Vitamin D is associated with the hypertriglyceridemic waist phenotype in Brazilian children

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ABSTRACT

Background Prevalence of cardiometabolic risk factors is increasing and vitamin D insufficiency/deficiency has become a worldwide public health problem, even in tropical countries. Therefore, we identified the prevalence of hypertriglyceridemic waist phenotype (HWP) and evaluate its relationship with vitamin D insufficiency/deficiency.

Methods A cross-sectional study with 378 children aged 8 and 9 enrolled in all urban schools in the city of Viçosa, MG, Brazil. Anthropometric measurements, body composition (dual energy X-ray absorptiometry), biochemical tests and clinical evaluation were performed. Poisson regression was used to analyze the association between vitamin D and HWP.

Results Prevalence of HWP was 16.4%. This prevalence was higher among children with vitamin D insufficiency and deficiency and in those with a greater number of other cardiometabolic risk factors. Multiple regression analysis showed that children with vitamin D insufficiency and deficiency had, respectively, prevalence 85% (95% CI: 1.03–3.30) and 121% (95% CI: 1.11–4.45) higher of HWP than the vitamin D sufficiency group.

Conclusion Vitamin D insuffiency and deficiency were associated with a higher prevalence of HWP among children, regardless of the presence of other cardiometabolic risk factors, indicating an additional risk of inadequate vitamin D status to cardiometabolic health in childhood.

Keywords children, vitamin D, hypertriglyceridemic waist, nutritional epidemiology

Introduction

Non-communicable chronic diseases are currently considered the leading cause of death worldwide.[1] Metabolic syndrome (MS) is a cluster of disorders—including central obesity, dyslipidemia, altered glucose metabolism and arterial hypertension—poorly understood in childhood due to the scarcity of studies, differences in age groups evaluated and the absence of consensus on how to diagnose it at this stage.[2] The lack of criteria for defining MS is partly due to the still inconclusive understanding of the developmental physiological changes associated with childhood and puberty.[3]

The hypertriglyceridemic waist phenotype (HWP) is characterized by the simultaneous presence of hypertriglyceridemia and increased waist circumference (WC).[4] It has been proposed as a predictor of the atherogenic metabolic triad defined by apolipoprotein B alteration, fasting insulinemia and small, dense particles of low density lipoprotein (LDL) cholesterol.[4] Increasing evidence suggests that HWP can be predictive of cardiovascular risk for its association with this metabolic triad and it also allows the tracking of other cardiometabolic risk factors in asymptomatic individuals.[4–6]

The HWP is considered a simpler and more practical method since it involves only two parameters.[7] Stands out for its high agreement with MS in the prediction of cardiovascular diseases and therefore it has been proposed as an alternative to MS, especially as an indicator of cardiovascular and metabolic risk.[8,9] Although HWP is little known and used, its prevalence has been investigated in adults, but studies with children are scarce, particularly in Brazil.[6,7,9]

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An interesting and relatively new aspect concerns vitamin D deficiency. It has been studied as a risk factor for the development of MS and cardiovascular disease, even in children and adolescents.[10,11] To date, according our knowledgement, only the National Health and Nutrition Examination Survey III has studied the relationship between vitamin D and HWP in adults. This study found that vitamin D was an independent predictor of HWP, and individuals with 25 (OH) D >28 ng/ml were significantly less likely to present this phenotype.[12]

From the foregoing, this study aimed to identify the prevalence of HWP and evaluate its relationship with vitamin D insufficiency/deficiency, considering the presence of other cardiometabolic risk factors in prepubertal children.

Methods

Study design and participants

This is a cross-sectional study with a representative sample of 8- and 9-year-old children enrolled in public and private schools in the city of Viçosa, MG, Brazil, from May to November 2015. Viçosa, MG is located in the Zona da Mata Region, at 227 km from the state capital Belo Horizonte (20° 45′ 14″ S latitude and 42° 52′ 53″ W longitude). According to the 2010 census, the municipality has a land area of 299.4 km^2 and 72 220 inhabitants, with 93.2% of the population living in urban areas. It has a gross domestic product per capita of R$9597.00 and a high Human Development Index (HDI) with a score of 0.775, higher than the HDI of the state (0.731) and the national average (0.755).

