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ARTICLE

Epidemiology

Cutoff point estimation for serum vitamin D concentrations to predict cardiometabolic risk in Brazilian children

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Abstract

Background/objectives To evaluate serum 25(OH)D concentrations and determine a cutoff point for cardiometabolic risk in children.

Subject/methods This is a cross-sectional study with a representative sample of 378 8–9-year-old children from all urban schools in the city of Viçosa, MG, Brazil. Sociodemographic data and information on lifestyle, and food consumption were collected. Biochemical evaluation included glucose, triglycerides, leptin, calcidiol [25(OH)D], and parathormone. Body composition was assessed by dual energy X-ray absorptiometry. Cardiometabolic risk was considered when nontraditional risk markers were detected, including triglyceride × glycemia index (TyG index), hyperleptinemia, and hypertriglyceridemic waist phenotype (HWP). The receiver operating characteristic curve (ROC) was used to define the cutoff point for serum 25 (OH)D to predict cardiometabolic risk.

Results 25(OH)D showed better predictive capacity for grouping of cardiometabolic risk markers than for either single or paired markers. The area under the curve for grouping of risk markers was 0.636 (95% CI: 0.585, 0.685, $P < 0.001$). The cutoff point to predict cardiometabolic risk was defined as 32.0 ng/mL.

Conclusion 25(OH)D presented good predictive capacity for cardiometabolic risk and 25(OH)D concentration higher than 32 ng/mL was associated with a 49% reduction of cardiometabolic risk prevalence in prepubertal Brazilian children.

Introduction

Vitamin D is an essential hormone for calcium absorption and therefore for bone health sustenance [1]. Nevertheless, hypovitaminosis, defined as vitamin D deficiency, is a growing problem and has become a worldwide public health problem [2, 3]. In tropical countries such as Brazil, it is not expected to find a population having this condition. However, recent studies have revealed alarming numbers of inadequate vitamin D in the Brazilian population [4, 5].

Efforts to assess optimal serum vitamin D levels have long focused on bone health, aiming to investigate the sufficient concentration to suppress the parathormone (PTH) [6, 7]. Although there is no globally accepted definition for a normal vitamin D level in a population, several studies have attempted to define an optimal cutoff point and results have varied according to the site researched [3, 8], reinforcing the importance of carrying out studies to determine cutoff points in different regions.

The complex vitamin D metabolism has taken almost the entire 20th century to be discovered [9]. The almost universal presence of vitamin D receptor (VDR) in many tissues and the large number of genes under the control of calcitriol ($1,25(OH)_2D$) point to a broader role of vitamin D [10]. Therefore, this vitamin has been extensively investigated for the possible role in reducing the incidences of neoplastic disease, cardiovascular disease, obesity, type 2 diabetes mellitus, neurological diseases, and global or cardiovascular disease mortality risk [11–13].

In recent years, obesity has been frequently associated with vitamin D deficiency, and important enzymes of vitamin D metabolism have been shown to be expressed in

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adipose tissue, which proves its role in this tissue [14, 15]. Studies suggest that excess adipose tissue may compromise the concentration of serum 25(OH)D in association with leptin, which is able to inhibit renal synthesis of 1α-hydroxylase, making the production of the active form of vitamin D difficult [16, 17]. Similarly, lower serum of vitamin D is also associated with lipid, glycolytic, and inflammatory alterations which are influenced by obesity [4, 14]. After VDR and 1α-hydroxylase enzyme have been identified in pancreatic β cells, the role of vitamin D in glucose homeostasis and insulin resistance became the target of studies [18]. In addition, studies have shown that adequate serum vitamin D concentrations have a positive influence on lipid profile, especially triglycerides [19, 20].

Growing research investigating the relationship between vitamin D and nonskeletal outcomes has gathered studies to estimate the best vitamin D concentration for multiple health outcomes; however, there is still no global recommendation, especially for children [21, 22]. Lower serum of vitamin D has also been associated to nontraditional cardiometabolic risk markers, such as the hypertriglyceridemic waist phenotype (HWP), models for insulin resistance estimation, and hyperleptinemia [23–25], which have the potential to increase the identification of risk by assisting in the prediction, identification, and early risk assessment.

As cardiometabolic diseases may start during childhood and progress silently, knowing the cutoff point for predicting them in this age group can help early assessment to prevent or delay their occurrence. Therefore, the objective of this study was to evaluate the serum vitamin D concentration and determine the cutoff point related to cardiometabolic risk in children.

