



Trabajo Original

Obesidad y síndrome metabólico

Cardiometabolic risk factors and hypovitaminosis D in adolescents with overweight from a sunny region in northeast Brazil: a cross-sectional study

Factores de riesgo cardiometabólico e hipovitaminosis D en adolescentes con sobrepeso de una región soleada del noreste de Brasil: un estudio transversal

Angélica Luiza de Sales Souza¹, Eduarda Pontes dos Santos Araújo², Thatyane Oliveira Souza¹, Jéssica Bastos Pimentel¹, Adriana Leão de Miranda Ferreira¹, David Franciole de Oliveira Silva³, Karine Cavalcanti Maurício Sena Evangelista¹, Ricardo Fernando Arrais⁴, Adriana Augusto de Rezende⁵, Severina Carla Vieira Cunha Lima¹

¹Postgraduate Nutrition Program. Centro de Ciências da Saúde. Universidade Federal do Rio Grande do Norte; ²Postgraduate Program in Health Sciences. Centro de Ciências da Saúde. Universidade Federal do Rio Grande do Norte; ³Postgraduate Program in Collective Health. Centro de Ciências da Saúde. Universidade Federal do Rio Grande do Norte; ⁴Department of Pediatrics. Universidade Federal do Rio Grande do Norte; and ⁵Department of Clinical and Toxicological Analyses. Universidade Federal do Rio Grande do Norte. Natal, Rio Grande do Norte. Brazil

Abstract

Background: obesity can influence vitamin D levels, which in turn might be associated with cardiometabolic risk factors.

Objectives: this study assessed the association between 25-hydroxyvitamin D [25(OH)D] levels and cardiometabolic risk factors in adolescents with overweight living in a region of northeastern Brazil.

Material and methods: a cross-sectional study was carried out by non-probabilistic sampling in adolescents diagnosed with overweight or obesity. The subjects were divided according to their 25(OH)D status into two groups: sufficient vitamin D and hypovitaminosis D. Biodemographic, lifestyle, cardiometabolic, and biochemical factors were evaluated. A logistic regression model was applied to determine the predictors of hypovitaminosis D.

Results: we found a high frequency of hypovitaminosis D (45.6 %) in adolescents. Weekly sun exposure was negatively associated with hypovitaminosis D (OR = 0.96; 95 % CI: 0.92-0.99), while significant positive associations were observed between hypovitaminosis D and blood pressure above the 95th percentile (OR = 4.00; 95 % CI: 1.19-13.37), body weight (OR = 1.04; 95 % CI: 1.01-1.07), and fasting insulin (OR = 1.13; 95 % CI: 1.05-1.22).

Conclusion: hypovitaminosis D showed a high prevalence in adolescents with overweight living in a sunny region of northeastern Brazil, and cardiometabolic risk factors such as systemic arterial hypertension, high body weight, and hyperinsulinemia are predictors of hypovitaminosis D.

Keywords:

Adolescent.
Overweight. Obesity.
Vitamin D. Vitamin
D deficiency. Risk
factors.

Received: 20/06/2021 • Accepted: 09/08/2021

Author contributions: AS, EA, AF wrote and edited the manuscript. AS, SL created all tables and figures. RA, AR, SL designed the study. TS, JP, EA, AF were involved in data collection. SL, KE, DS, AR were involved in data analysis. All authors have read and agreed to the published version of the manuscript.

Funding: this research was funded by Foundation of the State of Rio Grande do Norte (FAPERN) and the Coordination for the Improvement of Higher Education Personnel (CAPES) financing code 001, through Edital 006/2014 - "Support to graduate programs of Higher Education Institutions (IES) of the State of Rio Grande do Norte".

Conflicts of interest: the authors declare no conflicts of interest.

Souza ALS, Araújo EPS, Souza TO, Pimentel JB, Ferreira ALM, Silva DFO, Evangelista KCMS, Arrais RF, Rezende AA, Lima SCVC. Cardiometabolic risk factors and hypovitaminosis D in adolescents with overweight from a sunny region in northeast Brazil: a cross-sectional study. *Nutr Hosp* 2022;39(1):73-81

DOI: <http://dx.doi.org/10.20960/nh.03745>

Correspondence:

Angélica Luiza de Sales Souza.
Postgraduate Nutrition Program. Centro de Ciências da Saúde. Universidade Federal do Rio Grande do Norte. R. General Gustavo Cordeiro de Faria, 601. Ribeira. Natal, Rio Grande do Norte 59012-570. Brazil
e-mail: angelica_sales9@hotmail.com

Resumen

Introducción: la obesidad puede influir en los niveles de vitamina D, lo que a su vez podría estar asociado con factores de riesgo cardiometabólico.

Objetivos: este estudio evaluó la asociación entre los niveles de 25-hidroxivitamina D [25(OH)D] y los factores de riesgo cardiometabólico en adolescentes con sobrepeso que viven en una región del noreste de Brasil.

Material y métodos: se realizó un estudio transversal mediante muestreo no probabilístico con adolescentes diagnosticados de sobrepeso u obesidad. Los sujetos se dividieron según su estado de 25(OH)D en dos grupos: suficiente vitamina D e hipovitaminosis D. Se evaluaron factores biodemográficos, de estilo de vida, cardiometabólicos y bioquímicos. Se aplicó un modelo de regresión logística para determinar los predictores de la hipovitaminosis D.