The participants in this study came from the Schoolchildren Health Assessment Survey, a cross-sectional study with children enrolled in urban schools, to evaluate the cardiovascular health of this population in the city of Viçosa, MG, Brazil. In 2015, the municipality had 24 urban schools (17 public and seven private) for children aged 8 and 9 years. The sample size was calculated using the software Epi Open, version 3.03, based on the total number of students enrolled in urban schools in 2015 ($n = 1464$). Considering the analysis of multiple outcomes, the sample was calculated from 50% prevalence, 5% tolerated error, 95% confidence interval, 5% significance level, 10% refusals and losses and 10% confounding factor control, resulting in the sample size of 366 children.

The schoolchildren were selected by stratified random sampling. Each school sample met the proportionality ratio of students enrolled by age and gender. Students were selected by random simple draw until the necessary number for each school was obtained.

The children were invited to participate in the study after contact with the parents. The child was not included in the study if taking medication that interfered with the metabolism of vitamin D (corticosteroids, anticonvulsants and antifungals), glucose and/or lipids, as well as vitamin or mineral supplements.

The detailed description of the data collection as well as the collection of information on the demographic, socioeconomic and lifestyle characteristics were described in our previously published study.[11] The demographic and socioeconomic variables evaluated were gender, skin color, maternal schooling and per capita income. The behavioral variables were sedentarism, vitamin D intake and sun exposure.

This 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 (opinion n°. 663.171/2014). This study was also presented to the Municipal Department of Education, the Regional Superintendence of Education and the school principals. The informed consent form was signed by the parents.

Anthropometry and body composition

Weight and height were measured using an electronic digital scale (Tanita®, model BC 553, Arlington Heights, IL, USA), with 150 kg capacity and 100 g accuracy, and a 2-m portable stadiometer (Alturexata®, Belo Horizonte, MG, Brazil). The WC was measured for HWP evaluation at the midpoint between the iliac crest and the last rib using a flexible and inelastic tape measure.

The nutritional status of the children was evaluated by the anthropometric index, body mass index for age (BMI-for-age) using Z-score indices. The diagnosis of the nutritional status of the children was carried out according to the World Health Organization recommendation, which considers the BMI Z-score $> +1$ as excess of weight.[13]

Body composition was assessed by dual energy X-ray absorptiometry, in the morning, after an overnight fast with children in the supine position. The excess body fat was classified according to the cut-off point proposed by Lohman[14] when the percentage of fat was >20% for boys and 25% for girls.

Clinical and metabolic evaluation

Blood samples were collected after a 12-hour fast, by venipuncture into serum gel tubes for further analysis. Glucose, total cholesterol (TC), high density lipoprotein (HDL) and LDL, and triglycerides (TGs) were determined by the enzymatic colorimetric method using the commercial Bioclin® kit (Belo Horizonte, MG, Brazil), following the manufacturer's instructions, and measured in an automatic analyzer (Mindray BS-200®, Nanshan, China).

The lipid profile was classified using specific cut-off points for children. Values were considered altered when: CT $\geq$ 170 mg/dl; LDL $\geq$ 110 mg/dl; and HDL $\leq$ 45 mg/dl.[15]

Insulin and calcidiol (25(OH)D) were determined by chemiluminescent immunoassay. Serum insulin was quantified by the Elecsys Insulin® test with detection limit of 0.200–1000 μU/ml. 25(OH)D was determined by the ARCHITECT® 25-OH Vitamin D assay. Data from the laboratory show that the serum vitamin D assessment has correlation coefficient of 0.94 for serum samples compared with the assay DiaSorin LIAISON® 25-OH Total Vitamin D and 0.90 compared with liquid chromatography with mass spectrometry.

The Homeostasis Model Assessment Insulin Resistance (HOMA-IR) was calculated according to the equation described by Matthews *et al*.[16] Insulin resistance was measured when HOMA-IR ≥ 3.16, according to the 'I Atherosclerosis Prevention Guideline on Childhood and Adolescence of the Brazilian Society of Cardiology'.[17]

At present, no consensus exists on the cut-off points for the classification of serum 25(OH)D in clinical practice. Vitamin D deficiency has been defined as <20 ng/ml by many specialists, while sufficiency values range from 20 to 32 ng/ml.[18,19] In this study, vitamin D concentration was classified as deficient, insufficient and sufficient, using the cut-off values <20 ng/ml, 20–29.99 ng/ml and ≥30 ng/ml, respectively. In a previously published study, we found association of vitamin D status with cardiometabolic alterations using these cut-off points,[11] which was also in agreement with other studies with children and adolescents.[20,21]