Methods

This is a cross-sectional study with a representative sample of 8 and 9-year-old children from all urban schools, participants of the Schoolchildren's Health Assessment Survey (PASE). The objective of PASE is to investigate the cardiovascular health of these children in the municipality of Viçosa, Minas Gerais, southeastern Brazil (latitude 20° 45′ 14″ S). Information on the study design and sample calculation are described in published previous study [5]. The sample in this study consisted of 378 students.

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and approved by the Human Research Ethics Committee of the Federal University of Viçosa (UFV) (Opinion no. 663.171/2014). The study was also presented to the Municipal Department of Education, the Regional Superintendence of Education, and the school principals. An informed consent form was signed by the parents or legal guardians of all the children included in the study.

Socio-demographic, food consumption, and lifestyle data

A semi-structured questionnaire was used to collect sociodemographic, and lifestyle information. The questionnaire had been previously tested in a pilot study, which consisted of 10% of the sample in the same age group. After the pilot study, the format and order of the questions were adapted to make them clearer and more objective, thus, it was possible to establish an optimal interview time. The sample used in the pilot study was not included in this study.

The household's per capita income was classified according to the median of the total sample (US$ 155.0). Skin color was informed by the parents/guardians and categorized as white and non white (brown/brunette/mulatto and black).

Based on child's life habits, the sun exposure (h/day) and sedentary behavior were evaluated. Sedentary behavior, defined as activities that do not increase energy expenditure substantially above the rest level such as sitting, watching television or engaging in other forms of screen-based entertainment [26], was classified as screen time ≥2 h/day [27]. An evaluation of food consumption was also carried out from three 24-h dietary recalls (R24h) on nonconsecutive days, including one day of the weekend, through information declared by the mother/guardian and the child. This information was used to quantify vitamin D intake, used as an adjustment variable in the regression model as well as the season of the year.

More information on the data collection was described in a previously published study [5].

Anthropometry and body composition

Waist perimeter was measured at the midpoint between the iliac crest and the last rib [28] using a flexible and non-stretch measuring tape graduated in centimeters and subdivided in millimeters. Excessive abdominal adiposity was considered for values above the 75th percentile of the population, according to age and sex [29].

Body composition of the children was estimated by the dual energy X-ray absorptiometry (Lunar Prodigy Advance; GE Medical Systems Lunar, Milwaukee, WI, USA), with an automated test program with complete mechanical and electronic tests, global measurement calibration, and automated quality control with complete storage. Evaluations were performed in the morning in the diagnostic imaging sector of the Health Division of the Federal University of Viçosa with subjects fasting. Excess of body fat was classified when the fat percentage was higher than 20% for boys and 25% for girls [30].

Biochemical evaluation

We performed blood-sampling by venipuncture into serum separator tubes, after 12-h fasting, for further analysis in the laboratory of Clinical Analysis of the Division of Health of the Federal University of Viçosa. Glycemia, triglycerides, leptin, calcidiol [25(OH)D], and PTH were measured.

Glucose and triglycerides were measured by the colorimetric enzymatic method and PTH by the chemiluminescence immunoassay method using an automatic analyzer (BS-200 Mindray®, Nanshan, China) [31]. The following commercial kits were used according to the manufacturer's instructions. Bioclin® GLUCOSE MONOREAGENT test (Belo Horizonte, Brazil), with detection limit of 1.31 mg/dL, TRIGLICÉRIDES MONOREAGENTE Bioclin® test (Belo Horizonte, Brazil) with detection limit of 2.58 mg/dL, and Intact PTH Access® Immunoassay Systems (Fullerton, United States), with detection limit of 0.1 pmol/L.

The enzyme immunoassay was performed to evaluate leptin concentrations using the commercial kit Leptin-EASIA DiaSource ImmunoAssays S.A. (Louvain-la-Neuve, Belgium), with detection limit of 0.04 ng/mL [31]. Triglyceride levels were classified according to the Updated Brazilian Directive for Dyslipidemias and Prevention of Atherosclerosis (Update of the Brazilian Dyslipidemia and Atherosclerosis Prevention Guideline) [32].

