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ORIGINAL ARTICLE: OBESITY/INSULIN RESISTANCE, TYPE 2 DIABETES

Prevalence of type 2 diabetes among adolescents in Brazil: Findings from Study of Cardiovascular Risk in Adolescents (ERICA)

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Background: Type 2 diabetes mellitus (T2DM) in adolescents represents a clinical challenge related to lifestyle and obesity; however, only a few data are available in developing countries. Therefore, our aim was to investigate the prevalence of T2DM and prediabetes among Brazilian adolescents, as well as to describe the cardio-metabolic profile according to the diagnosis.

Methods: This is a cross-sectional school-based multicenter study including youth aged 12 to 17 years from cities with more than 100 000 inhabitants in Brazil (n = 37 854 students). Fasting glucose, hemoglobin A1c (HbA1c) and other cardio-metabolic risk factors were measured. Prediabetes was defined by glucose levels 100 to 125 mg/dL or HbA1c 5.7% to 6.4%. T2DM was defined by self-report, glucose ≥126 mg/dL or HbA1c ≥ 6.5%. Multinomial logistic regression was used to estimate the odds ratio (OR) of prediabetes or T2DM according to covariates.

Results: Prevalences of prediabetes and T2DM were 22.0% (95% confidence interval [CI] 20.6%-23.4%) and 3.3% (95% CI 2.9%-3.7%), respectively. This estimates represented 213 830 adolescents living with T2DM and 1.46 million adolescents with prediabetes in Brazil. Prevalences of cardio-metabolic risk factors were higher in adolescents with prediabetes and T2DM. In the multinomial logistic model, obesity (OR 1.59, 95% CI 1.20-2.11), high waist circumference (OR 1.51, 95% CI 1.13-2.01), and skipping breakfast (OR 1.48, 95% CI 1.21-1.81) were associated with an increased OR for T2DM, while studying at rural area (OR 0.56, 95% CI 0.41-0.78) was associated with a decreased OR for T2DM.

Conclusions: The prevalence of T2DM and prediabetes was high among Brazilian adolescents, which highlights that this disease became a public health challenge not only among adults in Brazil.

KEYWORDS
adolescents, Brazil, prediabetes, prevalence, type 2 diabetes mellitus

1 | INTRODUCTION

Type 2 diabetes mellitus (T2DM) prevalence has increased worldwide, especially in low and middle-income countries.[1] Global T2DM prevalence in adults rose from 4.7% to 8.5% in the past three decades,[2] reflecting the increase in obesity prevalence in most countries. T2DM prevalence varies widely among countries[2]; however, although 80% of the estimated cases of diabetes occur in less developed areas,[3] most available data come from high-income countries. Brazil, a middle-income country, has the fourth largest T2DM patient population in the world.[4] In a systematic review including more than one million people, T2DM prevalence in Brazil was found to be 11.9%, showing a progressive increase over the previous three decades.[5]

ABBREVIATIONS: BMI, body mass index; HbA1c, hemoglobin A1c; T2DM, type 2 diabetes mellitus.

Diabetes prevalence has increased over time not only in adults; in the last two decades, T2DM has become increasingly more frequent among youth worldwide, a trend that seems to be especially related to obesity.[6] The highest prevalence has been observed in the United States,[7] where T2DM represents 10% to 50% of new cases of diabetes among adolescents[8–10] and over 50% among minority groups, including Latin and Hispanic youth. In contrast, in Europe, T2DM is considered a rare disease, accounting for only 2% of new diabetes cases among youth.[11] Although it is known that the number of obese children and adolescents is increasing worldwide, only limited data are available regarding T2DM outside Europe and the United States.[12] In Brazil, a national survey recently showed that 8.4% of Brazilian adolescents were obese,[13] and over 20% of those had metabolic syndrome,[14] but prior to our study, no data were available on T2DM prevalence in this population.

The Study of Cardiovascular Risk in Adolescents (Portuguese acronym: Estudo de RIscos Cardiovasculares em Adolescentes "ERICA") was designed to estimate the prevalence of cardiovascular risk factors in adolescents aged 12 to 17 years.[15] Its aim was to evaluate the prevalence of prediabetes and T2DM in this population. We hypothesized that a high prevalence of prediabetes and T2DM would be found among obese/overweight youth, those from lower socioeconomic backgrounds and those with unhealthy lifestyle behaviors. Moreover, we expected a higher prevalence of cardiometabolic risk factors among adolescents with prediabetes and T2DM.