Blood pressure was measured with the child in the sitting position, after resting for at least 5 minutes, and the right arm on the same level as the heart. Blood pressure was measured three times, at intervals of ∼5 minutes. The mean values were used to classify children according to age, gender and height percentile following the 'VI Brazilian Guidelines on Hypertension'.[22] Systolic or diastolic pressure was considered altered when greater than the 90th percentile. Measurements were carried out using an Omron® automatic inflator (HEM 907, Vernon Hills, IL, USA), which was validated by El Assaad *et al*.[23]

The variable number of cardiometabolic risk factors was created from the sum of alterations presented by the child, considering excess weight and body adiposity, hypercholesterolemia, high LDL, low HDL, high blood pressure and insulin resistance.

HWP definition

HWP was considered present when the subject simultaneously showed increased WC and hypertriglyceridemia. Excess abdominal adiposity was considered for values above the 75th percentile of the population, according to age and sex, which has already been used in studies with children and adolescents as a derivation of a proposal for the definition of MS.[24] Hypertriglyceridemia classification was based on values ≥75 mg/dl.[15]

Statistical analyses

Statistical analyses were performed with the software STATA® version 13.0. Data were presented as distribution of absolute and relative frequencies. Pearson's chi-square test, Fisher's exact test and chi-square test for linear trend were used to examine the relationship between HWP and other variables in the study.

The association between the prevalence of HWP and the number of cardiometabolic risk factors (excess body weight and adiposity, hypercholesterolemia, high LDL, low HDL, high blood pressure and insulin resistance) was evaluated with the chi-square test for linear trend.

Poisson regression with robust variance was used to estimate the association between vitamin D and HWP. The prevalence ratio (PR) with 95% confidence interval (95% CI) was used as a measure of effect. Sex (female and male), skin color (white, pardo/brown/mulatto and black), sedentary behavior (hours/day), maternal schooling (completed years), per capita income (US $), season of the year, parathyroid hormone (nmol/ml), vitamin D intake (μg/day) and sun exposure (hours/day) were considered potential confounders.[7,9,25] The model adjusted was applied to the total sample and to the subgroup with at least one risk factor other than HWP.

The Hosmer and Lemeshow test was used to verify the goodness of fit for the final model, considering values >0.5 as good fit. The category 'vitamin D sufficiency' was adopted as reference in all models.

The significance level of 0.05 ($\alpha = 5\%$) was adopted for all tests.

Results

The prevalence of vitamin D deficiency and insufficiency were 12.2 and 43.4%, respectively, and 16.4% had HWP.

Children showed high prevalence of overweight and body fat (32.8 and 49.7, respectively). The highest prevalence of HWP was found in children with excess weight and body fat, hypercholesterolemia, low HDL, high LDL, insulin resistance, hypertension and vitamin D insufficiency and deficiency (Table 1). The prevalence of HWP was also significantly higher among children with a higher number of other cardiometabolic risk factors (Fig. 1).

The multiple regression analysis showed that the prevalence of HWP was 85% (95% CI: 1.03–3.30) higher in

Table 1 Sample characterization and prevalence of the hypertriglyceridemic waist phenotype (HWP) according to covariates in children. Viçosa, MG, Brazil, 2015