Resultados: encontramos una alta frecuencia de hipovitaminosis D (45,6 %) en los adolescentes. La exposición semanal al sol se asoció negativamente a la hipovitaminosis D (OR = 0,96; IC 95 %: 0,92-0,99), mientras que se observaron asociaciones positivas significativas entre hipovitaminosis D y presión arterial por encima del percentil 95 (OR = 4,00; IC 95 %: 1,19-13,37), peso corporal (OR = 1,04; IC del 95 %: 1,01-1,07) e insulina en ayunas (OR = 1,13; IC del 95 %: 1,05-1,22).

Conclusión: la hipovitaminosis D mostró una alta prevalencia entre los adolescentes con sobrepeso que viven en una región soleada del noreste de Brasil, y los factores de riesgo cardiometabólico, como hipertensión arterial sistémica, peso corporal elevado e hiperinsulinemia, son predictores de hipovitaminosis D.

Palabras clave:

Adolescente.
Exceso de peso.
Obesidad. Vitamina D.
Deficiencia
de vitamina D.
Factores de riesgo.

INTRODUCTION

The growing epidemic of obesity has been the most important metabolic disorder reported in many populations and age groups (1,2). In adolescents as well, the prevalence of overweight/obesity is increasing exponentially, with an estimated 25.5 % of adolescents in Brazil being overweight (3). Obesity in general can result in the appearance of several cardiovascular risk factors such as glycemic changes, dyslipidemia, high blood pressure, and metabolic syndrome (MS) (4). In addition, in adolescents, if not controlled, these risk factors can persist and cause adverse health events later in adulthood (5).

In this context, evidence has shown that vitamin D plays an important role in the pathogenesis of chronic non-communicable diseases such as obesity (6). Vitamin D belongs to a group of liposoluble secosteroids and is responsible for promoting the intestinal absorption of calcium, magnesium, and phosphate. To perform its functions, it needs to be converted into its active form, 1,25-dihydroxyvitamin D, also known as calcitriol or 1,25(OH)₂D (7). However, recently, its extra-skeletal role and the expression of more than 2,000 genes involved in the regulation of several mechanisms associated with cardiometabolic disorders have been discussed (8).

A study carried out in Norway demonstrated that serum concentrations of 25(OH)D below 50.0 nmol/L were associated with a significantly increased odds ratio (OR) for the incidence of obesity during follow-up (adjusted OR = 1.73, 95 % CI, 1.24-2.41) (9). In Brazil, a recent cohort study found that body weight, body mass index (BMI), and waist circumference increased over time in obese patients with low serum 25(OH)D concentrations, regardless of dietary vitamin D intake (10). The observed lower bioavailability of vitamin D in individuals with obesity is attributed, among other factors, to sequestration of this pre-hormone in adipose tissue (6).

Hypovitaminosis D can influence the homeostasis of the renin-angiotensin-aldosterone system and interfere with the pathogenesis of systemic arterial hypertension (SAH), compromising vascular health and culminating in elevated blood pressure (11). In a cohort of Iranian adolescents, low concentrations of 25(OH)D were reported to correlate negatively with SAH (12), whereas in American adolescents they were associated negatively with elevated systolic blood pressure and hyperglycemia (13).

Hypovitaminosis D is also associated with unfavorable outcomes related to atherogenic dyslipidemia, which affect high-density lipoprotein cholesterol concentrations (14). In addition, the presence of the vitamin D receptor in β -pancreatic cells demonstrates vitamin D activity in calcium-parathyroid hormone (PTH) homeostasis, with adequate concentrations of calcitriol preventing the development of insulin resistance (IR) and diabetes *mellitus* type 2 (15).

Given that vitamin D deficiency has become a global health problem in all age groups, monitoring vitamin D insufficiency/deficiency and its associated conditions in adolescents can optimize health in this cohort and prevent health issues in adulthood. Our aim was to evaluate the association between vitamin D status and cardiometabolic risk factors in adolescents with overweight living in a sunny urban region in northeastern Brazil.

MATERIALS AND METHODS

STUDY DESIGN

The cross-sectional study was approved by the Federal University of Rio Grande do Norte (UFRN) Research Ethics Committee (protocol number 1.614.945; CAAE 56763716.7.0000.5292), which complies with the Declaration of Helsinki. All participants completed and signed an informed consent form.

A total of 125 adolescents, of both sexes, diagnosed as overweight or obese, and who attended for the first time the Pediatric Clinic of a Federal University Hospital in Natal, RN, between September 2016 and November 2018, were enrolled (Fig. 1).

CLINICAL EVALUATION

During clinical evaluation, data on family, personal pathological antecedents, and sexual maturation were collected. The study included adolescents who 1) were between 10 and 19 years old, 2) had normal physical and cognitive functions, and 3) presented with a nutritional status classified as overweight or obese. The exclusion criteria were 1) presence of genetic syndromes associated with obesity or other diseases, 2) pregnant and lactating women, 3) use of vitamins and mineral supplements, 4) use of drugs to

treat insulin resistance or type-2 diabetes *mellitus*, and 5) adolescents presenting with some pathology impairing vitamin D metabolism (e.g., chronic renal failure, cancer, and heart failure).

Participants were classified in two groups: prepubertal (stage 1) and pubertal (stages 2 to 5) (16). Systolic and diastolic blood pressure was determined according to the protocols established by the 7th Brazilian Guideline on Hypertension (17).