2 | METHODS

2.1 | Study design and sample

ERICA is a national, school-based, cross-sectional multicenter study aimed at examining the prevalence of cardiovascular risk factors including obesity, diabetes, and metabolic syndrome in a representative sample of Brazilian adolescents. Eligible participants included regular students residing in Brazilian municipalities with more than 100 000 inhabitants. Data collection took place between February 2013 and November 2014. A thorough description of the study design and sampling procedures is available elsewhere.[15,16]

2.2 | Participants

The target population of ERICA was stratified into 32 geographical strata: 26 state capitals, one federal district, and five strata representing other municipalities in each macro-region of the country. Schools were selected based on number of students and a probability inversely proportional to the distance between the non-capital municipalities and the capital of the state. We selected three classes per school with different combinations of school schedule time (morning and afternoon) and grade (seventh, eighth, and ninth grade of elementary school, and first, second, and third grade of high school). All students in the selected classes were invited to participate. For the present analyses, we used data from students aged 12 to 17 years (n = 37 854), who lived in 124 municipalities and attended one of the 925 selected schools during the morning, as an overnight fasting was mandatory. The response rate for completion of all procedures, including blood collection, was 52%. A thorough description of the response rate in the ERICA is available elsewhere.[17]

All adolescents who agreed in participate in the study provided a written informed assent, and an informed consent signed by the parent or legal guardian. ERICA was approved by the Institutional Review Boards of all 27 federation units in Brazil.

2.3 | Data Collection

Trained researchers performed all the measurements according to written standardized procedures.[15] Height was measured using a portable stadiometer without shoes; body weight was measured using a digital scale in light clothing. These measures were used for calculating body mass index [BMI = weight (kg)/height (m^2)]. Nutritional status was determined by age-sex-specific BMI, according to the World Health Organization reference curves. [18] The categories were defined as follows: underweight if BMI z-score < −1; normal weight if BMI z-score ≥ −1 and ≤ 1; overweight if BMI z-score > 1 and ≤ 2; and obesity if BMI z-score > 2. Waist circumference was measured as a marker of central adiposity using an anthropometric tape. The measurement was taken at midway between iliac crest and lower costal margin. Abdominal obesity was defined according to the cutoff points recommended by the International Diabetes Federation based on the metabolic syndrome criterion for this age group (younger than 16 years old: ≥ 90th sex and age-specific percentile; older than or equal to 16 years old: ≥ 90 cm for boys and ≥ 80 cm for girls).[19]

Systolic and diastolic blood pressures were measured using an automatic oscillometric device (Omron 705-IT- Omron Healthcare, Bannockburn, IL), previously validated for use in youth.[20] Three consecutive measures were taken from each student's right arm after 5 minutes sitting in a quiet position, using an individually determined cuff size and, with an interval of at least 3 minutes between each measure. The second and third blood pressure readings were averaged and used in analyses. High blood pressure was defined as values of systolic or diastolic blood pressure ≥ 95th percentile for sex, age, and height.[21]

Before blood collection, participants were asked to keep an overnight fast of 12 hours. The following analytes were measured: glucose (hexoquinase method), insulin (chemiluminescence), hemoglobin A1c [(HbA1c) ion exchange chromatography], total cholesterol (enzymatic kinetics), high-density lipoproteins (HDL)-cholesterol (enzymatic colorimetric assay), and triglycerides (enzymatic kinetics). The high-density lipoproteins (LDL)-cholesterol was estimated indirectly by the Friedewald equation.[22] Lipid and insulin abnormalities were defined following Brazilian guidelines as previously reported: total cholesterol ≥150 mg/dL; HDL-cholesterol ≤45 mg/dL; LDL-cholesterol ≥100 mg/dL; triglycerides ≥100 mg/dL; and insulin ≥15 mU/L.[15] All blood samples were analyzed in a single laboratory following a standardized protocol.[23]

2.4 | Study-outcome definitions

Self-reported diagnosis of diabetes was assessed by a standard questionnaire that was self-administered by students and supervised by trained staff using a personal digital assistant (LG GM750Q).

Participants who reported insulin use were classified as having type 1 diabetes mellitus (n = 33) and were excluded from further analyses in this study. Type 1 diabetes autoantibodies were not evaluated in this study.

