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Severity of obesity is associated with worse cardiometabolic risk profile in adolescents: Findings from a Brazilian national study (ERICA)

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ABSTRACT

Objective: The prevalence of obesity and severe obesity among adolescents has increased dramatically in developing countries. However, the distribution of cardiometabolic risk factors through the severity of obesity continuum is relatively unknown among youth. The aim of this study was to evaluate the association of weight categories with cardiometabolic risk factors among Brazilian adolescents.
Methods: ERICA (The Study of Cardiovascular Risk in Adolescents) was a multicenter, school-based, cross-sectional study composed of Brazilian adolescents (12–17 y of age). Severity of obesity was classified according to the International Obesity Task Force reference values for body mass index (BMI) and several cardiometabolic risk factors were measured after clinical and biochemical exams and categorized using standard definitions of abnormal values.
Results: Among the 37 892 adolescents enrolled, 8708 had excess weight, being classified with overweight (17.2%), obesity (5.6%), and severe obesity (1.3%). Increasing severity of obesity was associated with a worse cardiometabolic profile in the overall sample. Multivariable models that controlled for age, sex, skin color, socioeconomic status, physical activity, and total energy intake, showed that individuals in higher categories of severity of obesity tended to have higher prevalence ratios of most cardiometabolic risk factors compared with the other weight groups, except for high fasting blood glucose among boys.
Conclusions: Progressive degrees of excess weight are positively associated with cardiometabolic risk factors in youth from a middle-income country, indicating the importance in classifying the severity of weight excess among adolescents and considering this to plan prevention programs against early development of obesity-related diseases.

Introduction

Obesity in children and adolescents has exponentially increased in the last decades, rising from 0.8% in 1975 to >6.8% in 2016 [1] . The same tendency can be seen in Brazil, where the prevalence of overweight and obesity in adolescents has increased six times in boys (4 to 28%) and three times in girls (8 to 23%) since the 1970s [2,3]. Severe obesity is the fastest growing subcategory of excess weight in adolescents, reaching >4% of all youth in the United States [4].

Weight excess in youth can lead to the development of many cardiovascular risk factors that, if not early controlled, tend to

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The data sets generated or analyzed during the present study are not publicly available due to issues in making them accessible online, such as storage difficulties. However, the data sets are available on reasonable request to the corresponding author.

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persist and increase the risk for early cardiovascular disease in adult life [5–7]. Cardiometabolic risk factors such as abnormal glucose levels, dyslipidemia, and hypertension are more prevalent in obese adolescents than in those with normal weight [8,9]. These conditions are associated with higher risk for coronary heart disease, stroke, diabetes mellitus, and all-cause mortality in adulthood [10]. However, weight reduction can significantly change these outcomes [11].

Data from a systematic review showed that the risk for all-cause mortality in adults with severe obesity (class II and III) is higher than in those with overweight or class I obesity [12]. In adolescents classified within the obese category, there is a variety of risks accompanying increases in body mass index (BMI); however, this association is still being investigated [11,13–17]. In the United States, results from the National Health and Nutrition Examination Survey (NHANES) 1999/2012, which included 8579 children and adolescents with excessive weight, showed that having severe obesity lead to an increased risk for low levels of high-density lipoprotein cholesterol (HDL-C), high systolic and diastolic blood pressure (SBP and DBP, respectively), and high levels of triglycerides (TGs) and glycated hemoglobin (HbA1c) [13]. Furthermore, differences by age, sex, and ethnicity were also observed in the relation between severity of obesity and cardiometabolic risk in youth [13,16].

In some low- and middle-income countries where quick nutritional transitions were observed in the last decades [18,19], the severity of obesity and its associated comorbidities among young people were insufficiently explored. Investigating the association between severity of obesity and cardiometabolic risk factors in Brazil can help us identify the individuals in higher risk groups and develop public health strategies against obesity-related outcomes early in life, which would apply to other low- and middle-income countries. Thus, the objective of this study was to evaluate the association of severity of obesity and known cardiometabolic risk factors in a representative sample of Brazilian adolescents.

Methods

Design and sample

ERICA (The Study of Cardiovascular Risk in Adolescents [*Estudo de Riscos Cardiovasculares em Adolescentes*]) was a multicenter, school-based, national cross-sectional study carried out in urban and rural settings in Brazil. The sample was composed of students between 12 and 17 y of age enrolled in private and public schools in Brazilian municipalities with ≥100 000 inhabitants. Data were collected between February 2013 and November 2014.

A complex sampling approach was performed. Thus, the population target was divided into 32 geographic strata: all 26 state capitals, the Federal District, and 5 more strata representing other municipalities with ≥100 000 inhabitants in each region of Brazil. The schools were selected based on probability proportional to size (number of students per school) and inversely proportional to the distance between the school municipality and the state capital. In all, 1247 schools in 124 municipalities were selected. Three classrooms were randomly selected from each school, and all students in these classes were invited to participate in ERICA. Further details regarding the sampling and design of the ERICA project can be found in previous publications [20,21]. The participation rate for adolescents who completed the questionnaires, anthropometric measures, and blood sampling in ERICA was 52% [22].