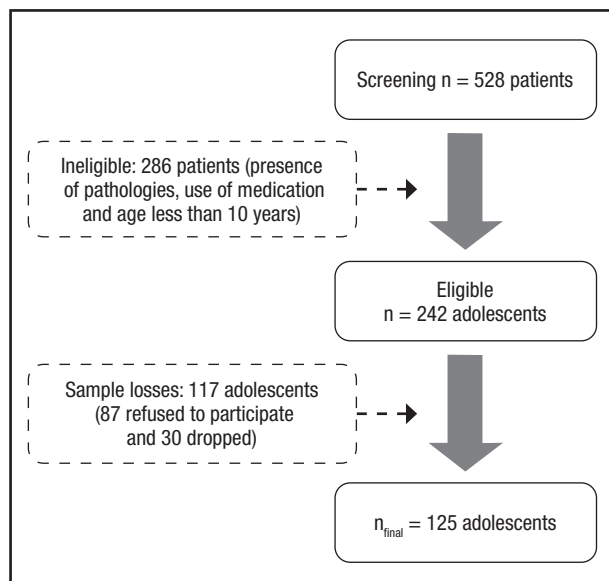


Figure 1.

Recruitment of participants.

ANTHROPOMETRIC EVALUATION

Anthropometric data on weight and height were collected according to Lohman et al. (1988) (18). BMI was calculated and the classification of anthropometric nutritional status was performed using the BMI-for-age anthropometric index (19). Abdominal circumference was measured to estimate cardiovascular risk based on the classification proposed by Taylor et al. (2000) (20) for adolescents (16). Neck circumference was measured and used to classify participants according to the cut-off points adapted for adolescents (21). All measurements were performed in duplicate by trained examiners.

BIOCHEMICAL ANALYSES

Blood samples were collected after fasting for 10 to 12 h. Fasting blood glucose, total cholesterol and its fractions, triglycerides, calcium, phosphorus, and C-reactive protein was analyzed using Wiener kits (Wiener Laboratories, Rosario, Argentina) following the manufacturer's instructions, and using the CMD-800 biochemical analyzer (Wiener Laboratories, Rosario, Argentina). Insulin and PTH were analyzed with the chemiluminescence method (Kit Liason XL, Diasorin, Stillwater, MN, USA).

Serum 25(OH)D was analyzed using the electrochemiluminescence method (COBAS 6000 Series Modular Analyzer,

Mannheim, Germany). The 25(OH)D status was diagnosed according to the recommendation established by the Endocrine Society using the following reference values: deficiency, if 25(OH)D \leq 20 ng/mL; insufficiency, if 25(OH)D between 21 and 29 ng/mL; and sufficiency, if 25(OH)D \geq 30 ng/mL (22). Participants were stratified into two groups: 1) sufficiency, which included those with 25(OH)D \geq 30 ng/mL, and 2) hypovitaminosis D, which included those with 25(OH)D deficiency and 25(OH)D insufficiency.

IR was assessed using the homeostasis model assessment for insulin resistance (HOMA-IR). A HOMA-IR cut-off point $>$ 3.16 was established for the diagnosis of IR (23). To assess the lipid profile, we applied the reference values recommended by the Update of the Brazilian Dyslipidemia and Atherosclerosis Prevention Directive (2017) for adolescents (24); low-density lipoprotein cholesterol was calculated using Friedewald's formula.

MS diagnostic criteria for adolescents were used according to the International Diabetes Federation (2007) (25). Adolescents between 10 and 16 years of age with abdominal obesity (\geq 90th percentile) and the presence of two or more of the following factors are considered to have metabolic syndrome: triglycerides $>$ 150 mg/dL, HDL $<$ 40 mg/dL, fasting glucose $>$ 100 mg/dL and PA $>$ p95.

SUN EXPOSURE AND PHYSICAL ACTIVITY

We assessed the adolescents' exposure to sunlight using the questionnaire proposed by Hanwell (2010) (26). We also investigated the adolescents' frequency of sunscreen application on different parts of the body and the performance of physical activity in the sun. The skin phototype was classified from I to VI, as proposed by Toda et al. (1973) and referred to by Astner and Anderson (2004) (27). Physical activity was assessed using the questionnaire developed and validated by Florindo et al. (2006) (28).

STATISTICAL ANALYSIS

The distribution of variables was analyzed using the Kolmogorov-Smirnov test. The data are presented as average or median, when appropriate. The Shapiro-Wilk test was used for statistical analysis. The frequency of hypovitaminosis D [25(OH)D \leq 30 ng/mL] was calculated based on the sample proportion, with a 95 % confidence interval (CI) and a 5 % margin of error. Student's *t*-test was performed for continuous variables with normal distribution in the groups.

Categorical variables were analyzed descriptively using absolute and relative frequencies and Pearson's chi-square test or Fisher's exact test were applied. Spearman's correlation was performed to assess the relationship between the dependent variable 25(OH)D and other continuous variables in the study. The binomial logistic regression model was applied to determine the effect of some of the tested variables in predicting hypovitaminosis D. Sexual maturation was used as an adjustment variable. The general statistical significance of the model was assessed by the Omnibus test. Interpretation of the adjusted models was based on the odds ratio (OR) and 95 % CI. The SPSS software

version 20.0 (SPSS, Chicago, IL, USA) was employed, and a significance level of 5 % was adopted for all analyses.