Calcidiol [25(OH)D] was determined by chemiluminescent immunoassay using the ARCHITECT® 25-OH Vitamin D assay [33]. According to the manufacturer's information, this method has limit of detection of 8.0 ng/mL and correlation coefficient ≥0.80 for serum samples when compared with the DiaSorin LIAISON® 25-OH assay for total Vitamin D, with imprecision ≤10% of the total coefficient of intra-laboratory variation. According to tests carried out by the manufacturer directly comparing liquid chromatography with mass spectrometry (LCMS), also using serum samples, the concentrations with the ARCHITECT 25-OH Vitamin D assay ranged from 20.5 to 176.25 nmol/L, and with the LCMS test method, the concentrations ranged from 18.75 to 161 nmol/L. The correlation was 0.90.

Cardiometabolic risk

A risk score was used to establish a cutoff point for serum 25(OH)D concentration related to cardiometabolic risk in children. This score was based on the sum of three markers (TyG index, HWP, and hyperleptinemia) because our previous studies conducted with this same sample showed a relationship of vitamin D with each of these markers (data in process of publication), which is in agreement with the literature. Moreover, studying these new risk markers may contribute to a better understanding of the genesis of cardiovascular disease. In the multiple regression analysis, we included sedentary behavior and body fat as potential confounders for the final model adjusted.

The TyG index was calculated using the equation by Simental-Mendia et al. [34] [Ln (fasting triglycerides (mg/dl) × fasting blood glucose (mg/dl)]/2.

The 80th percentile of the sample was used to classify the risk of insulin resistance (8.37) and hyperleptinemia (8.98) in children due to the absence of cutoff points for this age group. The HWP is characterized by the simultaneous presence of hypertriglyceridemia and increased waist circumference and increasing evidence suggests it can be a predictor of cardiovascular risk [35, 36].

Cardiometabolic risk markers can act concurrently, thus increasing the risks of developing chronic diseases [37]. Worldwide, occurrence of simultaneous risk markers is broad, and the frequency of at least two markers is predominant in relation to other, ranging from 36 to 82% [37, 38]. Therefore, we chose to evaluate each risk marker and their combinations. The occurrence of at least two of these alterations by the receiver operating characteristic (ROC) curve and by multiple regression analysis was considered risk.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences for Windows, version 20.0 (SPSS Inc. Chicago, USA). The Kolmogorov–Smirnov normality test was used to determine whether continuous quantitative variables were normally distributed. For all the tests performed, the level of significance was set at 0.05 ($\alpha = 5\%$).

Data descriptive analysis was performed using relative frequencies, means and standard deviation or medians and interquartile range. Means or medians between two independent groups were compared using Student's *t*-tests or Mann–Whitney tests, respectively. Pearson's chi-square test or Fisher's exact test were performed to compare prevalence.

The ROC curve was developed in the MedCalc® program to evaluate the ability of 25(OH)D to predict cardiometabolic risk. The ROC curves were summarized by the area under the curve and with 95% confidence interval (CI) estimation. Curves with areas >0.5, whose confidence interval did not include 0.5, were considered useful in identifying situations of interest. In addition, sensitivity (*S*), specificity (*E*), positive predictive value, and negative predictive value were estimated. The cutoff point for 25(OH)D was identified at the point equivalent to the balance between *S* and *E* determined by the Youden index.

The Poisson regression with robust variance was used to analyze the association between 25(OH)D and cardiometabolic risk. The prevalence ratio with 95% CI was considered

an effect measure. Sex (female and male), skin color (white, brown/brunette/mulatto, and black), per capita income (dollar), sedentary behavior (h/day), season of the year (autumn, winter, and spring), PTH (nmol/mL), vitamin D intake (μg/d), sun exposure (h/day), and body fat were considered as potential confounders. The first model was adjusted by sociodemographic variables; after adjusted by sedentary behavior in model 2 and determinants of 25(OH)D concentration in model 3, and, finally, by body fat in model 4. Cardiometabolic risk was considered the dependent variable and 25(OH)D concentration below the cutoff point identified was the reference category for all models.

Results

The sample consisted of 378 children, most female (52.1%), attending public schools (70.9%). The mean concentration of 25(OH)D and PTH was, respectively, 29.34 ng/mL and 24.76 nmol/L. The mean values for BMI, body fat, systolic and diastolic blood pressure were 17.49 kg/m^2, 24.21%, 102.92 and 60.82 mmHg, respectively. All children had vitamin D intake lower than the recommendation (400 IU/day). Cardiometabolic risk was identified in 63.8% of the sample, according to the cutoff point proposed in this study (≤32 ng/mL).

