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Apolipoprotein B-100/Apolipoprotein A-I Ratio in Overweight Brazilian Adolescents with or without Metabolic Syndrome

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Abstract

Background: Metabolic syndrome is defined as the presence of at least three cardiometabolic risk factors: abdominal obesity, hyperglycaemia or diabetes mellitus, dyslipidaemia, and hypertension, all of which are associated with insulin resistance.

Objectives: To investigate the association between the ratio of APOB-100/APOA-I and metabolic syndrome in Brazilian overweight adolescents.

Methods: A cross-sectional study of 2866 students aged 10-19 years, of both sexes, was conducted in 2011. They were randomly selected from public and private schools in Vitória de Santo Antão, Pernambuco. Metabolic syndrome was defined according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP-III) and the International Diabetes Federation (IDF).

Results: The prevalence of metabolic syndrome was 14.5% (95% CI: 10.4–19.5) and 18.5% (95% CI: 14–29) according to the IDF and NCEP-ATP III criteria, respectively. The median APOB-100/APOA-I ratio was significantly higher ($p < 0.005$) among adolescents with hypertriglyceridaemia, low HDL-c, hyperglycaemia, abdominal obesity, hypertension, insulin resistance, and components of metabolic syndrome. The Poisson regression analysis showed that, as independent predictors, a high APOB-100/APOA-I ratio, low HDL-c ($PR = 1.77$, 95% CI 1.2–2.6), and elevated serum LDL-c level ($PR = 3.3$, 95% CI 2.4–4.5) were present.

Conclusion: The ratio of APOB-100/APOA-I showed a significant association with components of metabolic syndrome in Brazilian adolescents. Given the importance of the apolipoprotein B-100/A-I ratio as a marker of cardiometabolic risk, it should be included in routine clinical practice.

Keywords: *Adolescents, APOA-I, APOB-100, Cardiometabolic risk, Hypertriglyceridaemia, Insulin resistance.*

Introduction

Obesity is a chronic non-communicable disease with roots in childhood, frequently accompanied over the years by substantial comorbidities such as hypertension, glucose intolerance, dyslipidemia, and metabolic syndrome (MetS).¹ The prevalence of MetS has increased significantly among adolescents in recent

decades, and Brazil has few national studies on the prevalence of MetS in adolescents, with ERICA being the main epidemiological support base on MetS in adolescents currently.²

MetS is defined as the presence of at least three cardiometabolic risk factors: abdominal obesity, hyperglycaemia or diabetes mellitus,

dyslipidaemia, and hypertension, all of which are associated with insulin resistance.³ In Brazil, the diagnostic criteria for MetS were established in the First Brazilian Guideline for the Diagnosis and Treatment of Metabolic Syndrome in 2005, in accordance with the National Cholesterol Education Program (NCEP-ATP-III) of 2001, endorsed by the American Heart Association and redefined by the International Diabetes Federation thereafter, in 2007.⁴⁻⁷ The combination of cardiovascular risk biomarkers, such as elevated triglycerides (TG), reduced HDL-c, and increased apolipoprotein B (APOB) and LDL-c, is frequent in individuals with MetS and Type 2 diabetes mellitus (DM2). These biomarkers are present from childhood, with apolipoproteins A-I and B-100 being particularly noteworthy.⁴

Recent epidemiological evidence, especially in adults, suggests that the APOB-100/APOA-I ratio reflects the balance between the transport of atherogenic and atheroprotective cholesterol, and constitutes a better independent predictor of cardiovascular risk than APOA-I, B-100 concentrations, or cholesterol indices in isolation.⁸⁻¹⁰ The APOB-100/APOA-I ratio values of relevance are ≥ 0.9 for men and ≥ 0.8 for women.⁷⁻¹⁰ However, the relationship between this ratio and MetS still requires more robust epidemiological investigations, especially in pediatric populations in Latin America. This study aimed to investigate the association between the APOB-100/APOA-I ratio and MetS and its components in overweight adolescents in a population-based probability sample.