The American Diabetes Association diagnostic criteria for prediabetes and diabetes were used in this study.[24] Prediabetes was defined by fasting glucose levels between 100 and 125 mg/dL (5.6-6.9 mmol/L) or HbA1c between 5.7% and 6.4% (39-47 mmol/mol). T2DM was defined by self-report (previous T2DM diagnosis reported and one or more positive responses for two questions regarding receiving any diabetes treatment recommendation and taking diabetes medication), fasting glucose ≥126 mg/dL (7.0 mmol/L), or HbA1c ≥6.5% (48 mmol/mol). The lab results in adolescents without self-reported diabetes were used to define previously undiagnosed T2DM.

2.5 | Covariates

Covariates were macro-regions (North, Northeast, Midwest, Southeast, and South), sex, age (categorized as 12-13, 14-15, and 16-17 years), self-reported skin color [white, black, mixed (brown), yellow, native, and not reported)], type of school (public or private) and school area (urban or rural).

Skipping breakfast (never/sometimes) was considered an indicator of unhealthy eating habits. Time spent in moderate-to-vigorous physical activity was assessed using an adapted version of the Self-Administered Physical Activity Checklist,[26] cross-culturally adapted and validated also in Brazilian adolescents.[27] To determine the weekly amount of time spent in physical activity, we multiplied self-reported duration and frequency for each activity listed and then dichotomized in <60 or ≥ 60 minutes/day.[28]

2.6 | Data analysis

ERICA was designed to provide representative estimates of the prevalence of major cardiovascular risk factors, including diabetes in Brazilian school-aged adolescents (12-17 years). All analyses were weighted to represent the total population of adolescents regularly attending schools in Brazilian municipalities with more than 100 000 inhabitants based on the 2011 National Educational Census.[16]

Prediabetes and T2DM prevalences, mean values and 95% confidence intervals (CIs) for behavioral and cardio-metabolic risk factors were estimated for the overall population and according to demographic and other covariates. Analyses were also conducted to describe the mean values of fasting glucose and HbA1c in those subgroups.

A multinomial logistic regression was used to examine the association of sociodemografic, lifestyle, and cardio-metabolic risk factors with the odds of a polytomic outcome: healthy (reference), prediabetes, and T2DM. Variables that resulted in a change of more than 10% in the multivariate model vis-à-vis the crude estimate were kept in the model. All tests were two-tailed and the analyses used Stata version 14 taking the study design (complex sample) into account. We followed the STROBE statement to prepare this report.[29]

3 | RESULTS

Overall, 37 854 ERICA participants were included in the analysis. Overall, the mean age was 14.6 (SD 1.6) years; 60.0% were female, 48.0% reported brown skin color, 77.8% were students from public schools, of which 95.6% were located in urban areas.

The overall prevalence of T2DM and prediabetes were 3.3% (95% CI 2.9-3.7) and 22.0% (95% CI 20.6-23.4), respectively. Considering the estimated population of school adolescents (12-17 years old) in Brazilian cities with more than 100 000 inhabitants, this prevalence represented 213 830 adolescents living with T2DM and 1.46 million adolescents with prediabetes in Brazil.

Adolescents with prediabetes, similarly to healthy adolescents, had lower HbA1c levels than adolescents with T2DM or other prediabetes criteria; students with altered HbA1c only, similarly to healthy adolescents, showed lower fasting glucose levels than adolescents with T2DM or other prediabetes categories (see Table 1). Adolescents with undiagnosed diabetes had higher levels of fasting glucose and HbA1c than those with previously diagnosed diabetes.

A linear trend was observed among adolescents with T2DM and prediabetes, in comparison to healthy youth, with regard to waist circumference (T2DM: 73.9 cm, prediabetes: 72.9 cm and healthy: 71.9 cm; *P* for trends <0.001), LDL-cholesterol (T2DM: 91.0 mg/dL, prediabetes: 86.9 mg/dL and healthy: 84.6 mg/dL; *P* for trends =0.001), triglycerides (T2DM: 84.5 mg/dL, prediabetes: 81.4 mg/dL, healthy: 76.9 mg/dL; p for trends <0.001), and insulin (T2DM: 10.8 mU/L, prediabetes: 10.6 mU/L, healthy: 9.1 mU/L; *P* for trends <0.001). Table 1 also shows the distribution of cardio-metabolic characteristics for prediabetes and T2DM through specific categories.

The prevalence of prediabetes was higher in males than in females, based on two criteria: altered fasting glucose only (3.5% vs 1.3%, $P < 0.001$) and altered HbA1c only (15.5% vs 20.9%, $P < 0.001$) (not shown in a table). On the other hand, no sex-related differences were observed for previously diagnosed and undiagnosed T2DM.