The concentrations of 25(OH)D were lower in 9-year-old children, with sedentary behavior, excess body adiposity, and in those that presented insulin resistance by the TyG index and HWP. Median values of the TyG index were higher in children with increased body fat and leptin levels, and with the HWP. Leptin concentrations were higher in girls, children with excess body fat, and with the HWP. All children with the HWP showed excess body fat. The prevalence of HWP was also higher in children with increased TyG index and leptin (Table 1).

The ROC curve analysis indicated that 25(OH)D had a better predictive capacity for grouping of risk markers than for either single or paired markers. The best parameters were found when assessing three grouped risk markers classified by the presence of at least two of them. The area under the curve was 0.636 (95% CI: 0.585, 0.685, $p < 0.001$) and indicated that 25(OH)D was associated with cardiometabolic risk. The 25(OH)D cutoff point at 32.0 ng/mL showed the best values for S and NPV to predict cardiometabolic risk (Table 2; Fig. 1). In this study, children with this concentration of 25(OH)D were more likely to be found true positives (children with at least two of the evaluated risk markers) and less likely to be false negatives (who present the risk but are not identified by the cutoff point).

The TyG index, leptin median and HWP prevalence were higher in children with 25(OH)D ≤ 32 ng/mL (Table 3).

The final Poisson regression model presented an inverse association between 25(OH)D and cardiometabolic risk, even after adjusting for confounding factors. The concentrations of 25(OH)D > 32 ng/mL were associated with a reduction of 49% in the cardiometabolic risk prevalence (Fig. 2).

Discussion

To date, this is the first study to investigate the 25(OH)D cutoff point and its predictive capacity for cardiometabolic risk conducted exclusively with children, according our knowledge. Our findings indicated 25(OH)D as a good predictor of cardiometabolic risk, and that its concentration higher than 32 ng/mL was associated with a 49% reduction in risk prevalence. These results corroborate with other studies that found association of serum 25(OH)D levels below 30 ng/mL with acute myocardial infarction, chronic diseases, global and cardiovascular mortality, and other non-skeletal diseases in adults [39, 40].

A study evaluating 18,225 men in the Health Professionals Follow-up Study showed that men with 25(OH)D deficiency (≤15 ng/mL) were at increased risk of myocardial infarction compared with those considered to have adequate 25(OH)D concentrations (>30 ng/mL) [41]. Moreover, data from the National Health and Nutrition Examination Survey III showed that the lowest 25(OH)D quartile was associated with the highest mortality from cardiovascular disease [42]. Currently, to our knowledge, only one study with children determined the cutoff point of 25(OH)D in relation to a non-bone parameter. In Iran, for 297 children between 7 and 11 years of age, the cutoff point for 25(OH)D was 11.6 ng/mL for insulin resistance, measured by HOMA-IR [13]. This finding was different from our study, possibly because this last study did not evaluate the sun exposure, and the HOMA-IR value used was different from our study, in which we considered the percentile of our children sample.

Literature reviews corroborate our findings. A review examining the ideal 25(OH)D serum concentrations for bone mineral density, reduction of fracture risk, oral health, and colorectal cancer prevention found that the most adequate 25(OH)D concentration for all outcomes is above 30 ng/mL, with the best values between 36 and 40 ng/mL [21]. Another large review concluded that 25(OH)D levels below 25 ng/mL are consistently associated with cardiovascular risks [22], and several other longitudinal studies have confirmed an association between low 25(OH)D concentration and cardiovascular events or stroke [39, 43, 44].

Although the adequate serum concentration of 25(OH)D is still controversial, lower concentrations have been associated, with clear scientific evidence, with deficient bone mineralization, which in severe condition leads to rickets in children and osteomalacia in adults [6]. There is no consensus as to

Table 1 Sample characteristics according to the serum 25(OH)D concentrations and cardiometabolic risk markers in children. Viçosa, MG, Brazil, 2015.