Methods

Study design and sample

This is a population-based, cross-sectional study of adolescents aged 10 to 19 years, of both sexes, enrolled in public and private schools in the city of Vitória de Santo Antão, Pernambuco, Northeast Brazil. The Northeast region of Brazil

has the lowest Human Development Index (HDI) in the country, with the concentration of major social problems in Brazil.

Ethical considerations

This study was conducted in accordance with Resolution 466/12 of the National Health Council and the Declaration of Helsinki, approved by the Ethics Committee for Research with Human Beings of the Federal University of Pernambuco, with approval number 262/2009.

Study population

All adolescents present in school at the time of data collection were included in the study. Those with mental health problems (reported by parents or teachers), physical disabilities that prevented anthropometric measurements, clinical pathologies, pregnancy (self-reported), or use of medications such as antihypertensives, corticosteroids, steroids, isotretinoin, and protease inhibitors were excluded. The study followed the STROBE Guidelines for observational studies.¹¹

Selection and description of participants

To estimate the sample size, the SampleXS program was used, employing the formula: $n = A / (E * E + (A / N))$, where n = corresponds to the sample size; $A = 3.8416PQW$, P = population prevalence in percentage; $Q = (100 - P)$; E = maximum acceptable sampling error; W = probable design effect; N = population size.¹² The sample size calculation was based on the estimated MetS prevalence of 3.0%.¹³ The reference population consisted of 21,515 enrolled adolescents, adopting a 95% confidence level, a sampling error of 1%, and a design effect of 2.5. The minimum sample size was 2,473 students. To make up for any losses or refusals identified in the pilot study, this value was increased by 15%, resulting in a final sample of 2,844 students. For the MetS diagnosis, the final sample comprised 248 students.

Sample selection was carried out by surveying all public (n = 31) and private (n = 8) schools offering education from the sixth grade of elementary school and/or high school onwards. The schools were organised by grade level into urban public, rural public, and private schools. They were randomly selected using a table of random numbers generated in the randomiser program [Social Psychology Network Association, Middletown, CT, USA]. The grade levels were defined as the study cluster, and a maximum of 40 students per classroom were considered.

Socioeconomic-demographic assessment

Data were collected by health professionals linked to the project and a public higher education institution. The coordinators trained the team to ensure inter- and intra-rater reproducibility, with only those with a Kappa index above 0.85 considered eligible. Project supervisors monitored data collection.

Personal, socioeconomic, and anthropometric information were obtained from schools through a questionnaire on socioeconomic, demographic, and lifestyle variables. The population was classified into social classes from A to E.¹⁴ The criterion of sexual maturation using Tanner's self-definition method was not adopted due to difficulties in analysing the criteria in the students, observed in the pilot study.

The practice of moderate to vigorous physical activity was analysed using the International Physical Activity Questionnaire (IPAQ), categorising adolescents as "insufficiently active" (≤ 60 min/day, ≥ 5 days/week) or "physically active".¹⁵

Anthropometric assessment

Weight and height were measured using a Balmak® Scale (100g precision) and an attached stadiometer (1 mm precision), calibrated by the

Brazilian measurement control body (Brazilian National Institute of Metrology, Standardisation and Industrial Quality). Adolescents were barefoot, without objects or adornments, standing upright, with the heels together, and looking forward.

We calculated body mass index (BMI) as weight (kg)/height (m)² and classified it according to the percentiles of the National Centre for Health Statistics: underweight (<P5), normal weight (P5-P85), overweight (P85-P95), and obesity ($\geq$ P95). Excess weight included overweight and obesity.