RESULTS

GENERAL CHARACTERISTICS OF ADOLESCENTS WITH OVERWEIGHT ACCORDING TO 25(OH)D STATUS

We identified a high frequency of hypovitaminosis D (45.6 %) among adolescents with overweight. The average concentration

of 25(OH)D was 32.73 (\pm 10.03) ng/mL in the total sample; however, the value was 39.39 (\pm 8.25) ng/mL in the sufficiency group and 24.38 (\pm 4.01) ng/mL in the hypovitaminosis D group. Table I lists the bio-demographic characteristics and lifestyle habits of adolescents with overweight and classifies them according to their 25(OH)D status. A statistically significant increase in hypovitaminosis D was recorded in all age groups (p = 0.024), except the first one (10-11 years). None of the other demographic parameters, such as exposure to sun, use of protective cream, skin color or sexual maturation were significantly different between the two groups.

Table I. Bio-demographic and lifestyle variables in adolescents with overweight grouped according to 25(OH)D status

Variable	25(OH)D Status		c ²	p-value
	Sufficiency > 30 ng/mL (n = 68)	Hypovitaminosis D ≤ 30 ng/mL (n = 57)		
	n (%)	n (%)		
<i>Gender</i>				
Male	40 (58.8)	25 (43.9)	2.78	0.095
Female	28 (41.2)	32 (56.1)		
<i>Age (years)</i>				
10–11	50 (73.5)	29 (50.9)	7.45	0.024 ^a
12–13	13 (19.1)	17 (29.8)		
≥ 14	5 (7.4)	11 (19.3)		
<i>Sexual maturation*</i>				
Prepubertal	7 (17.1)	17 (34.0)	3.45	0.178
Initial pubertal	21 (51.2)	19 (38.0)		
Final pubescent	13 (31.7)	14 (28.0)		
<i>Physical activity</i>				
Active (≥ 300 min/week)	20 (29.4)	12 (21.1)	1.14	0.286
Inactive (< 300 min/week)	48 (70.6)	45 (78.9)		
<i>Use of sunscreen</i>				
Yes	11 (16.2)	6 (10.5)	0.84	0.359
No	57 (83.8)	51 (89.5)		
<i>Exposure to sun during physical activity</i>				
Yes	30 (44.1)	16 (28.1)	3.43	0.064
No	38 (55.9)	41 (71.9)		
<i>Self-reported skin color</i>				
White	14 (20.6)	10 (17.5)	0.58	0.966 ^b
Black	9 (13.2)	7 (12.3)		
Brown	38 (55.9)	35 (61.4)		
Yellow	2 (2.9)	2 (3.5)		
Indigenous	5 (7.4)	3 (5.3)		
<i>Skin phototype</i>				
I	2 (3.0)	0 (0.0)	4.47	0.484 ^c
II	10 (14.7)	5 (8.8)		
III	16 (23.5)	10 (17.5)		
IV	30 (44.1)	31 (54.4)		
V	9 (13.2)	9 (15.8)		

Significance levels at * p < 0.05, based on the chi-square test. ^aCramer's V = 0.24. ^b40 % of cells have an expected frequency below 5 according to Fisher's exact test. ^c33 % of cells have an expected frequency below 5 according to Fisher's exact test. *Multiple imputations for missing data.

CLINICAL, ANTHROPOMETRIC, AND BIOCHEMICAL VARIABLES ASSOCIATED WITH 25(OH)D

The association between 25(OH)D status and the clinical, anthropometric, and biochemical variables of adolescents with overweight is shown in table II. Compared to the 25(OH)D sufficiency group, adolescents in the hypovitaminosis D group

presented a higher incidence of elevated blood pressure according to the 95th percentile (22.8 %; $p = 0.006$). In addition, there was a tendency for the group with hypovitaminosis D to include more adolescents diagnosed with MS (38,6 %; $p = 0.068$); neck circumference (61.4 %; $p = 0.016$) and elevated HOMA-IR (38.6 %; $p = 0.016$) were also significantly different between adolescents with hypovitaminosis D and the 25(OH)D sufficiency group.

Table II. Association between 25(OH)D status and cardiometabolic risk factors in adolescents with overweight

