels, which was seen before (24, 25). The high availability of sun associated with the fear of skin cancer could have interfered in the results, increasing the number of individuals taking multivitamins. Supplements and multivitamins contain on average 200 to 400 units of vitamin D, not enough to correct the vitamin D deficiency, as shown before (26). Even though multivitamins and supplements usually do not have the daily recommended amount of vitamin D, in this study they had a major effect, decreasing the odds of having vitamin D deficiency by 60%.

Higher latitude and BMI increased the odds of having vitamin D deficiency. At all sites most individuals were overweight

Table 4. Odds ratios for vitamin D deficiency (serum levels < 20 ng/mL) according to levels of predictor variables in men and women

	Men			Women			Total		
	Adjusted[a] OR	(95% CI)	*P*	Adjusted[a] OR	(95% CI)	*P*	Adjusted[a] OR	(95% CI)	*P*
Female vs male	–			–			1.09	(0.74-1.62)	.664
Age, y	1.01	(0.99-1.03)	.212	1.01	(1.00-1.03)	.174	1.01	(0.99-1.03)	.209
Race or ethnic group, White vs other	0.56	(0.38-0.84)	**.006**	0.56	(0.37-0.83)	**.005**	0.56	(0.38-0.85)	**.006**
Body mass index									
Normal or underweight, < 25.0	1 (ref)			1 (ref)			1 (ref)		
Above normal, 25.0-29.9	1.40	(0.88-2.24)	.155	1.41	(0.88-2.26)	.150	1.41	(0.88-2.26)	.150
Obesity I, 30.0-34.9	1.76	(1.02-3.04)	**.042**	1.76	(1.02-3.03)	**.043**	1.78	(1.03-3.08)	**.039**
Obesity II and III, ≥ 35.0	2.92	(1.54-5.55)	**.001**	2.97	(1.56-5.65)	**.001**	2.91	(1.53-5.53)	**.001**
Latitude	1.06	(1.01-1.10)	**.014**	1.06	(1.01-1.10)	**.009**	1.06	(1.01-1.10)	**.015**
Time spent under sun on weekday, min									
≤ 5	1 (ref)				1 (ref)				1 (ref)
5-15	0.56	(0.31-0.99)	**.046**	0.56	(0.32-1.00)	**.049**	0.55	(0.31-0.99)	**.045**
16-30	0.46	(0.25-0.86)	**.014**	0.48	(0.26-0.89)	**.020**	0.47	(0.25-0.87)	**.017**
> 30	0.29	(0.16-0.52)	**.000**	0.30	(0.17-0.54)	**.000**	0.30	(0.17-0.54)	**.000**
Part of body usually exposed to sun									
Whole body (with bathing suit) vs less	0.60	(0.30-1.22)	.158	0.60	(0.30-1.21)	.154	0.48	(0.22-1.03)	.060
Engage in outdoor activities on leisure time									
Rarely or a few times	1 (ref)			1 (ref)			1 (ref)		
Very often or always vs	0.72	(0.49-1.06)	.100	0.76	(0.51-1.12)	.169	0.72	(0.49-1.07)	.103
Leisure time physical activity									
Mainly sedentary/light to moderate activity	1 (ref)			1 (ref)			1 (ref)		
Regular sport and exercise/athletic training	0.73	(0.50-1.07)	.105	0.73	(0.49-1.07)	.102	0.74	(0.50-1.08)	.118
Type of housing									
Apartment or house without backyard	1 (ref)			1 (ref)			1 (ref)		
House with backyard	0.72	(0.42-1.23)	.230	0.72	(0.42-1.23)	.230	0.72	(0.42-1.23)	.208
Regular use of supplements									
No/past	1 (ref)			1 (ref)			1 (ref)		
Current	0.42	(0.22-0.83)	**.012**	0.43	(0.22-0.84)	**.013**	0.43	(0.22-0.84)	**.013**

Abbreviations: OR, odds ratio; ref, reference.
[a]Adjusted logistic regression model for all other predictor variables. Adjusted models included 979 (total), 491 (male), and 488 (female) participants with complete information on all considered variables. Bold = statistically significant.