	n (%)	25(OH)D mean (±SD)	TyG index mean (±SD)	LEPTIN median (IQR)	HWP *n* (%)
Total		29.48 (8.43)	8.02 (0.42)	2.00 (0,30; 6.79)	62 (16.4)
Sex					
Female	197 (52.1)	28.72 (7.62)	8.05 (0,43)	2.60 (0.45; 10.25)	35 (17.8)
Male	181 (47.9)	30.03 (9.18)	8.00 (0,41)	1.40 (0.20; 4.52)	27 (14.9)
p value		0.131	0.285	**0.003**	0.455
Age					
8 years	183 (48.4)	30.37 (8.26)	8.00 (0.45)	1.70 (0.20; 5.00)	30 (16.4)
9 years	195 (51.6)	28.39 (8.47)	8.05 (0.39)	2.20 (0.40; 7.93)	32 (16.4)
p value		**0.023**	0.263	0.198	0.996
Per capita income (US$)					
≥155.0	191 (50.5)	28.92 (8.80)	8.06 (0.42)	2.00 (0.50; 7.60)	31 (16.2)
<155.0	187 (49.5)	29.78 (8.00)	7.99 (0.42)	1.70 (0.20; 6.03)	31 (16.6)
p value		0.322	0.118	0.431	0.927
Sedentary behavior					
>2 h/d	180 (47.6)	28.28 (8.10)	8.05 (0.42)	2.05 (0.50; 7.15)	30 (16.7)
≤2 h/d	198 (52.4)	30.32 (8.61)	8.01 (0.42)	1.90 (0.10; 6.50)	32 (16.2)
p value		**0.019**	0.288	0.306	0.895
Overweight					
No	254 (67.2)	30.39 (8.57)	7.95 (0.38)	1.00 (0.10;3.00)	4 (1.6%)
Yes	124 (32.8)	27.21 (7.69)	8.19 (0.46)	10.00 (2.10;18.95)	58 (46.8)
p value		**0.001**	**<0.001**	**<0.001**	**<0.001**[a]
Body fat (%)					
Adequate	190 (50.3)	30.51 (8.20)	7.95 (0.38)	1.05 (0.10;2.60)	–
Increased	188 (49.7)	28.18 (8.49)	8.11 (0.44)	6.00 (0.70;14.70)	62 (33.0)
p value		**0.007**	**<0.001**	**<0.001**	**<0.001**[a]
TyG index					
≥percentile 80	70 (18.6)	26.47 (8.53)		2.10 (0.40; 15.25)	31 (44.3)
<percentile 80	307 (81.4)	30.00 (8.28)	–	1.80 (030; 6.00)	31 (10.1)
p value		**0.002**		0.122	**<0.001**
Leptin					
≥percentile 80	73 (20.0)	28.39 (7.50)	8.18 (0.51)		36 (49.3)
<percentile 80	292 (80.0)	29.73 (8.63)	7.98 (0.39)	–	24 (8.2)
p value		0.225	**<0.001**		**<0.001**
HWP					
Yes	62 (16.4)	26.16 (7.32)	8.46 (0.35)	14.10 (1.63; 22.93)	–
No	316 (83.6)	29.97 (8.49)	7.94 (0.38)	1.60 (0.15; 4.40)	
p value		**0.001**	**<0.001**	**<0.001**	

Student's *t* test, Mann–Whitney test, and Pearson's X^2 test.

TyG index triglyceride x glycemia index; *HWP* hypertriglyceridemic waist phenotype; *IQR* interquartile range. Values in bold indicate statistical significance ($P < 0.05$).

[a]Fisher's exact test.

whether the minimum range of desirable 25(OH)D should be 20 or 30 ng/mL, and whether there should be a vitamin D threshold for protection against cardiometabolic diseases [6, 7, 45, 46]. In Brazil, a study with young people between 17 and 35 years of age showed the cutoff point for bone health was 29.8 ng/mL, which is close to our result [47].

Increased HWP, TyG, and leptin levels are all considered as nontraditional risk markers for cardiometabolic risk and have showed an inverse association with serum 25(OH)D concentrations. HWP has been proposed as an alternative to the diagnosis of the metabolic syndrome [35, 36]. The TyG index has been proposed as a mathematical model that

Table 2 Areas under the receiver operating characteristic curve (ROC) and 25(OH)D cutoff points for assessing cardiometabolic risk in children. Viçosa-MG, Brazil, 2015.