	n (%)	*HWP*		*P*
		Yes	*No*	
Sex				
Girls	197 (52.1)	35 (17.8)	162 (82.2)	0.455
Boys	181 (47.9)	27 (14.9)	154 (85.1)	
Skin color[a]				
White	124 (32.8)	18 (14.5)	106 (85.5)	0.614
Pardo/brown/mulatto	211 (55.8)	37 (17.5)	174 (82.5)	
Black	43 (11.4)	7 (16.3)	36 (83.7)	
Sedentary behaviour				
≤2 h/d	198 (52.4)	32 (16.2)	166 (83.8)	0.895
>2 h/d	180 (47.6)	30 (16.7)	150 (83.3)	
Maternal education[a]				
Elementary school	138 (36.7)	25 (18.1)	113 (81.9)	0.743
High school	157 (41.8)	22 (14.0)	135 (86.0)	
Technical/Higher	81 (21.5)	14 (17.3)	67 (82.7)	
Per capita income (US$)				
≥Median (US$: 155,27)	191 (50.5)	31 (16.2)	160 (83.8)	0.927
<Median (US$: 155,27)	187 (49.5)	31 (16.6)	160 (83.4)	
Excess weight[b]				
≤Z-score + 1	254 (67.2)	4 (1.6)	250 (98.4)	<0.001*
>Z-score + 1	124 (32.8)	58 (46.8)	66 (53.2)	
BF (%)[b]				
Normal	190 (50.3)	—	190 (100.0)	<0.001*
Increased	188 (49.7)	62 (33.0)	126 (67.0)	
TC (mg/dl)				
<170	290 (76.9)	37 (12.8)	253 (87.2)	<0.001*
≥170	87 (23.1)	25 (28.7)	62 (71.3)	
HDL (mg/dl)				
>45	245 (65.0)	31 (12.7)	214 (87.3)	0.007*
≤45	132 (35.0)	31 (23.5)	101 (76.5)	
LDL (mg/dl)				
<110	318 (84.6)	44 (13.8)	274 (86.2)	0.001*
≥110	58 (15.4)	18 (31.0)	40 (69.0)	
HOMA-IR[b]				
<3.16	364 (97.6)	55 (15.1)	309 (84.9)	<0.001*
≥3.16	9 (2.4)	7 (77.8)	2 (22.2)	
BP				
<P90	352 (93.4)	45 (12.8)	307 (87.2)	<0.001*
≥P90	25 (6.6)	17 (68.0)	8 (32.0)	
25(OH)D (ng/ml)[a]				
Sufficiency	167 (44.4)	17 (10.2)	150 (89.8)	0.008*
Insufficiency	163 (43.4)	33 (20.2)	130 (79.8)	
Deficiency	46 (12.2)	12 (26.1)	34 (79.9)	

BF, body fat; TC, total cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; BP, blood pressure; P90, percentile 90.

[a]Chi-square test for linear trend.

[b]Fisher's exact test.

Pearson chi-square test. $^*P < 0.05$.

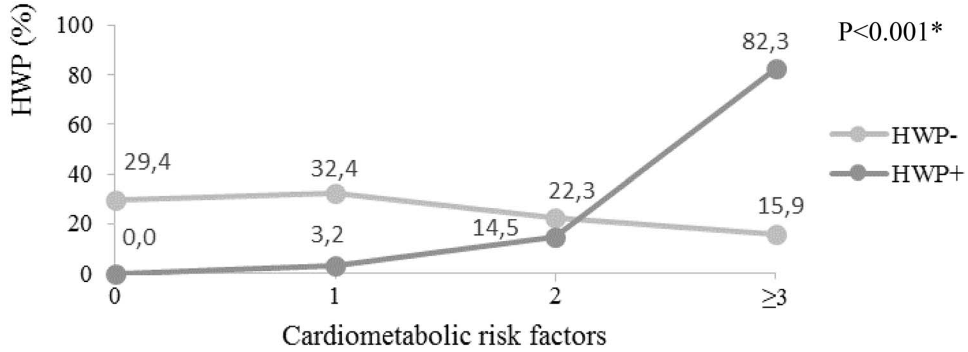

Fig. 1 Prevalence of hypertriglyceridemic waist phenotype (HWP) according to the number of other cardiometabolic risk factors in children. Viçosa, MG, Brazil, 2015. Risk factors: excess weight and body adiposity, hypercholesterolemia, high LDL, low HDL, hypertension and insulin resistance. *Chi-square test for linear trend.

Table 2 Crude and adjusted prevalence ratio for the association between vitamin D and the hypertriglyceridemic waist phenotype in children. Viçosa, MG, Brazil, 2015 ($n = 375$)

	PR crude	*95% CI*	*P* [a]
Insufficiency	1.95	1.13–3.37	0.016
Deficiency	2.41	1.24–4.70	0.010
	PR adjusted	*95% CI*	*P* [a]
Model 1			
Insufficiency	1.92	1.09–3.37	0.024
Deficiency	2.39	1.23–4.66	0.010
Model 2			
Insufficiency	1.89	1.08–3.32	0.027
Deficiency	2.36	1.22–4.59	0.011
Model 3			
Insufficiency	1.86	1.05–3.30	0.034
Deficiency	2.33	1.19–4.56	0.013
Model 4			
Insufficiency	1.85	1.03–3.30	0.039
Deficiency	2.21	1.11–4.45	0.025

Model 1: Adjusted by sex and skin color; Model 2: Model 1 + maternal education and per capita income; Model 3: Model 2 + sedentary behaviour; Model 4: Model 3 + season, parathyroid hormone, vitamin D intake and sun exposure.

