

Assessment of blood biomarkers in adolescents classified by body mass index and body fat percentage

Avaliação do perfil de biomarcadores sanguíneos em adolescentes classificados pelo índice de massa corporal e percentual de gordura corporal

Evaluación del perfil de biomarcadores sanguíneos en adolescentes clasificados por el índice de masa corporal y porcentaje de grasa corporal

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Abstract

The study aimed to compare biomarkers in groups of adolescents classified simultaneously according to body mass index (BMI) and body fat percentage measured by air displacement plethysmography. This was a cross-sectional study with 533 adolescents 18 to 19 years of age in São Luís, Maranhão, Brazil. BMI was classified as adequate ($< 25\text{kg/m}^2$) versus excess weight ($\geq 25\text{kg/m}^2$). High body fat percentage was defined as $\geq 25\%$ for males and $\geq 30\%$ for females. The adolescents were classified in four groups: "normal weight" (adequate BMI and body fat percentage), "normal weight obese" (adequate BMI with high body fat percentage), "excess weight with adequate body fat percentage", and "excess weight with high body fat percentage". Girls showed higher proportions of "normal weight obesity" (15.6%) and "excess weight with high body fat percentage" (17.1%). "Normal weight obese" adolescents exhibited higher mean values for total cholesterol (172.5mg/dL) and LDL-cholesterol (103.5mg/dL). Those with "excess weight and high body fat percentage" showed lower mean HDL-cholesterol (43.2mg/dL) compared to the other groups, higher mean interleukin-6 (2.7pg/mL) than "normal weight" and "excess weight and adequate body fat percentage" adolescents, and higher median triglycerides (114.0mg/dL) and C-reactive protein (0.14ng/mL) than "normal weight" and "normal weight obese" adolescents. Those with "excess weight and adequate body fat percentage" exhibited the same C-reactive protein levels as those with "excess weight and high body fat percentage". Assessment of nutritional status by BMI alone is limited, since 6.8% of the adolescents presented high body fat percentage despite normal BMI, and those who were "normal weight obese" had two biomarkers that were worse than for adolescents with "excess weight and high body fat percentage".

Body Mass Index; Adiposity; Biomarkers; Interleukin-6

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Introduction

Body mass index (BMI) has been the most widely used indicator for assessing nutritional status and was established as the basis for classification of obesity, defined as excess adiposity. Although BMI is capable of identifying excess body weight, it fails to distinguish between fat mass and fat-free mass. BMI thus significantly underestimates obesity prevalence ¹.

Due to this limitation, individuals with adequate BMI may present high body fat percentage, and are thus called normal weight obese ². There is a significant prevalence of individuals misclassified as healthy, simply because their BMI falls within the normal range, leaving a high percentage of false-negatives. Likewise, individuals with preserved or increased lean mass and adequate adiposity may be misclassified in the excess weight category according to BMI (although this percentage of false-positives is low) ³.

Studies have reported an association between high body fat percentage and increased risk of dyslipidemias, diabetes, metabolic syndrome, and cardiovascular mortality, even in individuals with adequate BMI ^{3,4}. Serrano et al. ⁵ found that female adolescents who were normal weight obese measured by bioelectrical impedance presented altered blood pressure and low-density lipoprotein cholesterol (LDL), similar to adolescents with excess weight.

Individuals with high body fat percentage may also present higher production and secretion of proinflammatory cytokines such as interleukin-6 and tumor necrosis factor alpha (TNF- α), a condition associated with the development of cardiovascular diseases, insulin resistance, and atherosclerotic processes. Thus, elevated rates of these cytokines can be considered indicators of cardiovascular risk and metabolic syndrome in obese individuals with normal weight ².

To ensure greater validity in nutritional diagnosis, it is necessary to use biomarkers and methods capable of valid estimation of body composition ⁵. The available methods feature air displacement plethysmography (ADP), which is valid in different populations, and whose estimate of body composition does not differ from that of hydrostatic weighing, considered the gold standard ⁶. The current study thus proposes to compare biomarkers in four groups of adolescents from the *RPS Cohort* in São Luís, Maranhão, Brazil, classified simultaneously by BMI and body fat percentage assessed by ADP.

Methods

Study design

This was a cross-sectional study whose data source was a birth cohort in São Luís, and entitled *Lifetime Determinants of Obesity, Precursors of Chronic Diseases, Human Capital, and Mental Health: A Contribution from the São Luís Birth Cohorts to the Brazilian Unified National Health System – SUS*. This study is part of the RPS Consortium, which includes other studies performed in the cities of Ribeirão Preto (São Paulo State) and Pelotas (Rio Grande do Sul State).