Overall, adolescents with prediabetes and T2DM had lower age than healthy ones. This finding, however, was observed in both males and females only for prediabetes; adolescents with T2DM were younger only in females. Also, higher BMI was observed in girls but not boys with prediabetes and T2DM (see Supporting Information Table S1).

The prevalence of T2DM was higher in adolescents who studied in urban areas in comparison to rural areas (3.3% vs 2.0%, $P < 0.001$). Moreover, skipping breakfast was shown to be associated with higher prevalence of T2DM (3.6% vs 2.7%; $P < 0.001$). Prediabetes was more frequent in boys, younger adolescents, students from public schools and urban areas, and adolescents with underweight or obesity when compared with normal weight (Table 2). Table S2 shows the distribution of mean values of fasting glucose e HbA1c according to selected covariates.

Figure 1 shows the prevalence of potential cardio-metabolic risk factors according to studied groups (healthy, prediabetes, and T2DM). Compared with healthy adolescents, those with prediabetes or T2DM have shown a higher prevalence of abdominal obesity, high blood

TABLE 1 Characteristics of study participants according to prediabetes and diabetes categories. ERICA 2013-2014

		Prediabetes categories			Type 2 diabetes categories	
	Healthy	Impaired fasting glucose	Altered HbA1c	Combined fasting glucose and HbA1c	Previously diagnosed diabetes	Previously undiagnosed diabetes
Overall, n (weighted %)	28 975 (74.8)	692 (2.4)	6615 (18.2)	339 (1.4)	1132 (3.0)	101 (0.2)
Variables	Weighted mean or %, (95% CI)					
Mean age (years)	14.7 (14.7-14.7)	14.3 (14.2-14.4)	14.4 (14.4-14.5)	14.2 (14.0-14.3)	14.5 (14.4-14.6)	14.3 (14.0-14.6)
Mean fasting plasma glucose (mg/dL)	85.1 (84.7-85.5)	103.8 (103.2-104.3)	86.9 (86.4-87.4)	103.4 (102.4-104.3)	88.3 (86.3-90.2)	123.3 (105.8-140.9)
Mean HbA1c (%)	5.3 (5.3-5.3)	5.3 (5.2-5.3)	5.8 (5.8-5.8)	5.9 (5.8-6.0)	5.4 (5.3-5.5)	6.8 (6.4-7.3)
Mean BMI (kg/m^2)	21.3 (21.2-21.5)	21.2 (20.3-22.1)	21.5 (21.2-21.8)	23.1 (21.8-24.3)	22.1 (21.6-22.6)	22.3 (20.7-23.4)
Mean waist circumference (cm)	71.9 (71.5-72.3)	73.0 (70.7-75.2)	72.6 (71.9-73.3)	76.9 (73.8-80.1)	73.9 (72.8-75.0)	74.1 (71.2-77.0)
Mean systolic BP (mm Hg)	111.2 (110.7-111.8)	112.6 (109.4-115.7)	111.6 (110.8-112.5)	116.6 (114.2-1118.9)	111.1 (109.8-112.4)	112.6 (109.2-116.0)
Mean diastolic BP (mm Hg)	66.5 (66.1-66.8)	66.5 (64.4-68.6)	66.2 (65.7-66.8)	68.6 (66.7-70.5)	66.3 (65.0-67.6)	67.1 (64.7-69.7)
Mean total cholesterol (mg/dL)	147.6 (146.5-148.7)	149.2 (145.3-153.1)	149.6 (147.9-151.3)	148.2 (141.3-155.1)	155.5 (147.8-163.1)	150.6 (139.4-162.1)
Mean HDL-cholesterol (mg/dL)	47.6 (47.0-48.2)	46.6 (44.8-48.5)	46.4 (45.5-47.3)	44.3 (41.6-47.0)	47.3 (45.9-48.7)	46.3 (43.8-48.7)
Mean LDL-cholesterol (mg/dL)	84.6 (83.7-85.5)	86.0 (82.6-89.4)	87.2 (85.8-88.5)	85.7 (80.6-90.7)	91.3 (84.2-98.3)	87.6 (78.6-96.6)
Mean triglycerides (mg/dL)	76.9 (75.4-78.4)	82.6 (77.5-87.8)	80.4 (78.0-82.9)	91.2 (80.8-101.7)	84.6 (78.9-90.2)	83.4 (70.5-96.4)
Mean insulin (mU/L)	9.1 (8.9-9.3)	14.0 (12.0-16.1)	9.8 (9.2-10.4)	14.8 (9.3-20.3)	10.5 (9.7-11.4)	13.8 (8.7-19.0)