In summary, ERICA's sample size calculation was performed considering that the prevalence of metabolic syndrome in adolescents is around 4%, a maximum estimation error of 0.9% and a 95% confidence level, the required size for a simple random sample would be 1821 students. However, considering that the sample is clustered by school, shift, grade, and class, a design effect of 2.97 was considered. Additionally, sample size was increased by 15% considering possible non-response and other losses. Finally, the calculation showed that it was necessary to enroll 6219 adolescents in each of the 12 domains (6 ages × 2 sexes), resulting in a total sample size of ≥74 628 adolescents [20].

For this study, we used data from students who attended school during the morning (925 schools), as overnight fasting was mandatory for the blood sampling. The final available sample size for this study was 37 892. The study was approved by the Research Ethics Committees in all 27 federation units in Brazil. All adolescents and their legal guardians provided written informed assent/consent to participate in the study.

Severity of obesity

Body mass index (weight [kg]/height [m^2]) was used to assess the severity of obesity. Weight and height were measured using a digital scale and a portable stadiometer, respectively. Both measures were taken with adolescents wearing light clothing and no shoes. The assessed anthropometric measures were performed following standard practices [23]. The severity of obesity was defined according to sex and age-specific cutoff points recommended by the International Obesity Task Force (IOTF) [24]. The BMI IOTF cutoffs for youth were calculated to represent BMI centile corresponding to BMI at 18 y of age (i.e., overweight ≥25 and <30 kg/m^2; obesity ≥30 and <35 kg/m^2; and severe obesity ≥35 kg/m^2). The IOTF-specific cutoff points of BMI for sex and age were previously published and can be accessed elsewhere [24,25].

Cardiometabolic risk factors

Blood pressure was verified using a digital monitor (Omron 705-IT) previously validated for use in youth [26]. Blood pressure was taken from each student's right arm using individual cuff sizes after 5 min of sitting still, with an interval of ≥3 min between each measure. The average values of the second and third readings were used in the analyses. High blood pressure was defined as values of SBP or DBP ≥95th percentile for sex, age, and height [27].

All participants were asked to refrain from eating for at least 10 to 12 h before blood sampling. Compliance with the overnight fast was confirmed by a questionnaire before venipuncture. Fasting blood samples were collected for measuring fasting glucose, HbA1c, insulin, total cholesterol, low-density lipoprotein cholesterol (LDL-C), HDL-C, and TGs. The reference values used to determine abnormal values of cardiometabolic variables are shown in Supplementary Table 1, which were in accordance with national and international guidelines [27–31]. All blood samples were analyzed by a single laboratory following a standardized protocol [32].

Metabolic syndrome (MetS) was defined according to the International Diabetes Federation criteria [33]. These include a high waist circumference as a mandatory component (<16 y: ≥90th percentile; ≥16 y, boys: ≥90 cm; and ≥16 y, girls: ≥80 cm), which was measured at midway between the iliac crest and the lower costal margin, and plus two or more of the following criteria: fasting plasma glucose (FPG) ≥ 100 mg/dL; SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg; TGs ≥ 150 mg/dL; HDL-C in adolescents <16 y: <40 mg/dL; HDL-C in adolescents ≥16 y: <40 mg/dL; and HDL-C in girls >16 y: <50 mg/dL.

Covariates

The covariates included in the analyses were sex, age (12–17 y), and self-reported skin color (white, black, brown, or others). Socioeconomic status (SES) was assessed with a similar instrument used by the Brazilian Demographic Census [34], which takes into account possession of specific goods and the presence of a housekeeper at home. Thereafter, for some analyses, this variable was categorized in tertiles.

Statistical analysis

All estimates and their 95% confidence intervals (CIs) were calculated using the ERICA's sample weights, taking into account the complex sample design and obtaining population-representative findings [20]. All the descriptive analyses were stratified by weight category (normal weight, overweight, obesity, and severe obesity). The mean values and 95% CI for cardiometabolic risk factors were estimated for the overall sample. TGs and fasting insulin do not follow a parametric distribution, thus, for this variable, median and interquartile range (IQR) are presented.

The prevalence of abnormal cardiometabolic risk factors according to the severity of obesity was calculated for overall sample and stratified by sex and age groups (12–14 and 15–17 y of age). The adjusted Wald's test for trend was calculated to evaluate the increase or decrease in the prevalence of abnormal cardiometabolic risk factors through the weight categories.