¹⁶

Waist circumference (WC) and neck circumference (NC) were measured in duplicate using a Sanny® measuring tape. NC was measured below the cricoid cartilage, with cutoff points from Hingorjo *et al.* (2012) (>35.5 cm for men, >32 cm for women). Waist circumference (WC) was measured between the last rib and the iliac crest, following the recommendation of the International Diabetes Federation⁷ (≥ 90 cm for abdominal obesity). The waist-to-height ratio (WHR) was calculated as WC/height, with abdominal obesity defined as WHR ≥ 0.5 .¹⁷⁻²¹

Clinical assessment

Blood pressure was measured using the auscultatory method as described in the literature, with a Unitec® mercury sphygmomanometer (300 mmHg, 2-mmHg range).^{22, 23} Systolic (SBP) and diastolic (DBP) pressures were identified by the Korotkoff sound phases 1 and 5, respectively. Measurements were taken after 10 to 15 minutes of rest, with the individual seated, back supported, feet on the floor, and arm at heart level. Three readings were taken at 10-minute intervals, and the average was adopted. If the variation between measurements exceeded 5 mmHg, the protocol was repeated and a new average taken. Blood pressure values were classified as hypertensive (Stages I to III) or normotensive (normal and borderline).

Biochemical evaluation

The blood samples were collected after a 10-12-hour fast by vacuum venipuncture using sterile, disposable materials in accordance with biosafety standards. The blood sample was stored in dry tubes with anticoagulant (EDTA, 1 mg/mL), kept in thermal boxes, and transported to the Multifunctional Laboratories of Federal University of Pernambuco and LAPAC®. Serum and plasma were separated at 3000 rpm at 4 °C for up to 2 hours after collection, with glucose and lipids (TC, TG, HDL-c, LDL-c) measured in duplicate. The remainder was stored at -20°C and analysed after 48 hours for insulin and apolipoproteins A-I and B-100. Lipid concentrations were determined by spectrophotometry (BioRad SmartSpec 3000, CA, USA) via enzymatic methods (Labtest, MG, BR). LDL-c and VLDL-c were calculated using the Friedewald equation or determined directly when TG > 400 mg/dL.²⁴

Apolipoproteins and insulin were analysed by immunoturbidimetry and chemiluminescence. Insulin resistance was calculated using HOMA-IR: $\text{HOMA-IR} = (\text{fasting insulin [mU/mL]} \times \text{fasting glucose [mmol/L]}) / 22.5$, considering HOMA-IR > 2 as insulin resistance.^{25,26}

The dyslipidemia criteria followed the First Brazilian Guideline for the Prevention of Atherosclerosis in Childhood and Adolescence (I DPAIA).²⁷ The established cutoff points were: Total cholesterol (TC) ≥ 170 mg/dL (elevated); LDL-c ≥ 130 mg/dL (elevated); HDL-c < 45 mg/dL (undesirable); Triglycerides (TG) ≥ 130 mg/dL (elevated). For the diagnosis of dyslipidaemias, elevated or altered values were adopted. The cutoff points used in the verification for hyperglycaemia (glucose ≥ 100 mg/dL) were defined by the IDF (2007), and for cardiovascular risk, the APOB-100/APOA-I ratio was considered ≥ 0.9 for men and ≥ 0.8 for women.^{7,28}

Definition of metabolic syndrome

The NCEP/ATP-III (2001) proposed the diagnosis of MetS in adolescents using the presence of three or more of the following components: systolic and/or diastolic blood pressure ≥ 90 th percentile for age, sex, and height percentile; triglycerides ≥ 130 mg/dL; HDL-c < 45 mg/dL; fasting glucose ≥ 100 mg/dL; and abdominal obesity defined by waist circumference ≥ 90 th percentile for age and sex.^{5,7,9} MetS was also determined using the IDF criterion,⁷ which considers abdominal obesity a "sine qua non" condition for its diagnosis; when this is present, two additional factors from the NCEP/ATP-III criteria are sufficient for diagnosis.

Data analysis

The tabulation was performed using EpiData 3.1 [EpiData Association, Odense, DK]. Validation was used to detect errors. The data were analysed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) statistical software and STATA/SE version 9.0 (StataCorp, College Station, TX, USA). In describing the proportions, the binomial distribution was approximated to the normal distribution using the 95% confidence interval (CI). The Mantel-Haenszel test and Pearson's Chi-Square test, or a linear trend test, were used to compare the proportions. Continuous variables were tested for normality using the Kolmogorov-Smirnov test. The means of normally distributed variables were compared using the Student's t-test for unpaired data, and the Mann-Whitney U test was used for variables that did not meet the normality criteria. For interpretation purposes, the limit for type I error was up to 5% ($p \leq 0.05$). Multivariate analysis was used to estimate the independent contribution of each variable to the odds of having a high APOB-100/APOA-I ratio. To construct the model, all variables that showed an association ($p < 0.2$) with a high APOB-100/APOA-I ratio in the bivariate analysis were tested. For this purpose, Poisson regression (PR)

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for clusters was used, with the Wald test, in Stata/SE version 9.0.