Abbreviations: BP, blood pressure; BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoproteins; LDL, low-density lipoproteins.
Diabetes categories, fasting glucose and HbA1c levels were categorized as follows: Healthy: fasting glucose <100 mg/dL, HbA1c <5.7% and without self-reported diabetes diagnosis; Isolated impaired fasting glucose: fasting glucose 100 to125 mg/dL and HbA1c <5.7%; Isolated impaired HbA1c: fasting glucose <100 mg/dL and HbA1c 5.7% to 6.4%; Combined impaired fasting glucose and HbA1c: fasting glucose 100 to 125 mg/dL and HbA1c 5.7% to 6.4%; Previously diagnosed diabetes: self-reported diabetes diagnosis by a physician or health professional; Previously undiagnosed diabetes: fasting glucose ≥126 mg/dL or HbA1c ≥ 6.5%, but without self-reported diabetes diagnosis by a physician or health professional. There was no superposition between the selected categories of prediabetes or type 2 diabetes.

pressure, high total and LDL-cholesterol, high triglycerides and high insulin concentrations.

In the adjusted multinomial logistic models, studying in urban areas, yellow skin color, skipping breakfast, and having general or abdominal obesity increased the odds of having T2DM (Table 3). Moreover, male sex, older ages (inversely), black or mixed-brown skin colors, studying in public schools and in urban areas, underweight status, general and abdominal obesity were associated with having prediabetes.

4 | DISCUSSION

The prevalence of T2DM varies broadly around the world, but most data relate only to the United States and some European countries.[12] This study was the first school-based report in Latin America to estimate the prevalence of T2DM and prediabetes among youth. Our results indicate that T2DM has reached epidemic proportions not only in adults,[5] but also in adolescents in Brazil. Extrapolation of our results to the adolescent population in cities with more than 100 000 inhabitants resulted in 200 000 living with T2DM and almost 1.5 million with prediabetes, a condition that has been shown to increase cardiovascular risk in this population.[30] Several previous studies have reported a rapid increase in the prevalence of diabetes in Brazil, mostly in adults.[5,31] However, most of these studies were based on self-reports. Also, because the American Diabetes Association only included HbA1c as a criterion for diabetes in 2009,[32] most past studies did not consider HbA1c in their diagnostic criteria. In our study, 8.2% were classified as previously undiagnosed cases, and this number could be even higher as we did not evaluate 75-g oral glucose tolerance test, and, although equally appropriate for diagnostic testing, the tests do not necessarily detect diabetes in the same individuals.[25] Unlike type 1 diabetes, symptoms may be less marked or even absent in T2DM and, thus, this disease may go undiagnosed for several years until diabetes-related complications occur.[2] A recently published study showed that 72% of teenagers with T2DM had evidence of at least one early diabetes-related complication.[33] Failure to diagnose diabetes close to its onset burdens the health care system, as the more severe this disease is at diagnosis, the more expensive it is to treat it—a problem that is particularly important in developing countries.[34]

It is well known that the presence of T2DM and prediabetes in adolescents increases the risk of future cardiovascular disease. Importantly, other risk factors may also be present early in life associated with T2DM, such as overweight and obesity.[12] Like T2DM, excess adiposity, is a risk factor for a cluster of metabolic conditions,

TABLE 2 Prevalence of prediabetes and type 2 diabetes in Brazilian adolescents by covariates. ERICA 2013-2014