Variable	25(OH)D Status		c ²	p-value
	Sufficiency > 30 ng/mL (n = 68)	Hypovitaminosis D ≤ 30 ng/mL (n = 57)		
	n (%)	n (%)		
<i>Blood pressure (mmHg)</i>				
< 95 th percentile	64 (94.1)	44 (77.2)	7.56	0.006 ^b
> 95 th percentile	4 (5.9)	13 (22.8)		
<i>Arterial pressure (mmHg)</i>				
< 130 × 85	64 (94.1)	44 (77.2)	7.56	0.006 ^b
> 130 × 85	4 (5.9)	13 (22.8)		
<i>Metabolic syndrome</i>				
< 3 criteria	52 (76.5)	35 (61.4)	3.33	0.068
≥ 3 criteria	16 (23.5)	22 (38.6)		
<i>BMI (kg/m²)</i>				
Overweight	19 (28.0)	14 (24.6)	3.58	0.167
Obesity	46 (67.6)	35 (61.4)		
Severe obesity	3 (4.4)	8 (14.0)		
<i>Abdominal circumference (cm)</i>				
< 80 th percentile	4 (5.9)	4 (7.0)	0.07	1.00 ^b
> 80 th percentile	64 (94.1)	53 (93.0)		
<i>Neck circumference (cm)</i>				
Men < 35,5; Women < 32	41 (60.3)	22 (38.6)	5.84	0.016 ^{ab}
Men > 35,5; Women > 32	27 (39.7)	35 (61.4)		
<i>Fasting blood glucose (mg/dL)</i>				
≤ 99	53 (77.9)	47 (82.5)	0.39	0.530
> 99	15 (22.1)	10 (17.5)		
<i>Fasting insulin</i>				
< 23	67 (98.5)	54 (94.7)	1.44	0.330 ^c
> 23	1 (1.5)	3 (5.3)		
<i>HOMA-IR index</i>				
< 3.16	55 (80.9)	35 (61.4)	5.84	0.016 ^{ab}
> 3.16	13 (19.1)	22 (38.6)		
<i>Total cholesterol (mg/dL)</i>				
< 170	33 (48.5)	29 (50.9)	0.07	0.794
≥ 170	35 (51.5)	28 (49.1)		
<i>LDL-cholesterol (mg/dL)</i>				
< 110	39 (57.4)	33 (57.9)	0.004	0.951
≥ 110	29 (42.6)	24 (42.1)		

(Continues on next page)

Table II (Cont.). Association between 25(OH)D status and cardiometabolic risk factors in adolescents with overweight

Variable	25(OH)D Status		c ²	p-value
	Sufficiency > 30 ng/mL (n = 68)	Hypovitaminosis D ≤ 30 ng/mL (n = 57)		
	n (%)	n (%)		
HDL-cholesterol (mg/dL)				
> 45	22 (32.4)	10 (17.5)	3.57	0.059
≤ 45	46 (67.6)	47 (82.5)		
Triglycerides (mg/dL)				
< 90	29 (42.6)	17 (29.8)	2.19	0.139
≥ 90	39 (57.4)	40 (70.2)		
Serum calcium (mg/dL)				
≤ 11	52 (76.5)	44 (77.2)	0.009	0.924
> 11	16 (23.5)	13 (22.8)		
PTH (pg/mL)				
< 67	55 (91.7)	42 (89.4)	0.16	0.746 ^c
> 67	5 (8.3)	5 (10.6)		
Phosphorus (mg/dL)				
≥ 4.5	58 (85.3)	45 (78.9)	0.86	0.353
< 4.5	10 (14.7)	12 (21.1)		
C-reactive protein (mg/L)				
< 5	55 (80.9)	50 (87.7)	1.08	0.299
> 5	13 (19.1)	7 (12.3)		

BMI: body mass index; HDL: high-density lipoprotein; HOMA-IR: homeostasis model assessment for insulin resistance; LDL: low-density lipoprotein; PTH: parathyroid hormone. Significance levels at * $p < 0.05$, based on the chi-square test. ^a $\phi = 0.22$. ^b $\phi = 0.25$. ^cFisher's test was applied.

CORRELATIONS BETWEEN VITAMIN D STATUS AND DIFFERENT PARAMETERS

Table III shows correlations between vitamin D status and different parameters. Significant positive correlations were found between 25(OH)D status, weekly sunlight exposure (score) ($p = 0.000$; $r = 0.321$), and physical activity (weekly

score) ($p = 0.034$; $r = 0.189$), indicating a low sun exposure and physical inactivity for the adolescents in this study. In addition, we identified negative correlations between 25(OH) D status and body weight ($p = 0.008$; $r = -0.236$), neck circumference ($p = 0.025$; $r = -0.200$), fasting insulin ($p = 0.000$; $r = -0.375$), HOMA-IR index ($p = 0.000$; $r = -0.386$), and PTH ($p = 0.020$; $r = -0.229$).

Table III. Correlations between 25(OH)D status and different parameters in adolescents with overweight

Variable	25(OH)D status	
	R	p-value
Sun exposure (weekly score)	0.321	0.000*
Physical activity practice (weekly score)	0.189	0.034*
Body weight (kg)	-0.236	0.008*
Systolic blood pressure (mmHg)	-0.288	0.001*
Neck circumference (cm)	-0.200	0.025*
Fasting insulin (μ U/mL)	-0.375	0.000*
Homa-IR index	-0.386	0.000*
PTH (pg/mL)	-0.229	0.020*

Data were analyzed using Spearman's correlation. Statistical significance was determined for * $p < 0.05$.

PREDICTING HYPOVITAMINOSIS D IN ADOLESCENTS WITH OVERWEIGHT

Table IV shows the logistic regression model as adjusted to predict hypovitaminosis D in adolescents with overweight. We recorded a significant negative association between weekly sunlight exposure (OR = 0.960; 95 % CI, 0.923-0.999) and hypovitaminosis D, and significant positive associations between body weight (OR = 1.040; 95 % CI, 1.012-1.069) and fasting

insulin (OR = 1.133; 95 % CI, 1.049-1.224) as predictors of hypovitaminosis D. Specifically, adolescents with blood pressure > 95th percentile and those with arterial hypertension (diagnostic criterion for MS) exhibited a four times greater chance of hypovitaminosis D (OR = 4.005; 95 % CI, 1.199-13.375 and OR = 4.727; 95 % CI, 1.446-15.455, respectively). Finally, the linear regression model confirmed the association between elevated blood pressure and hypovitaminosis D observed by the classification of the 95th percentile and MS criteria.