Poisson regression models were used to examine the association of severity of obesity (adolescents with normal weight were the reference group) with abnormal cardiometabolic risk factors. All models were adjusted for sex, age, skin color, SES, physical activity and total energy intake; and the inclusion of these variables was decided a priori and is in accordance with the literature [13,14,16]. These analyses were performed for overall sample and by sex.

All tests were two-tailed, and the analyses were performed in Stata version 14 (StataCorp, College Station, TX, USA) taking the study design (complex sample) into account. $P < 0.05$ denotes statistical significance. We followed the STROBE statement to prepare this report [35].

Results

Among the sample of 37 892 adolescents, 8708 had weight excess, being classified with overweight (17.2%), obesity (5.6%),

Table 1
Distribution of obesity severity and demographic and clinical characteristics among Brazilian adolescents: ERICA 2013–2014.

Characteristics	Normal weight Weighted % (95% CI)	Overweight	Obesity	Severe obesity
Overall (n = 37 892)	75.9 (74.5–77.2)	17.2 (16.2–18.3)	5.6 (5.1–6.2)	1.3 (1.1–1.5)
Sex				
Female	75.9 (74.0–77.8)	17.8 (16.3–19.4)	5.1 (4.5–5.7)	1.2 (0.9–1.5)
Male	75.0 (73.0–77.7)	16.6 (15.0–18.4)	6.1 (5.3–7.0)	1.3 (1.0–1.7)
Age (years)				
12–14	74.0 (71.4–76.5)	18.7 (17.0–20.6)	6.0 (5.2–6.9)	1.2 (0.9–1.6)
15–17	77.6 (75.9–79.1)	15.9 (14.7–17.3)	5.2 (4.4–6.1)	1.3 (1.0–1.6)
Skin color				
White	74.5 (72.5–76.5)	17.3 (16.0–18.7)	6.5 (5.6–7.7)	1.6 (1.2–2.2)
Black	75.3 (69.9–80.0)	17.8 (13.3–23.5)	5.2 (3.9–7.0)	1.6 (1.0–2.6)
Brown (mixed)	77.2 (75.3–79.1)	17.1 (15.6–18.7)	4.7 (4.0–5.5)	1.0 (0.8–1.2)
Others	74.8 (69.3–79.5)	17.0 (14.0–20.4)	7.5 (4.1–13.3)	0.8 (0.5–1.3)
SES (tertiles)				
First	78.8 (77.0–80.5)	14.7 (13.3–16.3)	5.5 (4.6–6.5)	1.0 (0.7–1.4)
Second	76.4 (73.6–78.9)	16.8 (15.1–18.6)	5.9 (4.7–7.3)	1.0 (0.8–1.3)
Third (Higher)	71.9 (68.8–74.8)	20.8 (18.7–23.1)	5.4 (4.3–6.8)	1.9 (1.4–2.5)
Region				
North	79.9 (78.1–81.5)	14.9 (13.6–16.4)	4.1 (3.5–4.8)	1.1 (0.8–1.5)
Northeast	75.6 (72.9–78.2)	18.1 (16.1–20.4)	5.0 (4.3–5.8)	1.2 (0.9–1.6)
Southeast	76.2 (73.9–78.4)	16.8 (15.1–18.7)	6.0 (5.1–7.1)	1.0 (0.7–1.3)
South	71.5 (69.1–73.9)	19.9 (18.4–21.5)	6.0 (5.1–7.1)	2.5 (1.6–3.9)
Midwest	78.0 (76.6–79.3)	15.7 (14.6–16.8)	5.0 (4.3–5.7)	1.4 (0.9–2.1)
		Weighted mean (95% CI)		
Weight (kg)	52.4 (52.1–52.7)	69.1 (68.5–69.8)	83.7 (82.8–84.7)	101.9 (98.6–105.2)
BMI (kg/m^2)	19.6 (19.5–19.6)	25.5 (25.4–25.5)	30.3 (30.1–30.5)	37.0 (36.4–37.6)
Waist circumference (cm)	68.1 (67.9–68.3)	81.0 (80.6–81.4)	93.2 (92.5–93.9)	105.8 (104.3–107.3)
SBP (mm Hg)	109.2 (108.7–109.7)	117.0 (116.3–117.7)	121.5 (120.4–122.7)	121.7 (119.6–123.8)
DBP (mm Hg)	65.5 (65.1–65.9)	68.3 (67.8–68.9)	71.6 (70.8–72.5)	72.6 (71.2–74.0)
Cholesterol (mg/dL)	146.8 (145.7–148.0)	151.2 (149.5–153.0)	156.1 (152.5–159.8)	160.4 (156.4–154.3)
LDL-c (mg/dL)	83.7 (82.9–84.5)	88.9 (87.4–90.4)	94.2 (91.2–97.2)	97.4 (94.3–100.4)
HDL-c (mg/dL)	48.3 (47.6–49.0)	45.2 (44.6-45.9)	41.5 (40.5–42.5)	38.8 (37.6–40.0)
Triglycerides* (mg/dL)	67.0 (66.0–68.0)	76.0 (74.0–78.0)	88.0 (81.1–94.9)	113.0 (102.2–123.8)
HbA1c (%)	5.38 (5.36–5.39)	5.39 (5.36–5.41)	5.48 (5.44–5.53)	5.52 (5.46–5.58)
Fasting insulin* (mU/L)	7.5 (7.3–7.7))	10.8 (10,5–11.1)	15.8 (15.1–16.5)	18.5 (16.2–20.8)
Fasting plasma glucose (mg/dL)	86.0 (85.5–86.4)	87.2 (86.6–87.8)	88.2 (87.3–89.1)	89.4 (87.7–91.1)