	AUC (95% CI)	Cutoff point (ng/mL)	*S* (95% CI)	*E* (95% CI)	PPV	NPV	*P* value
1 RISK FACTOR							
HWP	0,642 (0.591;0.690)	26.2	59.7 (46.5–71.9)	66.6 (61.0;71.8)	26.1	89.3	<0.001
↑TyG	0.627 (0.576;0.676)	24.6	47.3 (35.6;59.2)	75.8 (70.5;80.5)	32.4	85.4	<0.001
↑LEP	0.556 (0.503;0.608)	31.4	72.4 (60.9;82.0)	41.5 (35.8;47.4)	24.6	85.1	0.121
≥1 RISK FACTOR							
HWP, ↑TyG	0.633 (0.582;0.682)	26.8	56.7 (46.7;66.4)	66.5 (60.6;72.1)	39.3	80.1	<0.001
HWP, ↑LEP	0.597 (0.546;0.647)	26.2	51.5 (41.3;61.6)	67.3 (61.4;72.8)	36.6	79.1	0.002
TyG,↑LEP	0.594 (0.542;0.644)	26.6	50.0 (41.0;59.0)	66.5 (60.3;72.4)	43.5	72.1	0.002
HWP, ↑TyG, ↑LEP	0.606 (0.555;0.656)	26.6	51.5 (42.8;60.0)	68.1 (61.7;73.9)	48.3	70.7	<0.001
2 RISK FACTORS							
HWP,↑TyG	0.664 (0.614;0.712)	26.8	68.6 (50.0;83.9)	62.8 (57.4;67.9)	14.7	95.6	<0.001
HWP, ↑LEP	0.594 (0.543;0.644)	26.1	54.1 (36.9;70.5)	65.2(59.9;70.3)	14.5	92.9	0.042
TyG, ↑LEP	0.624 (0.573;0.673)	24.6	54.5 (32.2;75.6)	72.6 (67.6;77.2)	11.0	96.3	0.027
≥2 RISK FACTORS							
HWP, ↑TyG, ↑LEP	0.636 (0.585;0.685)	32.0	82.5 (70.1;91.2)	39.5 (34.1;45.1)	19.6	92.6	<0.001

AUC area under the curve, *95% CI* 95% confidence interval, *S* sensitivity, *E* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *HWP* hypertriglyceridemic waist phenotype, *TyG* triglycerides × glycemia index, *LEP* leptin.

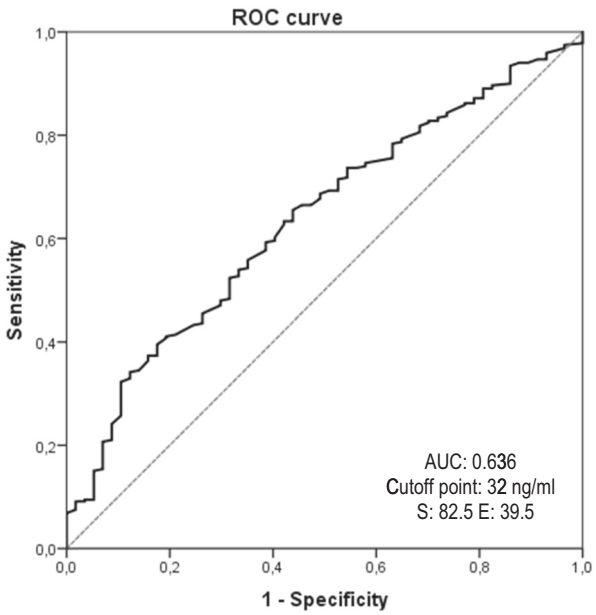

Fig. 1 Receiver operating characteristic curve (ROC) for vitamin D to assess cardiometabolic risk in children. Viçosa, MG, Brazil, 2015.

predicts the risk of insulin resistance from triglycerides and fasting glycemia [34]. Leptin has been associated with several factors related to the metabolic syndrome and increased cardiovascular risk [48, 49]. Results similar to our findings were found, in which adults having serum 25(OH)D levels >28 ng/mL were less likely to present HWP [23]. The inverse association between serum concentrations of 25(OH)D and leptin has also been found and much discussed, despite findings that are still inconclusive and little explored in childhood [25, 50, 51]. The inverse relation between vitamin D and insulin resistance is related to the binding of the active form of vitamin D to its VDR receptor in the beta cell, as well as to the conversion of proinsulin to insulin [52, 53].

We also observed that HWP, TyG index, and leptin were positively associated with each other. In fact, risk markers tend to occur simultaneously, and there may be a multicausal network [37, 54]. In the ROC curve analysis, 25(OH)D presented predictive capacity for each of these markers alone, except for leptin, and for their pair combinations, although the curve showed no good estimates of S, E, VPP, and VPN.