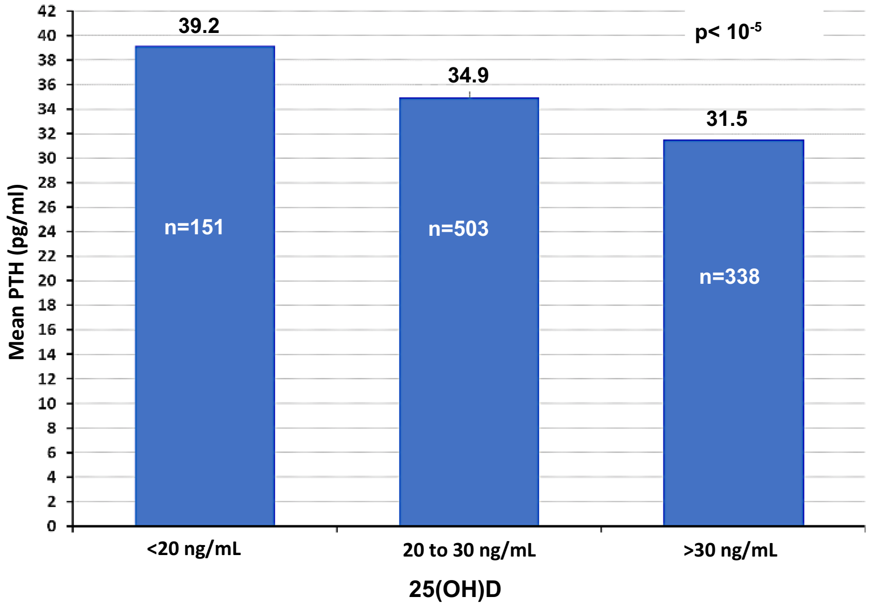

Figure 1. Mean concentration of serum parathyroid hormone (PTH) levels and serum 25-hydroxyvitamin D (25(OH)D) levels.

or obese and the odds of having vitamin D deficiency increased progressively with the increase in BMI, which agrees with the literature showing a decrease of 25(OH)D levels with increasing latitude and BMI (27). A metanalysis of 23 studies also found a higher prevalence of vitamin D deficiency in obese (35%) and overweight (24%) individuals compared to the eutrophics (28). These data could motivate the population to increase outside physical activity, mainly in regions with high sun availability. In Brazil there is no policy for food fortification with vitamin D, as seen in other countries such Canada and Finland. Nevertheless, our data indicate that even healthy people living in the tropics would benefit from the addition of vitamin D in food to avoid deficiency.

Even in this healthy population, PTH was negatively related to vitamin D levels. Nevertheless, besides the 20% with 25(OH)D deficiency, secondary hyperparathyroidism was seen in a lower percentage, as seen before in other studies (29). This raises 2 points for discussion. First is the upper limit of the PTH reference value, which is usually determined without corrections to 25(OH)D levels. If only individuals with adequate levels of 25(OH)D are considered, the upper limit of normal for PTH levels would decrease by 25% to 30%, as suggested by Souberbielle et al (30). In this case, the percentage of secondary hyperparathyroidism would increase in our population. Second, this healthy population was relatively young, and PTH concentrations generally increase with aging and unfortunately, our study was not powered to analyze skin color, PTH, and 25(OH)D levels by age.

The strength of this study was the representative sample size of healthy individuals; the evaluation in cities from 3 different regions and latitudes of the country; well-distributed age and sex between sites; the exclusion of people taking vitamin D supplements in the past month; the sample collection in summer following the same methodology for collection and analysis; and the assessment and ample investigation of risk factors for vitamin D deficiency. A limitation was a possible use of vitamin D supplements in the past year, which could have interfered with vitamin D levels because of its long half-life.

This study confirmed the high prevalence of vitamin D deficiency even in the midsummer in a healthy population in Brazil. It confirms that vitamin D levels are associated with sun exposure, latitude, skin color, BMI, and use of supplements.

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Data Availability

Some or all data sets generated during and/or analyzed during the present study are not publicly available but are available from the corresponding author on reasonable request.

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