Results

The prevalence of MetS among overweight adolescents was 14.5% (95% CI: 10.4-19.5) and 18.5% (95% CI: 14-29) according to the IDF and NCEP/ATP-III criteria, respectively. There was homogeneity in the distribution of MetS across age groups. Male adolescents had a higher prevalence of MetS when defined using the NCEP/ATP-III criteria. The APOB-100/APOA-I ratio was elevated in 35.5% (95% CI: 29.5-41.8) of overweight adolescents. The mean APOB-100/APOA-I ratios differed by age (Table I).

Clinical, biochemical, and anthropometric characteristics of the study participants are shown

in Table II. No significant associations were observed between clinical and anthropometric variables and the APOB-100/APOA-I ratio. However, significant differences in the progression of quartiles of the APOB-100/APOA-I ratio were identified for all biochemical parameters except glucose, HOMA index, and APOA-I.

In turn, the median APOB-100/APOA-I ratios were significantly higher among adolescents who presented with the components of MetS (Table III).

The multivariate Poisson regression analysis identified low HDL-c concentrations (<45 mg/dL) and high serum LDL-c levels (≥ 130 mg/dL) as independent risk factors for a high APOB-100/APOA-I ratio (Table IV).

Table Ia: Mean values of the APOB-100/APOA-I ratio according to the socioeconomic-demographic and behavioural characteristics of overweight adolescents

Socioeconomic-demographic and behavioural characteristics	APOB/APOA-I Ratio		
	n	mean $\pm$ DP	p-value [†]
Gender			0.24
Male	102	0.74 $\pm$ 0.22	
Female	146	0.77 $\pm$ 0.23	
Age (years)			0.049
10-14	169	0.78 $\pm$ 0.23	
15-19	79	0.72 $\pm$ 0.22	
Home address			0.417
Urban	220	0.76 $\pm$ 0.23	
Country	28	0.80 $\pm$ 0.23	
Work			0.325
Yes	19	0.71 $\pm$ 0.22	
No	229	0.77 $\pm$ 0.23	
Live with family			0.511
Yes	181	0.77 $\pm$ 0.24	
No	67	0.75 $\pm$ 0.21	
Maternal education (years) ^a			0.705
> 9	69	0.75 $\pm$ 0.23	
≤ 9	129	0.74 $\pm$ 0.21	

Results are expressed as means $\pm$ standard deviation. ^aANOVA test. [†]Independent Student's t-test. ^a50 students did not respond or did not know. ^bEight students did not respond or did not know. ^c24 students did not respond or did not know. ^done student did not respond or did not know. ^e21 students did not respond or did not know.

Table Ib: Mean values of the APOB-100/APOA-I ratio according to the socioeconomic-demographic and behavioural characteristics of overweight adolescents

Socioeconomic-demographic and behavioural characteristics	APOB/APOA-I		
	N	mean±DP	p-value [†]
Father's education level (years) ^a			0.995
> 9	53	0.76±0.24	
≤ 9	145	0.76±0.22	
Economic classes ^b			0.784*
A/B	57	0.75±0.24	
C	127	0.77±0.22	
D/E	56	0.74±0.25	
Consider obese parents or siblings			0.962
Yes	135	0.75±0.21	
No	89	0.75±0.25	
Habitual alcohol consumption			0.166
Yes	3	0.58±0.25	
No	244	0.76±0.23	
Physical activity			0.082
Insufficiently active	189	0.75±0.22	
Physically active	59	0.81±0.24	
Daily frequency of television viewing on weekdays (hours/day) ^c			0.683
≥ 3	164	0.76±0.23	
< 3	63	0.77±0.23	
Daily frequency of television viewing on weekends (hours/day)			0.922
≥ 3	110	0.76±0.22	
< 3	138	0.76±0.23	

Results are expressed as means ± standard deviation. *ANOVA test. [†]Independent Student's t-test. ^a50 students did not respond or did not know. ^bEight students did not respond or did not know. ^c24 students did not respond or did not know. ^done student did not respond or did not know. ^e21 students did not respond or did not know.