[a]Poisson regression. Reference group was sufficiency (>30 ng/ml).

children with insufficiency and 121% (95% CI: 1.11–4.45) higher in children with deficiency than in children with vitamin D sufficiency (Table 2). We examined these associations in the group of children with at least one cardiometabolic risk factor besides HWP and found that the association remained, indicating that vitamin D insufficiency/deficiency contributes to an additional risk in these individuals (Fig. 2).

Discussion

Main findings of this study and what is already known on this topic

The findings of this study show a high prevalence of HWP (16.4%). Vitamin D insufficiency/deficiency was associated with a higher prevalence of this phenotype among children, regardless of the presence of other cardiometabolic risk factors. Nevertheless, the prevalence of HWP was higher in children with a higher number of cardiometabolic risk factors and in children with vitamin D insufficiency/deficiency.

HWP describes a subtype of high-risk obesity and provides a promising approach to assess cardiometabolic risk. However, differences in body composition and metabolic complications associated with age, gender and ethnicity still need to be better assessed in different populations, since cut-off points may differ between them.[7,26] So far, a careful study of the literature reveals that the prevalence of HWP in children and its association with vitamin D status in childhood have not been thoroughly investigated.

The prevalence of HWP in this study was higher (16.4%) than in other studies with children and adolescents (6.4–10.6%) reported in the UK,[9] China,[26] Iran,[7,27] and Brazil.[28–30] It is important to note that the criteria used to define HWP varied among the studies. However, the prevalence found in this study was lower than in a population of 10 to 14-year-old children in Paraná (20.7%),[31] which also used the 75th percentile for WC, but a higher cut-off point for TG (≥100 mg/dl). Besides cut-off points, differences in the prevalence of HWP among populations may also involve the age range studied. In this regard, we found no studies with the same age group of our study for comparison.

The main finding of this study is that vitamin D insufficiency and deficiency were associated with higher HWP prevalence. Thus, this finding suggests an association of vitamin D insufficiency and deficiency with cardiometabolic risk

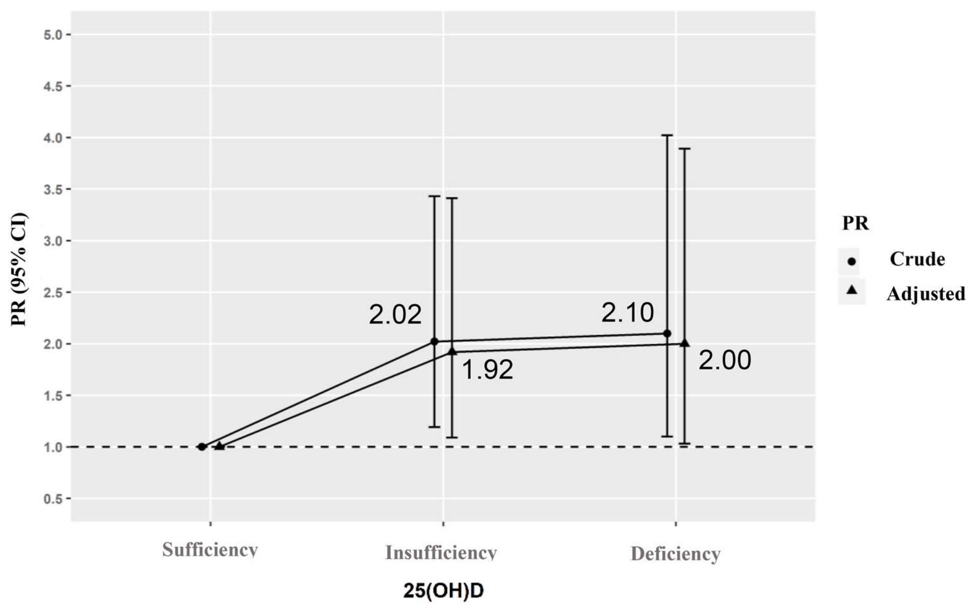

Fig. 2 Crude and adjusted prevalence ratio for the association between vitamin D and the HWP in children with at least one risk factor other than HWP. Viçosa, MG, Brazil, 2015. ($n = 278$). Adjusted by sex, skin color, maternal education, per capita income, sedentary behaviour, season, parathyroid hormone, vitamin D intake and sun exposure. Poisson regression.