Table IV. Logistic regression model adjusted to predict hypovitaminosis D in adolescents with overweight

Variable	B	SE	p-value	OR	IC 95 % for OR	
					Inferior	Superior
Weekly sun exposure	-0.041	0.020	0.045*	0.960	0.923	0.999
Constant	0.292	0.381	0.443	1.339	0.292	
Body weight (kg)	0.039	0.014	0.006*	1.040	1.012	1.069
Constant	-2.624	0.901	0.004*	0.073		
Fasting insulin (µIU/mL)	0.125	0.039	0.002*	1.133	1.049	1.224
Constant	-1.577	0.479	0.001*	0.207		
Blood pressure ^a	1.388	0.615	0.024*	4.005	1.199	13.375
Constant	0.292	0.381	0.443	1.339	0.292	
Blood pressure ^b	1.553	0.604	0.010*	4.727	1.446	15.455
Constant	-0.375	0.196	0.056*	0.688		

B: regression coefficient; SE: standard error; OR: odds ratio = Exp (B); CI: confidence interval. *p < 0.05. ^aReference category: < 95th percentile. ^bReference category: MS < 130 × 85. Sexual maturation was a control variable.

DISCUSSION

Our study identified a high prevalence of hypovitaminosis D among adolescents with excess weight and consequent metabolic changes, such as higher percentages of blood pressure, higher prevalence of metabolic syndrome, greater body weight, higher neck circumference, hyperinsulinemia, and insulin resistance.

We identified an association between individual nutritional status and vitamin D concentrations in the adolescents evaluated. Although our population was composed only of individuals with overweight, after the adjusted analysis high body weight augmented by 1.04 times the chance of adolescents presenting with hypovitaminosis D. This relationship of vitamin D with excess weight and a greater deposition of body fat can be explained by its fat-soluble nature, which can favor uptake by the adipose tissue, decreasing bioavailability and activation of the hypothalamus to develop a cascade of reactions that results in an increased feeling of hunger and decreased energy expenditure (6).

Similar results were also confirmed in the study by Oliveira et al. (2014) (29), who evaluated a population of adolescents aged 15 to 17 years and demonstrated that vitamin D levels were lower in adolescents with overweight and abdominal obesity.

Although the high prevalence of hypovitaminosis D has been evident throughout the world, the determinants of this phenomenon are not yet fully understood. It is known that the major part of vitamin D synthesis in the body is due to exposure to the sun (80 %); hence, places that remain sunny for most of the year, such as the northeastern region of Brazil, should have a low prevalence of hypovitaminosis D. However, we identified significant positive correlations between the 25(OH)D status and weekly sun exposure or the participation in physical activity (weekly score). This indicates that in spite of living in a sunny region all year round, these adolescents have adopted life habits of sedentary individuals that predispose them to hypovitaminosis D. These findings corroborate the study by Araújo et al. (2016) (30), who also identified a high prevalence of hypovitaminosis D in adolescents in a sunny capital of northeastern Brazil.

Other anthropometric parameters, in addition to weight and BMI, have been studied in the adolescent population as indicators of cardiometabolic risk. In our study, a large neck circumference was more frequent in adolescents with hypovitaminosis D. Neck perimeter has been used as a simpler but more reliable anthropometric indicator than waist circumference, and its increase is associated with cardiometabolic risks as strongly as is abdominal visceral fat (31). The BCAMS study, involving a cohort of individuals aged 14 to 28 years, found that concentrations of 25(OH)D were negatively correlated with neck circumference and body fat percentage, and that levels of 25(OH)D were significantly lower in participants with obesity or MS compared to their respective counterparts (32). Such data reinforce that vitamin D deficiency is more common in the population of young people who are at risk of MS; however, the mechanisms that justify this relationship still need to be elucidated in additional studies.

In general, changes in weight and body composition are associated with the appearance of complications such as hypertension and insulin resistance. The tested sample confirmed an association between being overweight and HOMA-IR. Such relationship may be linked to the increased anabolic effect of insulin and growth hormone during puberty (33). In addition, our findings agree with reports of a high prevalence of IR in female adolescents (34,35). The different prevalence of IR between the sexes can be explained, in part, by differences in the distribution of body fat or pubertal stage, as girls usually enter puberty about two years before boys, this justifying the investigation of the relationship between puberty as a control variable (36).

The negative correlation between low vitamin D concentrations and high insulin values shown in our study was also found by Gul et al. (2017), demonstrating the influence of vitamin D on the mechanisms underlying IR and hyperinsulinemia (37). The latter is a predictor of hypovitaminosis D in adolescents, which confirms the influence of hypovitaminosis D on the calcium-PTH axis and its role in the pathogenesis of diabetes *mellitus* type 2 (38).

It is worth noting that hyperinsulinemia contributes also to increased blood pressure, meaning that primary prevention measures for cardiometabolic risk factors should be implemented in adolescents (34). Morais et al. (2016) observed a significant association between IR and blood pressure and the impact of IR on blood pressure (34). Other studies also indicate that adolescents with IR are at higher risk of having altered blood pressure (13,15).

We confirmed the results of the association between hypovitaminosis D and presence of SAH in the adjusted analysis of the linear regression model. In our population, adolescents with blood pressure higher than the 95th percentile were about four times more likely to develop hypovitaminosis D when compared to others. Some evidence shows that vitamin D can participate in the regular renin-angiotensin-aldosterone system at clinical, pathophysiological, and molecular levels in animal and human studies (39).