As a limitation, this study had a cross-sectional design, which did not allow us to explore the causal relation. In addition, the ROC curve analysis was not stratified by age or sex due to the sample size, and it was not possible to classify increased serum leptin and TyG index due to the absence of cutoff for this age group. However, there are several strengths of our study that should be considered. This is the first study, according our knowledge, that

Table 3 Cardiometabolic risk markers according to the 25 (OH)D cutoff point for children obtained from the receiver operating characteristic curve. Viçosa, MG, Brazil, 2015.

	25(OH)D		*P* value
	≤32 ng/mL ($n = 240$)	>32 ng/mL ($n = 136$)	
TyG index, mean (±SD)	8.08 (0.42)	7.93 (0.41)	0.002
Leptin, Median (IQR)	2.20 (0.50; 8.15)	1.40 (0.10; 4.40)	0.012
HWP, *n* (%)	50 (20.8)	12 (8.8)	0.003

Student's *t* test, Mann–Whitney test, and Pearson's X^2 test.

TyG index triglycerides × glycemia index, *HWP* hypertriglyceridemic waist phenotype, *IQR* interquartile range.

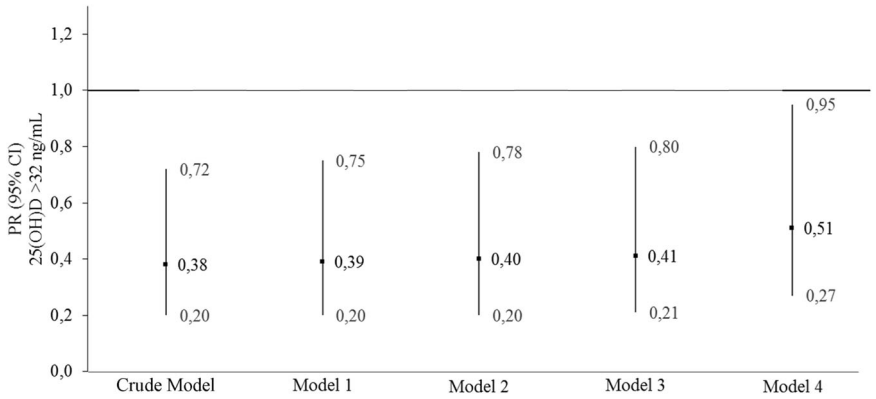

Fig. 2 Poisson regression for the association between vitamin D and cardiometabolic risk (dependent variable) in children. Viçosa, MG, Brazil. PR: prevalence ratio. 95% CI: 95% confidence interval. Reference category: 25(OH)D ≤ 32 ng/ml. Model 1: Adjusted by sex, age and per capita income. Model 2: Model 1 + sedentary behavior. Model 3: Model 2 + season of the year, parathyroid hormone, vitamin D intake, skin color and sun exposure. Model 4: Model 3 + body fat.

evaluated a representative sample of Brazilian prepubescent children, establishing a cutoff point for 25(OH)D and its predictive capacity for cardiometabolic risk in early stages of life. The proposed cutoff in this study (32 ng/mL) is important because it considers characteristics of the geographic region and population, such as season, age group, ethnicity, and sun exposure, which influence serum concentrations of 25(OH)D. In addition, it showed good sensitivity, which is relevant for screening diagnosis and could be analyzed for future application in cardiometabolic risk screening for this population or with similar characteristics, although our results should not be generalizated to all populations. On the other hand, despite a good sensitivity, the proposed cutoff point showed low specificity; however, from the public health point of view, it is especially important that the diagnostic method of cardiometabolic risk have good sensitivity, in order to identify the highest possible number (preferably 100%) of children at risk. Therefore, it is less serious to misclassify some risk-free children as being at risk (who would be evaluated in more detail for a treatment) than to fail to detect at-risk children, who, if left untreated, will have a higher risk of developing diseases that can remained in adulthood, with great damage to health. Further studies, in populations of different age, race/ethnicity are required to clarify the values of serum 25 (OH)D threshold as a marker of cardiometabolic risk.

We conclude that 25(OH)D presented a good predictive capacity for cardiometabolic risk, and its concentration higher than 32 ng/mL was associated to a 49% risk reduction in prepubertal Brazilian children. Additional studies among different populations, and preferably with larger sample sizes, are required to determine the cutoff value of 25(OH)D as a marker of cardiometabolic risk, mainly in childhood.

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Compliance with ethical standards

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

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