	Healthy	Prediabetes	Type 2 diabetes
Covariates	% (95% CI)	% (95% CI)	% (95% CI)
Overall	74.8 (73.2-76.2)	22.0 (20.6-23.4)	3.3 (2.9-3.7)
Sex		*P* < 0.001*	*P* = 0.091*
Female	79.0 (77.2-80.7)	17.9 (16.3-19.6)	3.0 (2.6-3.6)
Male	70.5 (68.4-72.4)	26.1 (24.2-28.1)	3.4 (2.9-4.1)
Age group (years)		*P* < 0.001**	*P* < 0.001**
12-13	70.8 (68.3-73.1)	25.3 (23.1-27.6)	4.0 (3.3-4.8)
14-15	74.4 (72.2-76.4)	22.7 (20.8-24.6)	3.0 (2.4-3.7)
16-17	78.5 (76.3-80.5)	18.6 (16.6-20.7)	3.0 (2.3-3.8)
Region		*P* = 0.225*	*P* = 0.128*
North	72.5 (70.8-74.2)	24.2 (22.6-25.9)	3.2 (2.8-3.8)
Northeast	74.2 (71.9-76.4)	22.8 (20.5-25.1)	3.1 (2.6-3.7)
Southeast	74.8 (72.2-77.2)	21.7 (19.4-24.1)	3.6 (3.0-4.3)
South	76.5 (72.7-79.9)	21.0 (17.4-25.1)	2.5 (1.9-3.4)
Midwest	75.4 (73.2-77.4)	21.9 (19.9-24.1)	2.7 (2.2-3.3)
School type		*P* < 0.001*	*P* = 0.067*
Private	78.4 (76.2-80.5)	17.6 (15.5-20.0)	4.0 (3.4-4.6)
Public	73.7 (71.9-75.4)	23.2 (21.6-25.0)	3.0 (2.6-3.6)
School area		*P* = 0.007*	*P* < 0.001*
Rural	80.6 (76.8-83.9)	17.4 (14.4-21.0)	2.0 (1.5-2.7)
Urban	74.5 (73.1-75.8)	22.2 (20.9-23.6)	3.3 (3.0-3.7)
Skin color		*P* < 0.001*	*P* = 0.319*
White	78.0 (76.2-79.7)	18.9 (17.3-20.6)	3.1 (2.5-3.7)
Black	68.6 (64.0-72.8)	28.9 (24.6-33.6)	2.6 (1.9-3.5)
Mixed (brown)	73.1 (71.0-75.2)	23.5 (21.8-25.3)	3.4 (2.7-4.1)
Yellow	72.9 (67.0-78.1)	21.8 (16.8-27.9)	5.3 (3.2-8.6)
Native	78.8 (70.0-78.3)	16.9 (11.3-24.6)	4.2 (1.9-9.0)
Not reported	73.1 (67.3-78.3)	23.6 (18.6-29.4)	3.3 (2.0-5.4)
BMI category		*P* < 0.001*	*P* = 0.007*
Underweight	67.8 (61.2-73.7)	30.3 (24.3-37.0)	1.9 (0.8-4.4)
Normal weight	76.1 (74.6-77.5)	21.0 (19.6-22.3)	3.0 (2.6-3.4)
Overweight	75.4 (72.6-77.9)	20.7 (18.0-23.6)	4.0 (2.9-5.4)
Obesity	65.2 (60.8-69.3)	30.5 (26.7-34.6)	4.3 (3.4-5.4)
Physical activity (min/day)		*P* < 0.001*	*P* = 0.250*
<60	76.3 (74.6-77.9)	20.7 (19.1-22.5)	3.2 (2.7-3.6)
≥60	72.1 (70.2-74.0)	24.4 (22.6-26.3)	3.5 (2.8-4.4)
Skip breakfast		*P* = 0.076*	*P* < 0.001*
No	76.2 (74.4-78.0)	21.1 (19.5-22.8)	2.7 (2.2-3.2)
Yes	73.6 (71.8-75.4)	22.7 (20.9-24.5)	3.6 (3.2-4.1)

Abbreviation: BMI, body mass index; CI, confidence interval
*Adjusted Wald's test for heterogeneity, **Adjusted Wald's test for trends.
Prediabetes: fasting glucose 100 to 125 mg/dL or HbA1c 5.7% to 6.4%; Type 2 diabetes: fasting glucose ≥126 mg/dL or HbA1c ≥ 6.5% or self-reported diabetes diagnosis. BMI categories: underweight BMI Z-scores < −1; normal weight BMI Z-scores ≥ −1 and ≤ 1; overweight BMI Z-scores >1 and ≤ 2; and obesity BMI Z-scores >2.

including hyperglycemia, insulin resistance, dyslipidemia, and hypertension.[35] A cluster of these risk factors has been shown to be three times more frequent in adolescents with, than in those without diabetes.[35] Our study identified a graded (dose-response) pattern of increase among adolescents with prediabetes and T2DM, when compared to healthy youth, not only for obesity, but also for insulin resistance and dyslipidemia. In agreement with our study, previous data from the SEARCH study had already indicated that dyslipidemia prevalence increased significantly with increasing HbA1c in adolescents with T2DM.[36] With regard to hypertension, our data found an association only with prediabetes. We hypothesized that lifestyle changes likely recommended to youth previously diagnosed with T2DM in our study may have decreased blood pressure levels in T2DM adolescents.