BMI, body mass index; DBP, diastolic blood pressure; HbA1c, Glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; SES, socio-economic status; SBP, systolic blood pressure, LDL-c, low-density lipoprotein cholesterol.
*Weighted median and interquartile range.

and severe obesity (1.3%). The mean age in the overall sample was 14.6 y (SE 0.01) and was higher in the group with severe obesity. Regarding the prevalence of each weight category, we did not observe associations with sex and age group; however, adolescents with brown (mixed) skin color showed a slightly lower prevalence of obesity and severe obesity, especially when compared with white (Table 1). Regarding the concentration levels of the cardiometabolic risk factors, HDL-C decreased and all others increased through the weight categories. Similarly to what was observed in the overall sample, when the analysis was stratified by sex, both boys and girls with higher severity of obesity showed a poor cardiometabolic profile (data not shown).

Figure 1 shows the prevalence of abnormal cardiometabolic risk factors according to the severity of obesity. There was an increase in the prevalence of higher levels for blood pressure, total and LDL-C, TGs, HbA1c, FPG, fasting insulin, and MetS with increasing severity of obesity ($P < 0.01$ for all). The prevalence of low HDL-C levels was proportional to increase in severity of obesity ($P < 0.01$).

Table 2 shows the prevalence of abnormal values for cardiometabolic risk factors by sex and age group. The prevalence of most risk factors increased by severity of obesity in both sexes; however, this association was not significant for high FPG in boys. Boys in all weight categories had a significantly higher prevalence of low HDL-C than girls. Girls with normal weight and overweight, compared with boys in the same respective weight category, had higher prevalence of abnormal levels of total and LDL-C, but lower levels of elevated HbAc and high blood pressure. Difference in prevalence between sexes in the obesity and severe obesity groups were discreet. When the data was analyzed by age, increasing severity of obesity was correlated with higher presence of all cardiometabolic risk factors in both age groups, except for FPG in adolescents 12 to 14 y of age.

Excluding adolescents with normal weight (in which <0.1% had MetS), the prevalence of MetS increased along with severity of obesity in both sex and age categories (data not shown). Overall, the prevalence of MetS was 4.7% (95% CI, 3.7–5.9%), 23.8 (95% CI, 19.6–28.6%), and 30.5% (23.3–38.8%) among adolescents with overweight, obesity, and severe obesity, respectively.

Table 3 shows the prevalence ratios for the abnormal cardiometabolic risk factors adjusted for sex, age, skin color, SES, physical activity level, and total energy intake. Prevalence ratios of the majority of cardiometabolic risk factors tended to increase with higher severity of obesity in the overall sample. Among sexes, the same association was found, except for high FPG in boys (P_{trend} = 0.579). Prevalence of MetS, compared with adolescents with overweight, was significantly higher among those with obesity or severe obesity in the overall sample and in both sexes.

Discussion

The present study, involving 37 892 Brazilian youth, showed that severe obesity should be considered a public health concern