The present study has also some limitations. First, it is a cross-sectional study carried out without continuous monitoring of participants, which prevented further clarification of how some

risk factors impacted on vitamin D status. Second, the questionnaire used to assess the sun exposure score had not been validated for adolescents. Third, even though diet has a negligible impact on the concentration of 25(OH)D, the study did not assess the influence of food and dietary intake on vitamin D status. Finally, memory bias could influence the recollection of weekly physical activity and sun exposure supplied in the questionnaires.

CONCLUSIONS

Taken together, the present results indicate a high prevalence of hypovitaminosis D in adolescents, and important associations between cardiometabolic risk factors such as SAH, high body weight, and hyperinsulinemia with hypovitaminosis D. Such correlations emphasize the urgent need for public policies aimed at preventing and treating adolescents with overweight, as well as monitoring cardiometabolic risk factors and hypovitaminosis D in this age group.

REFERENCES

1. Bluher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol* 2019;15:288-98. DOI: 10.1038/s41574-019-0176-8
2. Abarca-Gómez L, Ziad AA, Hamid ZA. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017;390:2627-42. DOI: 10.1016/S0140-6736(17)32129-3
3. Bloch KV, Klein CH, Szklo M, Kuschnir MCC, Abreu GA, Barufaldi LA, et al. ERICA: prevalences of hypertension and obesity in Brazilian adolescents. *Rev Saúde Pública* 2016;50(1s).
4. Sbaraini M, Cureau FV, Sparrenberger K, Teló GH, Kuschnir MCC, Oliveira JS, et al. Severity of obesity is associated with worse cardiometabolic risk profile in adolescents: Findings from a Brazilian national study (ERICA). *Nutrition* 2020;75-76:110758. DOI: 10.1016/j.nut.2020.110758
5. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. *Obes Rev* 2012;13:985-1000. DOI: 10.1111/j.1467-789X.2012.01015.x
6. Vanlint S. Vitamin D and obesity. *Nutrients* 2013;5:949-56. DOI: 10.3390/nu5030949
7. Maeda SS, Borba VZC, Camargo MBR, Silva DMW, Borges JLC, Bandeira F, et al. Recommendations of the Brazilian Society of Endocrinology and Metabolism (SBEM) for the diagnosis and treatment of hypovitaminosis D. *Arq Bras de Endocrinol & Metabol* 2014;58:411-33. DOI: 10.1590/0004-2730000003388
8. Charoengnam N, Holick MF. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients* 2020;12:2097. DOI: 10.3390/nu12072097
9. Mai XM, Chen Y, Camargo Jr CA, Langhammer A. Cross-sectional and prospective cohort study of serum 25-hydroxyvitamin D level and obesity in adults. *Am J Epidemiol* 2012;175:1029-36. DOI: 10.1093/aje/kwr456
10. Cembranel F, D'Orsi E, Wagner KJP, Giehl MWC, Moreno YMF, González-Chica DA. Obesity and 25(OH)D Serum Concentration Are More Important than Vitamin D Intake for Changes in Nutritional Status Indicators: A Population-Based Longitudinal Study in a State Capital City in Southern Brazil. *Nutrients* 2019;11:2366. DOI: 10.3390/nu11102366
11. Andersen LBJ, Przybyl L, Haase N, Versen-Hoyneck F, Qadri F, Jorgensen JS, et al. Vitamin D depletion aggravates hypertension and target-organ damage. *J Am Heart Assoc* 2015;4:1-11. DOI: 10.1161/JAHA.114.001417
12. Ghobadi S, Rostami ZH, Marzijarani MS, Faghih S. Association of vitamin D status and metabolic syndrome components in Iranian children. *Int J Prev Med* 2019;10:1-6.
13. Lee M, Ebert JR, Kadakia MP, Zhang J, Czerwinski SA. Inverse associations between cardiometabolic and 25-hydroxyvitamin D risk factors in obese