in childhood. We found no other study focusing on the relationship between vitamin D and HWP in children, but these results corroborate with a research involving 2301 US adults, in which vitamin D was also identified as an independent HWP predictor.[12] In addition, the association of vitamin D insufficiency and deficiency with increased prevalence of HWP was maintained when evaluated in children with at least one other risk factor, indicating that low levels of vitamin D are an additional risk in cardiometabolic health.

We believe that the association of vitamin D insufficiency and deficiency with HWP may be related to the visceral obesity in these individuals, since it has a greater influence on serum vitamin D levels than subcutaneous levels.[32,33] This is clinically important because vitamin D insufficiency/deficiency and HWP are related to the MS components, increasing the cardiometabolic risk.[8,10,11] In addition, the concentration of vitamin D has been inversely associated with dyslipidemia in some studies, especially the concentration of TGs, which makes up the diagnosis of HWP.[34–37] Therefore, this result is plausible considering the already documented inverse association between visceral fat and TGs with vitamin D.

Furthermore, in this study, HWP was associated with a greater number of cardiometabolic risk factors and its prevalence was higher in children who had at least one other risk factor. In 2000, Lemieux *et al*.[4] in their pioneering work reported the association between HWP and increased cardiometabolic risk in adults, mainly in association with the atherogenic triad (hyperinsulinemia, high concentrations of apolipoprotein B and small dense particles of cholesterol LDL). Later, researchers pointed out that HWP could be used for the screening of populations at risk, as a good predictor of MS in adults.[7,9,38] Although the prevalence of MS has been less investigated in children and adolescents, studies suggest that the presence of HWP is associated with other cardiometabolic risk factors.[8,14,24,39]

HWP may be important for identifying cardiometabolic risk in children, since there are no well-defined criteria for the classification of MS in this age group.[2,27] In addition, the literature highlights the use of the phenotype as a screening tool equally or more relevant than the current MS criteria, even for epidemiological studies with children and adolescents, being a more practical and useful predictor for using only the WC and serum TGs.[7,9,27,39] It is important to carry out studies to propose the standardization of methods and cut-off points for WC and hypertriglyceridemia to facilitate the interpretation and comparison of the studies in childhood.

What this study adds

The possibility of identifying asymptomatic individuals at risk for cardiovascular and metabolic diseases may have important implications for public health, with a view to improving prevention strategies. Maintaining adequate serum vitamin D levels, for example, may be a relevant health prevention strategy to reduce cardiometabolic risk in childhood.

Some strengths of this study should be mentioned. This is the first study to assess HWP and its association with vitamin D insufficiency/deficiency and other cardiometabolic risk factors in childhood and the first study on vitamin D with a representative sample of Brazilian children. Because the prevalence of cardiometabolic risk factors is increasing and vitamin D insufficiency/deficiency has become a world-wide public health problem, even in tropical countries such as Brazil, it is important to assess the relationship between these factors and vitamin D status in childhood. Emphasis should be placed on the HWP, which is little studied in the child population. In this study, all the confounding variables described in the literature were used for adjustments in the statistical analyses.

Limitations of this study

It is important to note that the criteria used to define HWP varied among the studies. Different cut-off points are used to estimate the prevalence of HWP, for both the classification of the high WC and hypertriglyceridemia, which hinder comparison with similar studies. Another aspect that makes comparison difficult is the lack of standardization of WC measurement site on the body.

We concluded that vitamin D insufficiency and deficiency were associated with a higher prevalence of HWP, regardless of the presence of other cardiometabolic risk factors. HWP may be a useful indicator in assessing cardiometabolic risk in pediatric clinical practice, especially in basic healthcare services, for being a simple, practical and low cost method. In addition, combating vitamin D insufficiency/deficiency may become an important strategy for reducing cardiometabolic risk in children, even in sunny countries.

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Conflict of interest

The authors declare no conflicts of interest.

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