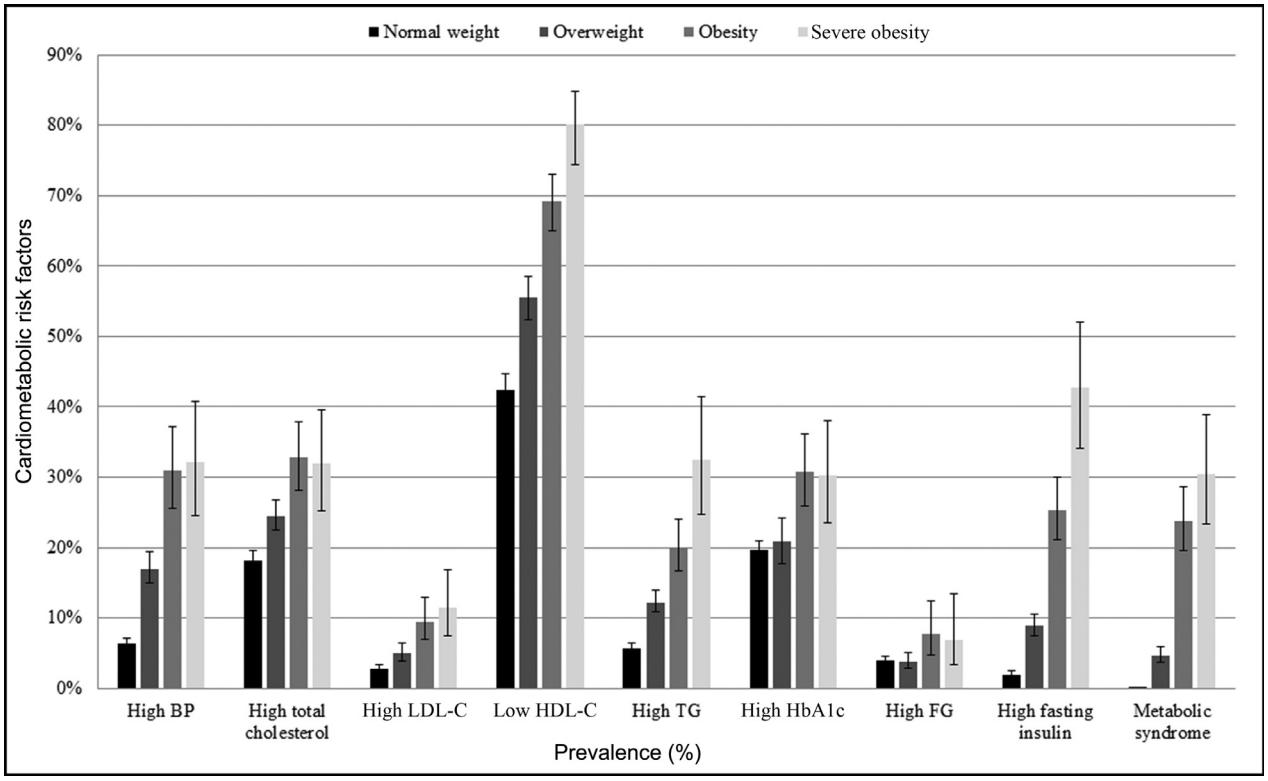

Fig. 1. Prevalence of abnormal cardiometabolic risk factors according to the severity of obesity. ERICA 2013–2014. BP, blood pressure; FG, fasting glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides.

owing to the observed prevalence and suggests that there is a positive association between severity of obesity and worst cardiometabolic profile in this age group. In 2013, the American Heart Association released a scientific statement recommending the division of childhood obesity into class I, II, and III [15]. It was justified by greater precision for categorizing this population and better identification of individuals with higher number of cardiovascular risk factors. However, the Brazilian Ministry of Health still recommends stratification of childhood obesity in only two classes, following the World Health Organization's 2007 reference [36,37].

Our adjusted models showed that increasing weight excess severity tends to be accompanied with a concomitant rise in the prevalence of cardiometabolic risk factors. However, in other populations, such as in high-income countries, obesity-related cardiometabolic risk factors can differ. A Korean study with 1326 adolescents showed a correlation with obesity level for all studied variables except FPG and DBP [14]. On the other hand, in North American children and adolescents, only SBP, HDL-C, and FPG levels were related to severity of obesity [13]. These divergent results may be explained by different cutoffs for abnormal values used in both studies, a much broader age inclusion criteria (3–19 y) in the study from the United States, and differences in the socioeconomic parameters of the populations. It can also be related to specific diet patterns and sugar consumption in each region—countries from the Americas have the highest intake of sugar-sweetened beverages; whereas those from Asia have the lowest [38].

In ERICA, the prevalence of cardiometabolic risk factors increased with obesity class in both sexes, except for FPG in boys. Low HDL-C was more prevalent in boys than in girls across all weight categories, just as elevated blood pressure and high Hb1Ac. Girls tended to have more elevated fasting insulin than boys. Furthermore, in the present study, differences between sexes were more prominent in the normal weight and overweight groups; whereas in those with obesity and severe obesity, they were subtle. Data regarding these associations by sex are still controversial. During puberty, owing to changes in hormonal levels, body fat percentage increases in girls and decreases in boys [39]. A study with Italian youth with obesity showed that girls were more insulin resistant and had higher body fat percentage and lower lean body percentage than boys, independently of Tanner stage [40]. Previous studies also showed that Brazilian girls are more physically inactive [41], eat snacks more frequently in front of the television [42], and have diets containing higher levels of sugar than boys [43], all factors that could contribute to higher insulin resistance in this group.

A graded relationship between severity of obesity and unfavorable cardiometabolic profile were found in participants on both age groups (12–14 and 15–17 y), without a significant difference between them. Our findings disagree with those of Lambert et al., in which older adolescents were more likely to have higher number of cardiometabolic risk factors compared with those younger, especially boys [44]; however, only 9-, 13-, and 16-y-old youth were included in the study, and obesity was used as a single category, not divided into classes of BMI. Prior work has also shown that older adolescents were more likely to have MetS and its components than their younger counterparts, mostly owing to the expected increase of visceral fat deposits with age [45]. Disproportions of pubertal stages among groups, independently of age, could help explain these differences.