This São Luís birth cohort included live hospital births to mothers living in the municipality, from March 1997 to February 1998. Participants in this cohort were assessed in three life phases: birth, childhood (7 to 9 years), and adolescence (18 to 19 years). The current study used data from the third phase.

Participants

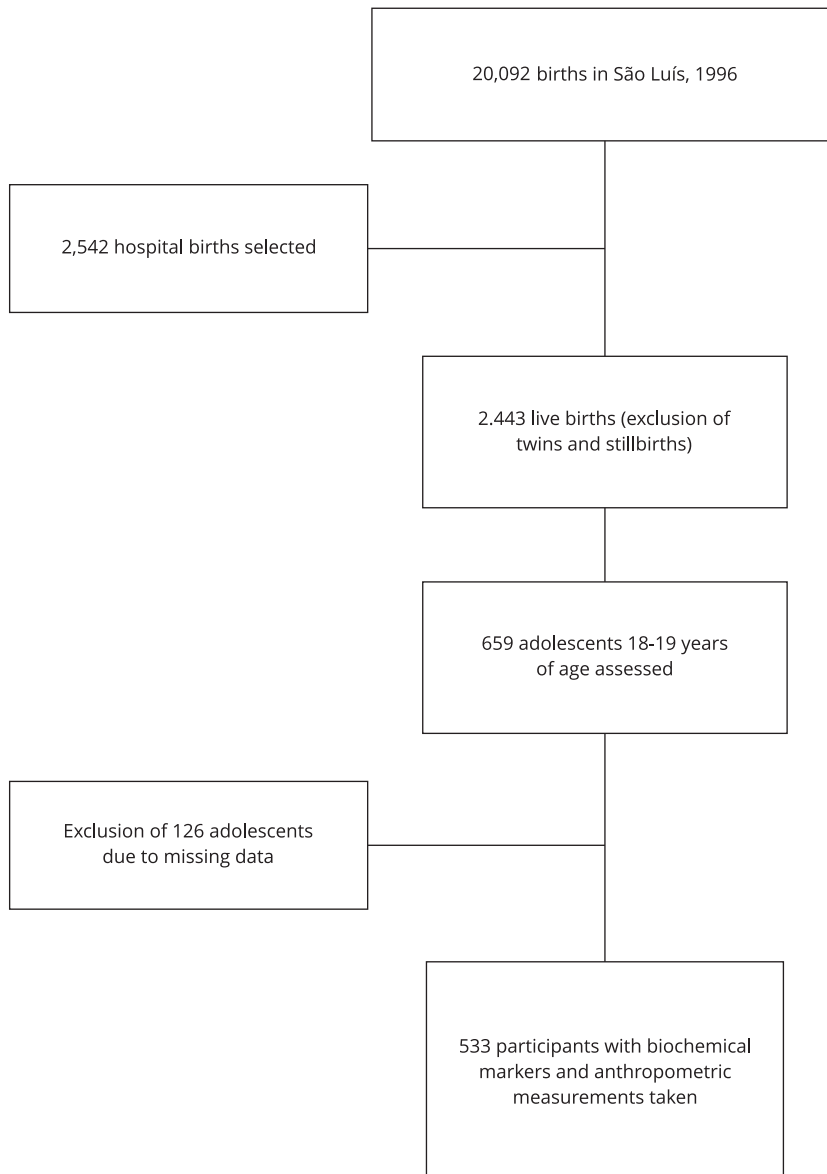
The birth cohort was conducted in ten public and private hospitals providing obstetric care. Systematic sampling was used with stratification proportional to the number of births in each hospital. One out of seven births were recruited in each hospital, covering 2,542 births in this phase of the cohort. The target population covered 96.3% of all births in São Luís (20,092) in the year 1996. With the exclusion of twins and stillbirths, the final sample in this first phase totaled 2,443 live births ⁷.

In the third phase of the cohort, participants were located through searches in school and university enrollment lists, at the addresses and telephone contacts recorded during the first and second phases of the cohort, on the military enlistment rosters for boys, and on social media. A total of 659

adolescents were identified and agreed to participate and appeared for the data collection. The current study considered data from 533 participants, since 106 did not have their biomarkers measured, while 20 lacked anthropometric data (Figure 1).