Discussion

This study, involving a representative sample of school-aged adolescents in a municipality in Northeast Brazil, an area with high water scarcity and a low human development index, showed a significant association between the APOB-100/APOA-I ratio and the lipid profile and components of MetS. Important studies, such as those by Zhang and Balling, have shown that the APOB-100/APOA-I ratio is not only the most potent explanatory factor for the risk of acute myocardial infarction, but is also the most prevalent risk factor among conventional risk factors, independent of sex, age, race, and other lipid parameters.^{25,26} In turn, several reports have

emphasised the association between the APOB-100/APOA-I ratio and MetS.^{27,28}

Recent studies have shown that the APOB-100/APOA-I ratio is associated with MetS and its components.²⁸ The findings were consistent with other studies; patients with an increased number of factors constituting MetS had a parallel increase in the APOB-100/APOA-I ratio, regardless of which criteria were used to define MetS.²⁹ Wallenfeldt *et al.* described a relationship between the APOB-100/APOA-I ratio and MetS.³⁰ They studied 313 Caucasian men with a mean age of 58 years, with varying degrees of obesity and insulin sensitivity. The study reported a close association between the

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APOB-100/APOA-I ratio and the factors that constitute MetS. However, the study was conducted in a different population, did not

include women, and used only the WHO definition of MetS.

Table II. Clinical characteristics according to quartiles of the APO B-100/APOA-I ratio in overweight adolescents. Vitória de Santo Antão, Pernambuco, Brazil

Clinical Characteristics	Quartiles				Differences between groups	p-value [†]
	I (n=61)	II (n=60)	III (n=62)	IV (n=65)		
Age (years)	14 (12-15)	13 (12-15)	13 (12-14)	13 (11-15)	-	0.243
Body Mass Index (Kg/m ²)	25.6 (23.4-27.8)	25 (23.7-27.6)	25.7 (23.7-27.5)	25.9 (23.8-29.4)	-	0.518
Waist Circumference (cm)	81 (73.8-89)	81.1 (75-86)	79.7 (74-86.2)	82.6 (77-88.6)	-	0.481
Waist-to-Height Ratio	0.51 (47-54)	0.50 (47-54)	0.50 (48-53)	0.51 (0.48-0.56)	-	0.301
Neck Circumference (cm)	34.1 (32.1-35.7)	34 (32-36.2)	33.9 (32.2-36)	34.6 (32.4-37.1)	-	0.284
Systolic Blood Pressure (mmHg)	114.6 (106.6-119.3)	116.6 (107.3-124.6)	113.3 (104.6-121.6)	114 (106.1-122.6)	-	0.532
Diastolic Blood Pressure (mmHg)	68.3 (60-78.6)	74 (67-82)	72.6 (64.3-78)	72 (67-80.6)	-	0.159
Glucose (mg/dl)	83 (76-89)	84 (76.2-92)	82 (75.6-88.5)	83 (78-90.5)	-	0.455
CT (mg/dL)*	158±1.2	166.63±1.23	171.25±1.19	206.9±1.21	I≠IV, II≠IV, III≠IV	<0.001**
HDL – Cholesterol (mg/dL)	43.94±1.23	41.23±1.29	39.63±1.21	38.98±1.21	I≠IV	<0.050**
LDL – Cholesterol (mg/dL)	92.82±25.10	100.74±25.76	106.74±30.3	110.41±33.54	I≠IV, II≠IV, III≠IV	<0.001**
VLDL – Cholesterol (mg/dL)	102 (80-139)	114 (87-160)	109 (80.5-161.5)	134 (99-205)	I≠IV, II≠IV, III≠IV	<0.050
TG (mg/dL)	97 (75-134)	109 (82-155.5)	104 (75.5-156.5)	129 (94-200)	I≠IV, II≠IV, III≠IV	<0.050
Ratio CT/HDL-c (mg/dL)*	3.58±1.23	4.04±1.26	4.31±1.24	5.3±1.24	I≠II, I≠III, I≠IV, II≠IV, III≠IV	<0.001**
Ratio LDL-c/HDL-c (mg/dL)*	2.03±1.34	2.34±1.35	2.56±1.4	3.47±1.3	I≠III, I≠IV, II≠IV, III≠IV	<0.001**
Ratio TG/HDL-c (mg/dL)*	2.32±1.74	2.82±1.85	2.87±1.83	3.60±1.7	I≠IV	0.001**
HOMA Index *	2.78±2.25	2.43±2.26	2.51±1.92	2.92±1.88	-	0.627**
APO A-I (mg/dL)	109 (84-143)	101 (72.2-136.2)	117.8 (77-144.5)	93 (71-134.5)	-	0.100
APO B-100 (mg/dL)*	51.83±1.47	66.32±1.53	83.48±1.50	99.45±1.52	I≠II, I≠III, I≠IV, II≠III, II≠IV	<0.001**