It is important to consider that obesity and its associated comorbidities are a considerable burden for health systems around the world. A systematic review of 12 studies from the United States estimated an annual medical expenditure per person with obesity of

Table 2
Prevalence of cardiometabolic risk factors by severity of obesity and stratified by sex and age: ERICA 2013–2014.

Characteristics	Normal weight Weighted % (95% CI)	Overweight	Obesity	Severe obesity	*P* value
High blood pressure					
Sex					
Female	5.0 (4.1–6.2)	12.4 (10.4–14.7)	23.3 (16.5–31.7)	31.0 (20.5–43.9)	<0.001
Male	7.5 (6.6–8.6)	22.0 (18.1–26.5)	37.5 (29.7–45.9)	33.0 (22.4–45.6)	<0.001
Age (years)					
12–14	6.5 (5.4–7.8)	15.5 (13.2–18.2)	32.2 (25.6–39.6)	28.9 (18.5–42.0)	<0.001
15–17	6.1 (5.0–7.4)	18.5 (15.3–22.3)	29.8 (23.1–37.5)	34.7 (24.6–46.5)	<0.001
High total cholesterol					
Sex					
Female	23.8 (22.2–25.5)	28.9 (25.3–32.9)	30.4 (23.6–38.2)	30.8 (23.8–38.9)	<0.001
Male	12.6 (11.1–14.2)	19.8 (16.5–23.5)	34.8 (28.5–41.7)	32.9 (22.3–45.6)	<0.001
Age (years)					
12–14	18.9 (17.1–20.8)	24.6 (21.4–28.1)	32.9 (27.0–39.5)	33.6 (22.1–47.4)	<0.001
15–17	17.6 (15.9–19.6)	24.5 (21.6–27.7)	32.7 (26.3–39.7)	30.5 (23.1–39.1)	<0.001
High LDL-c					
Sex					
Female	3.5 (2.8–4.5)	6.5 (4.6–9.3)	8.1 (5.3–12.1)	10.5 (6.5–16.4)	<0.001
Male	2.0 (1.4–2.7)	3.4 (2.6–4.4)	10.7 (7.3–15.5)	12.1 (6.3–21.9)	<0.001
Age (years)					
12-14	2.8 (2.0–3.9)	5.0 (3.5–7.2)	10.2 (6.7–15.2)	11.2 (5.5–21.4)	<0.001
15-17	2.7 (2.2–3.3)	5.0 (3.6–7.0)	8.8 (6.0–12.8)	11.5 (7.3–17.8)	<0.001
Low HDL-c					
Sex					
Female	32.9 (30.4–35.6)	48.0 (44.8–51.2)	59.4 (51.2–67.1)	71.9 (63.5–78.9)	<0.001
Male	51.9 (49.4–54.3)	63.6 (58.8–68.1)	77.3 (71.3–82.4)	86.9 (78.0–92.5)	<0.001
Age (years)					
12–14	38.9 (35.8–42.1)	55.3 (50.1–60.3)	74.4 (68.6–79.5)	83.3 (74.0–89.8)	<0.001
15–17	45.3 (42.4–48.2)	55.7 (51.9–59.6)	63.9 (57.1–70.1)	77.3 (69.6–83.4)	<0.001
High triglycerides					
Sex					
Female	6.7 (5.8–7.8)	11.1 (9.3–13.1)	15.5 (11.7–20.4)	27.9 (20.2–37.1)	<0.001
Male	4.4 (3.3–5.7)	13.5 (11.2–16.3)	23.9 (19.2–29.3)	36.3 (24.7–49.8)	<0.001
Age (years)					
12–14	5.7 (4.8–6.7)	12.8 (10.8–15.1)	19.7 (14.9–25.6)	39.4 (26.3–54.2)	<0.001
15–17	5.4 (4.4–6.7)	11.6 (9.5–14.2)	20.6 (16.0–26.0)	26.4 (19.0–35.3)	<0.001
High HbA1c					
Sex					
Female	16.6 (15.0–18.4)	17.3 (14.8–20.1)	29.4 (23.0–36.8)	29.0 (21.3–38.3)	<0.001
Male	22.7 (20.8–24.8)	24.5 (20.1–29.5)	32.0 (24.7–40.3)	31.3 (20.9–44.2)	0.010
Age (years)					
12–14	22.1 (20.0–24.3)	22.6 (18.5–27.2)	35.8 (29.3–42.8)	32.2 (21.4–45.3)	<0.001
15–17	17.7 (16.1–19.4)	18.9 (14.8–23.8)	25.9 (19.5–33.4)	28.6 (20.6–38.3)	0.002
High fasting plasma glucose					
Sex					
Female	2.2 (1.7–2.9)	2.7 (1.8–3.8)	8.7 (4.1–17.6)	9.3 (3.4–22.9)	<0.001
Male	5.5 (4.3–7.2)	5.1 (3.5–7.4)	7.1 (3.7–13.0)	4.7 (2.0–11.0)	0.802
Age (years)					
12–14	4.7 (3.7–6.0)	3.4 (2.4–4.7)	8.5 (3.7–16.1)	8.4 (3.7–18.1)	0.179
15–17	3.1 (2.4–4.1)	4.3 (2.9–6.4)	7.1 (3.5–14.0)	5.6 (2.3–12.9)	0.015
High fasting insulin					
Sex					
Female	2.6 (2.0–3.4)	11.0 (8.9–13.6)	27.2 (21.7–33.5)	48.4 (37.4–59.6)	<0.001
Male	1.4 (1.0–2.0)	6.7 (5.0–8.8)	23.8 (18.3–30.3)	38.2 (26.7–51.2)	<0.001
Age (years)					
12–14	2.3 (1.8–3.0)	10.6 (8.4–13.1)	25.7 (19.5–32.9)	41.4 (28.8–55.3)	<0.001
15–17	1.8 (1.3–2.5)	7.2 (5.5–9.4)	25.0 (19.8–31.0)	44.0 (33.5–55.0)	<0.001