Figure 1

Sampling flowchart for the birth cohort *Lifetime Determinants of Obesity, Precursors of Chronic Diseases, Human Capital, and Mental Health: A Contribution from the São Luís Birth Cohorts to the Brazilian Unified National Health System-SUS*.



Data collection and study variables

The data were collected by trained health professionals. The information was recorded in the online program Research Electronic Data Capture (REDCap. <https://www.project-redcap.org/>)⁸. The variables sex (male and female) and age (years) were collected with a questionnaire.

Anthropometric and body composition assessments were performed. Height was measured in centimeters with a stadiometer (Altuxata, Belo Horizonte, Brazil). Total body mass was obtained in kilograms with a Filizola scale (São Paulo, Brazil). BMI was calculated as weight in kilograms divided by height in meters squared, and was classified as adequate versus excess weight (overweight and obesity) according to World Health Organization (WHO) guidelines ($\geq 25\text{kg/m}^2$)⁹. Waist circumference (in centimeters) was obtained with the Dimensional Photonic Scanner - 3DPS ([TC]² Labs, Cary, United States), which produces a 3D image of the body.

The adolescents had their body fat percentage assessed with ADP (Bod Pod Gold Standard, COSMED – Rome, Italy). Based on the body volume measured by ADP and body mass, the equipment calculated the body density, which was used in the Siri equation to determine the adolescents' fat mass¹⁰. The adolescents wore a cap to hold down their hair and light clothing to minimize the potential error from isothermal air that can be trapped in the clothing and hair. They were barefoot, with no earrings, rings, dental prostheses, or other types of metallic materials. The equipment was calibrated daily with a known volume of 50 liters. Body fat percentage was classified according to the Williams criteria¹¹ (1992) as normal ($< 25\%$ for males and $< 30\%$ for females) versus high ($\geq 25\%$ for males and $\geq 30\%$ for females).

Muscle mass (in kilograms) was measured by dual-emission x-ray absorptiometry (DEXA) based on enCORE and the Lunar Prodigy model (GE Healthcare – Chicago, United States).

Level of physical activity was measured with the 24-Hour Physical Activity Survey, based on an adaptation of the *Self-Administered Physical Activity Checklist* (SAPAC)¹². Level of physical activity was calculated by the number of metabolic task equivalents (MTEs) per week, where the time spent on each activity was multiplied by the activity's MTE and the number of days the adolescent practiced that activity. MTEs for each activity were obtained from the Compendium of Physical Activities (CPA)¹³. Classification of level of physical activity used the cutoff points from the *International Physical Activity Questionnaire* (IPAQ) in MTEs/week: sedentary (0), low (1 to < 600), moderate (600 to $< 3,000$), and high ($\geq 3,000$)¹⁴.

Blood samples (40 ml) were drawn aseptically from the cubital vein by a technician with experience in this procedure. The samples were stored in a freezer at adequate temperatures for each type of analysis (-20 or -80°C) until tested. The blood analysis measured interferon gamma (IFN- γ) in pg/mL, interleukin-4 (IL-4) in pg/mL, interleukin-17 (IL-17) in pg/mL, vascular endothelial growth factor (VEGF) in pg/mL, C-reactive protein (CRP) in ng/mL, interleukin-6 (IL-6) in pg/mL, hepatocyte growth factor (HGF) in pg/mL, tumor necrosis factor alpha (TNF- α) in pg/mL, and regulated on activation, normal T-cell expressed and secreted (RANTES) in pg/mL. These biomarkers were analyzed with Milliplex MAP Human Cytokine Kit (Merck, Darmstadt, Germany) (Table 1).

A four-group classification was defined, using BMI and body fat percentage simultaneously: "normal weight" (adequate BMI and body fat percentage), "normal weight obese" (adequate BMI with high body fat percentage), "excess weight with adequate body fat percentage", and "excess weight with high body fat percentage".

Statistical analysis

Data were analyzed with the Stata software, version 14.0 (<https://www.stata.com>). Categorical variables were described by absolute and relative frequencies. Chi-square test was performed to verify whether there was a difference between the groups' frequencies, gender, and level of physical activity. Normal distribution of the continuous variables was verified with the Shapiro-Wilk test and asymmetry and kurtosis coefficients. Continuous variables with normal distribution were presented by the mean and standard deviation and analyzed by the ANOVA test, and those without normal distribution were described by the median and interquartile range and analyzed by the Kruskal-Wallis test to verify differences in the measure of central tendency between the groups. We opted not to perform

Table 1

Coefficients of intra- and inter- assay variability for biomarkers assessed by Milliplex MAP Human Cytokine Kit.