Results expressed as medians and interquartile ranges. *Results expressed as mean ± standard deviation. †Kruskal-Wallis test. **ANOVA test. WC: neck circumference; TC: total cholesterol; HDL-c: high-density lipoprotein; LDL-c: low-density lipoprotein; VLDL: very low-density lipoprotein; TG: triglyceride; HOMA: Homeostasis Model Assessment - Insulin Resistance; APOA: Apolipoprotein A-I; APOB: Apolipoprotein B-100.

Previous studies have already demonstrated the association between different apolipoproteins and cardiovascular risk factors for more than two decades. In a sample of 1,522 men and women aged 40 to 69 years in three ethnic groups, with insulin resistance and atherosclerosis, Sattar *et al.* compared the associations of APOB and non-HDL-c lipids with other cardiovascular risk factors in individuals with MetS. Individuals with higher APOB-100 levels had a significantly higher proportion of MetS components than

patients with higher LDL-c and normal APOB-100 levels.³¹

Apolipoproteins regulate and stabilise the structure, synthesis, and metabolism of lipoprotein particles. The total APOB value indicates the amount of potentially atherogenic lipoproteins. APOA-I is important in removing excess cholesterol from tissues and incorporating it into HDL-c via reverse transport to the liver. The APOB-100/APOA-I ratio thus reflects the

balance of cholesterol transport, with higher values indicating a greater propensity for cholesterol deposition and, consequently, a greater risk of atherogenesis.^{8, 32, 33} The evidence in this case series supports the paradigm that abnormalities in lipoproteins, as part of the set of

metabolic risk factors, and their association with insulin resistance, hyperglycaemia, low HDL-c concentrations, hypertriglyceridaemia, abdominal obesity, and hypertension can provide important insights into the complexity of MetS.

Table III: Medians and quartile ranges of the APOB-100/APOA-I ratio according to the components of Metabolic Syndrome in overweight adolescents

Components of Metabolic Syndrome	APOB/APOA-I Med (IQR)		p-value*
	High	Normal	
Triglyceride ≥ 130 mg/dL	1.01 (0.91-1.10)	0.66 (0.57-0.75)	<0.001
HDL-c <45mg/dL	1.01 (0.88-1.10)	0.64 (0.55-0.73)	<0.001
Glucose ≥ 100 mg/dL	1 (0.92-1.1)	0.64 (0.46-0.67)	0.001
Abdominal circumference $\geq P_{90}$ (cm)	1.05 (0.93-1.14)	0.65 (0.57-0.74)	<0.001
Blood Pressure $\geq P_{95}$ (mmHg)	0.93 (0.9-1.03)	0.66 (0.60-0.75)	<0.001
Diagnostic criteria			
NCEP/ATP III (≥ 3 components)	1.06 (0.93-1.117)	0.65 (0.60-0.74)	<0.001
IDF (abdominal obesity + 2 components)	1.03 (0.91-1.12)	0.66 (0.61-0.75)	<0.001
Insulin resistance (HOMA-IR >2)	0.98 (0.88-1.1)	0.64 (0.54-0.74)	<0.001