Wald's test for trends was used to obtain the *P* values presented.
HbA1c, Glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.

$1901 in 2014 USD, reaching nationally almost $150 billion [46]. In Brazil, studies have shown a yearly cost of diseases related with overweight and obesity of $2.1 billion, in which >40% were due to cardiovascular diseases and diabetes [47]. Considering that most children and adolescents with obesity remain in the same BMI category in adulthood, early strategies to prevent this disease and its related costs are usually cost-effective and should be stimulated [48,49].

Treatment options for adolescents with severe obesity are initially based on lifestyle modifications, such as adhering to a healthy diet and increasing physical activity. However, this kind of intervention provides discrete short-term changes in weight, and individuals usually remain in the same BMI category [15]. Other treatments for obesity in adolescents involve drugs (such as orlistat and sibutramine in Brazil) and bariatric surgery [50]. Although effective in weight loss and improvement of cardiometabolic risk factors, long-term effects of this procedure on morbimortality of adolescents are still unknown, owing to the short follow-up time in previous studies. Due to the challenging aspects of treating adolescents with any class of obesity, it is important to establish preventive actions during childhood, finding new ways to promote

Table 3
Adjusted* prevalence ratios for cardiometabolic risk factors by severity of obesity and sex in adolescents: ERICA 2013–2014.

Risk factors	Overall PR (95% CI)	Girls PR (95% CI)	Boys PR (95% CI)
High blood pressure	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	Reference	Reference	Reference
Overweight	2.8 (2.3–3.5)	2.5 (2.0–3.3)	3.0 (2.3–3.9)
Obesity	4.8 (3.9–6.0)	4.7 (3.3–6.8)	4.9 (3.9–6.3)
Severe obesity	5.2 (3.7–7.1)	6.3 (3.0–10.1)	4.5 (3.0–6.8)
High total cholesterol	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	Reference	Reference	Reference
Overweight	1.3 (1.2–1.5)	1.2 (1.1–1.4)	1.5 (1.3–1.9)
Obesity	1.8 (1.6–2.1)	1.3 (1.0–1.6)	2.8 (2.2–3.4)
Severe obesity	1.7 (1.4–2.2)	1.3 (1.0–1.7)	2.4 (1.6–3.5)
High LDL-c	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	Reference	Reference	Reference
Overweight	1.8 (1.3–2.6)	2.0 (1.3–3.1)	1.8 (1.2–2.6)
Obesity	3.5 (2.5–4.8)	2.4 (1.5–3.8)	5.3 (3.5–8.1)
Severe obesity	4.1 (2.6–6.4)	3.3 (1.9–5.8)	5.9 (3.0–11.8)
Low HDL-c	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	Reference	Reference	Reference
Overweight	1.3 (1.3–1.4)	1.5 (1.3–1.6)	1.3 (1.2–1.3)
Obesity	1.6 (1.5–1.8)	1.8 (1.6–2.1)	1.5 (1.4–1.7)
Severe obesity	2.0 (1.8–2.1)	2.2 (1.9–2.5)	1.8 (1.6–2.0)
High triglycerides	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	Reference	Reference	Reference
Overweight	2.2 (1.8–2.7)	1.6 (1.2–2.1)	3.2 (2.3–4.3)
Obesity	3.7 (3.0–4.6)	2.4 (1.8–3.2)	5.7 (4.2–7.9)
Severe obesity	5.9 (4.4–7.9)	4.4 (3.1–6.1)	8.7 (5.6–13.9)
High HbA1c	$P < 0.001$	$P < 0.001$	$P = 0.008$
Normal weight	Reference	Reference	Reference
Overweight	1.1 (0.9–1.2)	1.0 (0.9–1.2)	1.1 (0.9–1.2)
Obesity	1.6 (1.4–1.9)	1.8 (1.4–2.2)	1.5 (1.2–2.0)
Severe obesity	1.6 (1.2–2.0)	1.8 (1.3–2.5)	1.4 (0.9–2.0)
High fasting plasma glucose	$P = 0.003$	$P < 0.001$	$P = 0.579$
Normal weight	Reference	Reference	Reference
Overweight	1.0 (0.8–1.4)	1.2 (0.8–1.7)	1.0 (0.7–1.5)
Obesity	2.0 (1.2–3.4)	3.8 (1.8–8.0)	1.3 (0.7–2.7)
Severe obesity	1.9 (0.9–3.9)	4.4 (1.7–11.4)	1.0 (0.4–2.3)
High fasting insulin	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	Reference	Reference	Reference
Overweight	4.4 (3.5–5.6)	4.1 (3.1–5.5)	4.8 (3.1–7.3)
Obesity	12.7 (9.9-16.3)	10.2 (7.8-13.4)	17.7 (11.6–26.8)
Severe obesity	21.5 (15.6–29.6)	17.8 (11.6–27.4)	27.9 (17.2–45.2)
Metabolic syndrome	$P < 0.001$	$P < 0.001$	$P < 0.001$
Normal weight	NI	NI	NI
Overweight	Reference	Reference	Reference
Obesity	5.20 (3.78–7.14)	3.91 (2.33–6.57)	6.21 (4.09–9.44)
Severe obesity	6.85 (4.82–9.72)	6.33 (3.65–10.9)	7.88 (4.65–13.4)