Interestingly, our results have also identified underweight to be associated with a higher prevalence of prediabetes, even after

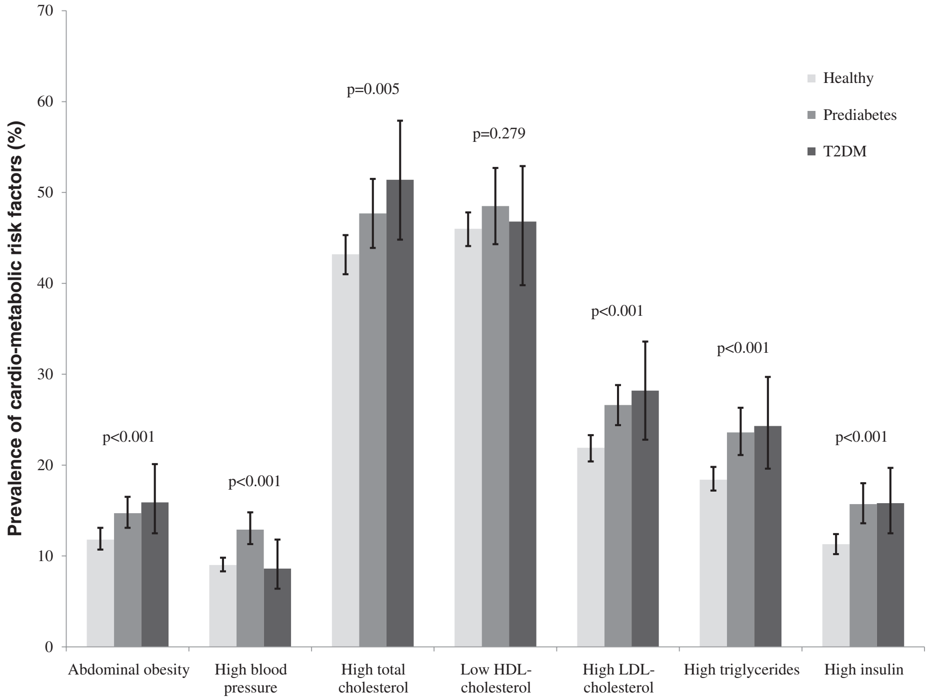

FIGURE 1 Prevalence of cardio-metabolic risk factors by groups: healthy, prediabetes, and diabetes. Healthy: fasting glucose <100 mg/dL, HbA1c <5.7% and without self-reported diabetes diagnosis; Prediabetes: fasting glucose 100 to125 mg/dL or HbA1c 5.7% to 6.4%; Type 2 diabetes: fasting glucose ≥126 mg/dL or HbA1c ≥6.5% or self-reported diabetes diagnosis. Abdominal obesity ≥90th; high total cholesterol ≥150 mg/dL; high HDL-cholesterol ≤45 mg/dL; high LDL-cholesterol ≥100 mg/dL; high triglycerides ≥100 mg/dL and high insulin ≥15 mU/L. Adjusted Wald's test for trends was used to obtain *P*-values

adjustment for sociodemographic characteristics. This finding has been observed in previous studies and it is likely explained by iron deficiency, which may increase red blood cells survival and hence glycosylation.[37] In the NHANES study, iron deficiency had a dose-response association with HbA1c independently of fasting glucose levels.[38] Iron deficiency was not evaluated in our study and, thus, this hypothesis should be evaluated in future studies.

Most studies evaluating T2DM in youth showed that 65% to 70% of T2DM adolescents were females, usually from ethnic minorities.[12] However, some studies suggested that boys have higher glycemic levels than girls.[39] In our study, male sex was found to be associated with increased odds of having prediabetes only. Also, the prevalence of both prediabetes and T2DM were higher among younger adolescents. We hypothesized that this finding may be explained by the fact that older adolescents are in their final puberty period, which is characterized by the end of transient insulin resistance.[40]

With regard to socioeconomic findings, although a very high prevalence of T2DM has been seen in non-White groups, this disease may happen in all ethnic groups.[6] Brazil has a large mixed-race population, mostly represented by brown skin color. In our study, adolescents with brown skin color presented the highest prediabetes prevalence. Previous studies have shown, as we did in our study, that skin color seems to be an important socioeconomic marker associated with diabetes.[41] Another characteristic related to socioeconomic status in our study was studying in public schools, which reflects a lower socioeconomic status[42] and which increased the odds of prediabetes. Previously published data also showed that foods available in public schools are generally unhealthy,[42] which may have contributed to the findings in our study. Also, although studying in rural areas was shown to be less associated with T2DM than urban areas, this study included very few schools in rural areas, which limited the value of this finding.