- American children and adolescents. *Am J Hum Biol* 2016;28:736-42. DOI: 10.1002/ajhb.22863
14. Filgueiras MS, Suhett LG, Silva MA, Rocha NP, Novaes JF. Low vitamin D intake is associated with low HDL cholesterol and vitamin D insufficiency/deficiency in Brazilian children. *Public Health Nutr* 2018;21:2004-12. DOI: 10.1017/S1368980018000204
 15. Rodrigues KF, Pietrani NT, Bosco AA, de Sousa MCR, Silva IFO, Silveira JN, et al. Lower Vitamin D Levels, but Not VDR Polymorphisms, Influence Type 2 Diabetes Mellitus in Brazilian Population Independently of Obesity. *Medicina* 2019;55:188. DOI: 10.3390/medicina55050188
 16. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child* 1969;44:291-303. DOI: 10.1136/adc.44.235.291
 17. Malachias MVB, Souza WKSB, Plavnik FL, Rodrigues CIS, Brandão AA, Neves MFT, et al. 7th Brazilian Guideline on Hypertension 2016;107:1-83.
 18. Lohman TG, Roche AF, Martorell R. Anthropometric Standardization Reference Manual. Champaign, Illinois: Human Kinetics Books; 1988.
 19. WORLD HEALTH ORGANIZATION. Who child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. Methods and development. WHO (non serial publication). Geneva, Switzerland: WHO; 2006
 20. Taylor RW, Jones LE, Williams SM, Goulding A. Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3-19 y. *Am J Clin Nutr* 2000;72:490-5. DOI: 10.1093/ajcn/72.2.490
 21. Hingorjo MR, Qureshi MA, Mehdi A. Neck circumference as a useful marker of obesity: a comparison with body mass index and waist circumference. *J Pak Med Assoc* 2012;16:36-40.
 22. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2011;96:1911. DOI: 10.1210/jc.2011-0385
 23. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose / insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. *Pediatrics* 2005;115:500-3. DOI: 10.1542/peds.2004-1921
 24. Faludi AA, Izar MCO, Saraiva JFK, Chacra APM, Bianco HT, Afione A Neto, et al. Brazilian Society of Cardiology. Update of the Brazilian guideline on dyslipidemia and prevention of atherosclerosis. *Arq Bras Cardiol* 2019;113:1-91.
 25. Zimmet P, Alberti KGMM, Kaufman F, Tajima N, Silink M, Arslanian S, et al. IDF Consensus Group. The metabolic syndrome in children and adolescents – an IDF consensus report. *Pediatric Diabetes* 2007;8:299-306. DOI: 10.1111/j.1399-5448.2007.00271.x
 26. Hanwell HE, Vieth R, Cole DE, Scillitani A, Modoni S, Frusciante V, et al. Sun exposure questionnaire predicts circulating 25-hydroxyvitamin D concentrations in Caucasian hospital workers in southern Italy. *Steroid Biochem Mol Biol* 2010;121:334-7. DOI: 10.1016/j.jsbmb.2010.03.023
 27. Astner S, Anderson RR. Skin phototypes 2003. *J Invest Dermatol* 2004;122:1-2. DOI: 10.1046/j.1523-1747.2003.22251.x
 28. Florindo AA, Romero A, Peres SV, Silva MV, Slater B. Development and validation of a physical activity assessment questionnaire for adolescents. *Rev Saúde Pública* 2006;40:802-9. DOI: 10.1590/S0034-89102006000600009
 29. Oliveira R, Novaes J, Azeredo L, Cândido A, Leite I. Association of vitamin D insufficiency with adiposity and metabolic disorders in Brazilian adolescents. *Public Health Nutrition* 2014;1:787-94. DOI: 10.1017/S1368980013001225
 30. Araujo EPS, Queiroz DJM, Neves JPR, Lacerda LM, Gonçalves MCR, Carvalho AT. Prevalence of hypovitaminosis D and associated factors in adolescent students of a capital of northeastern Brazil. *Nutr Hosp* 2017;34:1416-23.
 31. Silva CC, Zambon MP, Vasques ACJ, Rodrigues AMB, Camilo DF, Antonio MARGM, et al. Neck circumference as a new anthropometric indicator for prediction of insulin resistance and components of metabolic syndrome in adolescents: Brazilian Metabolic Syndrome Study. *Rev Paul Pediatr* 2014;32:221-9. DOI: 10.1590/0103-0582201432210713
 32. Fu J, Han L, Zhao Y, Li G, Zhu Y, Li Y, et al. Vitamin D levels are associated with metabolic syndrome in adolescents and young adults: The BCAMS study. *Clin Nutr* 2019;38:2161-7. DOI: 10.1016/j.clnu.2018.08.039
 33. Smolarek AC, Mascarenhas LPG, Junior TPS, Oliveira CS, Boguszewski MC, Laet EF, et al. Association of anthropometric indicators with insulin resistance and function of pancreatic beta cells in pubescent adolescents. *Rev Bras Obes Nutr Emagrec* 2018;12:804-11.
 34. Morais PRS, Sousa ALL, Jardim TSV, Nascente FMN, Mendonça KL, Povoá TIR, et al. Correlation of insulin resistance and anthropometric measures with adolescent blood pressure. *Arq Bras Cardiol* 2016;106:1-8. DOI: 10.5935/abc.20160041
 35. Chissini RBC, Oliveira CL, Giannini DT, Kuschnir MCC. Childhood and adolescent obesity: association of inflammation and insulin resistance with metabolic changes. *Braz J Health Biomed Sci* 2015;14:41-9.
 36. Mauvais-Jarvis F. Sex differences in metabolic homeostasis, diabetes, and obesity. *Biol Sex Differ* 2015;6:1-9. DOI: 10.1186/s13293-015-0033-y
 37. Gul A, Ozer S, Yilmaz R, Sonmezgoz E, Kasap T, Takcı S, et al. Association between vitamin D levels and cardiovascular risk factors in obese children and adolescents. *Nutr Hosp* 2017;34:323-9. DOI: 10.20960/nh.412
 38. Wimalawansa SJ. Associations of vitamin D with insulin resistance, obesity, type 2 diabetes, and metabolic syndrome. *Steroid Biochem Mol Biol* 2018;175:177-89. DOI: 10.1016/j.jsbmb.2016.09.017
 39. Tomaino K, Romero KM, Robinson CL, Baumann LM, Hansel NN, Pollard SL, et al. Association between serum 25-hydroxy vitamin D levels and blood pressure among adolescents in two resource-limited settings in Peru. *Am J Hypertens* 2015;28:1017-23. DOI: 10.1093/ajh/hpu264