*Weighted Poisson regression models adjusted for sex, age, skin color, socioeconomic status, physical activity and total energy intake; Wald's test for trends was used to obtain the *P* values presented.HbA1c, Glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; NI, not informed; PR, prevalence ratios.

change of unhealthy habits; or even during intrauterine life, providing favorable conditions for fetal development [51].

The present study has some potential limitations. Because it is a cross-sectional study, it is not possible to establish a causal relationship between severity of weight excess and cardiometabolic risk factors. However, considering previous studies [52], it is acceptable to think that an increase in adiposity leads to a worse cardiometabolic profile, rather than the opposite. Smaller numbers of participants in the obesity and severe obesity groups (5.6 and 1.3% of the sample, respectively) could have led to imprecision, especially when subdividing in sex or age for subgroup analysis. Also, we did not plan to stratify adolescents by pubertal status, which has a known effect on metabolism changes such as glucose homeostasis and could account for differences in cardiovascular variables [16]. Nevertheless, the reliability of this self-referenced information is low, and it is reasonable to assume that age could be used as a surrogate because it accompanies puberty stage.

The main strength of our findings resides in the large, multiethnic, representative national sample of adolescents enrolled from a middle-income country. Data collection, anthropometric measures, and biochemical analysis were standardized and followed a specific protocol [21]. Regression models were adjusted for several possible confounding factors, and maintained the association between severity of obesity and worsening of cardiometabolic profile. Adolescents were also stratified in two classes of obesity rather than one, and results were compared with the normal weight group, further reinforcing the parallel of increasing cardiometabolic risk factors with severity of obesity.

Conclusion

Prevalence of obesity in adolescence has been increasing exponentially in the past few years, emerging as an alarming health problem globally. This study is the first representative study with Brazilian adolescents showing that abnormal levels in biomarkers of cardiometabolic risk, such as lipids and glucose profile, appear to increase with severity of obesity. Worsening of cardiometabolic profile accompanying BMI categories in adolescents from low- and middle- income countries indicate the need to stratify this population further and highlight the importance of public health strategies to stop progression to higher obesity classes and associated health problems.

CRediT authorship contribution statement

Mariana Sbaraini: Conceptualization, Methodology, Data curation, Writing - original draft, Writing - review & editing. **Felipe Vogt Cureau:** Conceptualization, Methodology, Formal analysis, Data curation, Writing - review & editing. **Karen Sparrenberger:** Conceptualization, Methodology, Writing - review & editing. **Gabriela Heiden Teló:** Writing - review & editing. **Maria Cristina Caetano Kuschnir:** Writing - review & editing. **Juliana Souza Oliveira:** Writing - review & editing. **Vanessa Sá Leal:** Writing - review & editing. **Katia Vergetti Bloch:** Supervision, Writing - review & editing. **Beatriz D. Schaan:** Supervision, Writing - review & editing.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2020.110758.

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