The present study has some limitations. Although ERICA was a large school-based study, it had a cross-sectional design subjected to both temporal and survival biases (although in adolescents the latter bias is less likely to occur). Also, even though the large sample size of ERICA and the careful planning and execution of this study reinforce the findings, the response rate for completion of all procedures was 52% and this may influence our results.[17] In addition, many characteristics included in this study were based on self-report, which may have resulted in information bias and misclassification. Another possible source of misclassification was that, although our protocol specified that blood collection should be done after an overnight fasting period, we could not be sure that all adolescents complied with this request. Notwithstanding these potential biases, the present study is, to the best of our knowledge, the first country-wide, population-based representative study to assess the prevalence of diabetes and prediabetes in Latin American adolescents using, as part of its criteria, measured glucose and HbA1c.

In conclusion, this school-based study assessed prediabetes and T2DM data in a national sample of adolescents in Brazil, and showed that the prevalences of both prediabetes and T2DM were very high, and mainly associated with obesity and low socioeconomic status.

TABLE 3 Multivariable adjusted odds ratios[a] for prediabetes and diabetes in Brazilian adolescents. ERICA 2013-2014

Covariates	Prediabetes $OR_{adjusted}$ (95% CI)	Type 2 diabetes $OR_{adjusted}$ (95% CI)
Sex		
Female	1	1
Male	1.63 (1.43-1.87)	1.25 (0.96-1.64)
Age group (years)		
12-13	1	1
14-15	0.80 (0.71-0.90)	0.74 (0.53-1.04)
16-17	0.62 (0.53-0.73)	0.71 (0.49-1.02)
Region		
North	1.09 (0.83-1.41)	1.25 (0.88-1.77)
Northeast	1.08 (0.82-1.43)	1.13 (0.79-1.61)
Southeast	1.04 (0.79-1.37)	1.42 (1.00-2.01)
South	1	1
Midwest	1.03 (0.79-1.35)	1.03 (0.71-1.48)
School type		
Private	1	1
Public	1.49 (1.23-1.81)	0.90 (0.70-1.14)
School area		
Rural	1	1
Urban	1.64 (1.26-2.14)	1.76 (1.27-2.43)
Skin color		
White	1	1
Black	1.64 (1.29-2.08)	0.99 (0.68-1.44)
Mixed (brown)	1.30 (1.14-1.48)	1.22 (0.88-1.68)
Yellow	1.26 (0.92-1.74)	1.88 (1.06-3.33)
Native	0.75 (0.44-1.29)	1.32 (0.57-3.06)
Not reported	1.10 (0.79-1.53)	1.06 (0.60-1.89)
Physical activity		
<60 minutes/day	1	1
≥60 minutes/day	1.06 (0.95-1.19)	1.08 (0.80-1.46)
Skip breakfast		
No	1	1
Yes	1.12 (0.99-1.28)	1.48 (1.21–1.81)
BMI category		
Underweight	1.52 (1.09-2.13)	0.72 (0.31-1.68)
Normal weight	1	1
Overweight	1.01 (0.87-1.17)	1.33 (0.92-1.91)
Obesity	1.71 (1.44-2.02)	1.66 (1.26-2.18)
Abdominal obesity		
No	1	1
Yes	1.47 (1.27-1.71)	1.51 (1.13–2.01)

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.
Prediabetes: fasting glucose 100 to 125 mg/dL or HbA1c 5.7% to 6.4%; Type 2 diabetes: fasting glucose ≥126 mg/dL or HbA1c ≥ 6.5% or self-reported diabetes diagnosis. BMI categories: underweight BMI Z-scores < −1; normal weight BMI Z-scores ≥ −1 and ≤ 1; overweight BMI Z-scores >1 and ≤ 2; and obesity BMI Z-scores >2.
[a] Multinomial logistic regression was used to adjust the odds ratios for the following variables: sex, age, skin color and BMI. Odds ratios for waist circumference were not adjusted for BMI.

Our findings highlight T2DM as an important public health challenge not only among adults in Brazil, but also in adolescents. Considering the modifiable nature of T2DM cardio-metabolic risk factors, strategies aimed at prevention must be considered by public health authorities in Brazil.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

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