Results are expressed as medians (Med) and interquartile ranges (IQR). *Mann-Whitney U test. HOMA: Homeostasis Model Assessment - Insulin Resistance. HDL-c: high-density lipoprotein. NCEP/ATP-III: National Cholesterol Education Program. IDF: International Diabetes Federation. APOA: Apolipoprotein A-I; APOB: Apolipoprotein B-100.

Table IV: Independent predictors of high APOB-100/APOA-I ratio in overweight adolescents, according to Poisson regression

Risk factors	Final Model			
	n	Adjusted PR [†]	IC _{95%}	p-value*
	237			
HDL-c				<0.001
Low < 45 mg/dL		1.77	[1.2-2.6]	
LDL-c				<0.001
High ≥ 130 mg/dl		3.28	[2.4-4.5]	

PR: Prevalence rate; CI: 95% confidence interval. *Wald test for heterogeneity of proportions. †Model adjusted for the variables: sex; age; neck circumference; waist-to-height ratio; blood pressure; physical activity; socioeconomic class; glucose; triglyceride; metabolic syndrome. HDL-c: high-density lipoprotein. LDL-c: low-density lipoprotein.

There are still controversies about which definition best characterises MetS and the contribution this set of components makes to cardiovascular risk prediction. The basis for constructing a concept encompassing a set of risk factors is that insulin resistance is the primary pathophysiological disorder, accompanied by atherogenic dyslipidaemia, hypertension,

hyperglycaemia, and a prothrombotic and proinflammatory state, which can ultimately increase cardiovascular risk. In the present model, we included insulin resistance as a diagnostic criterion for MetS. However, aside from the WHO recommendation, current definitions of MetS do not include this parameter.

This study of an adolescent population deserves to be highlighted, considering that it is one of the first in adolescent groups outside of metropolitan areas and large cities, in addition to the reduced number of investigations addressing this relationship in Brazil, and the importance of early diagnosis for the prevention and control of cardiometabolic risks with age progression. The identification of low HDL-c concentrations and high LDL-c levels as independent predictors of a high APOB-100/APOA-I ratio, as demonstrated by the adjusted Poisson regression, has practical implications for the use of these two biomarkers in clinical research, particularly given the high costs of apolipoprotein analyses. It is generally agreed that MetS alone cannot predict the overall risk for cardiovascular disease. There is a need to include other metabolic risk markers. Therefore, the APOB-100/APOA-I ratio should be considered when including cardiovascular risk diagnosis as an important risk factor linked to the set of metabolic risk markers.

Limitations

The study has limitations that should be taken into account when interpreting the results. It is a cross-sectional study in which cause-and-effect relationships between the APOB-100/APOA-I ratio and MetS cannot be determined. In addition, all adolescents investigated for MetS were overweight, and the refusal rate for blood sampling was high, which may have affected the sample's randomness. Another limitation of the study is the potentially high correlation between APOA-I and HDL-c, which has already been well defined in other studies.²⁸ Such a correlation was expected, given that HDL-c is included in the APOA-I measurement. However, in this study, the Pearson correlation between HDL-c and APOA-I was $r = 0.15$, ruling out potential collinearity in the multivariate analysis.

Conclusion

The APOB-100/APOA-I ratio showed a significant association with MetS components in Brazilian adolescents. Low HDL-c concentrations and high serum LDL-c levels were identified as independent predictors of an elevated APOB-100/APOA-I ratio. Given the importance of the apolipoprotein B-100/A-I ratio as a marker of cardiometabolic risk, it should be incorporated into biomedical models for preventive clinical practice.

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