Biomarkers	Coefficient of intra-assay variability	Coefficient of inter-assay variability
Interleukin-6 (pg/mL)	10.3	2.7
TNF- α (pg/mL)	85.0	20.0
CRP (ng/mL)	16.2	3.9
Interleukin-17 (pg/mL)	21.2	3.7
HGF (pg/mL)	33.8	22.2
VEGF (pg/mL)	11.7	20.5
IFN- γ (pg/mL)	35.1	3.9
RANTES (pg/mL)	1.6	4.5
Interleukin-4 (pg/mL)	27.1	22.4

TNF- α : tumor necrosis factor alpha; CRP: C-reactive protein; HGF: hepatocyte growth factor; IFN- γ : Interferon gamma; RANTES: T cell expressed and secreted; VEGF: vascular endothelial growth factor.

the analysis between groups and the biomarkers separated by sex, since there were only four boys with “normal weight obesity” and four girls with “excess weight and high body fat percentage”.

Ethical and legal aspects

The study was approved by the Institutional Review Board of the University Hospital, Federal University of Maranhão, protocol number 1.302.489. All participants signed a free and informed consent form.

Results

The study assessed 533 adolescents, 18 to 19 years of age, of whom 61.5% were boys. Boys showed a higher proportion of “excess weight and adequate body fat percentage” (8.3%) compared to girls, who had higher proportions of “normal weight obesity” (15.6%) and “excess weight with high body fat percentage” (17.1%) (Table 2).

Higher mean waist circumference was seen in adolescents with “excess weight and high body fat percentage” (96cm) compared to “normal weight” and “normal weight obese” individuals, besides higher mean body fat percentage in adolescents with “excess weight and high body fat percentage” (35.1%) and “normal weight obesity” (34.2%) compared to “normal weight” (14.4%) and “excess weight and adequate body fat percentage” (18.8%) individuals. Adolescents with “excess weight and adequate body fat percentage” exhibited higher mean muscle mass (54.5kg) and higher rates of high physical activity (32.2%) and moderate physical activity (35.5%). “Normal weight obese” adolescents were more sedentary (66.7%) (Table 3).

In relation to biomarkers, “normal weight obese” adolescents presented the highest mean total cholesterol (172.5mg/dL) and LDL-cholesterol (103.5mg/dL) among all the groups. Those with “excess weight and high body fat percentage” exhibited lower mean high-density lipoprotein cholesterol (HDL-cholesterol – 43.2mg/dL) than the other groups; higher mean IL-6 (2.7pg/mL) than the “normal weight” and “excess weight and adequate body fat percentage” adolescents; and higher median triglycerides (114.0mg/dL) and CRP (0.14ng/mL) compared to their “normal weight” and “normal weight obese” peers. Adolescents with “excess weight and adequate body fat percentage” presented CRP equal to those with “excess weight and high body fat percentage” (0.14ng/mL), but higher than the “normal weight” adolescents (0.06ng/mL) (Table 4).

Table 2

Classification according to body mass index (BMI) and body fat percentage in adolescents. São Luís, Maranhão State, Brazil 2016.

Groups	Males % (n)	Females % (n)	Total % (n)
Normal weight	82.0 (269)	65.4 (134)	75.6 (403)
Normal weight obese	1.2 (4)	15.6 (32)	6.8 (36)
Excess weight and adequate body fat percentage	8.3 (27)	1.9 (4)	5.8 (31)
Excess weight and high body fat percentage	8.5 (28)	17.1 (35)	11.8 (63)
Total	100.0 (328)	100.0 (205)	100.0 (533)

Note: p-value < 0.001.

Normal weight: adequate BMI and body fat percentage; Normal weight obese: adequate body mass and high body fat percentage; Excess weight and adequate body fat percentage: excess weight according to BMI and adequate body fat percentage; Excess weight and high body fat percentage: excess weight according to BMI and high body fat percentage.

Table 3

Body composition and level of physical activity according to groups classified simultaneously by body mass index (BMI) and body fat percentage in adolescents. São Luís, Maranhão State, Brazil, 2016.

	Normal weight (n = 403)	Normal weight obese (n = 36)	Excess weight and adequate body fat percentage (n = 31)	Excess weight and high body fat percentage (n = 63)
Body composition				
BMI (kg/m ²) *	20.0 (18.6-2.0) **,***,##	22.6 (21.2-23.5) ***,###,##	25.7 (25.2-27.0) **,##	27.8 (26.2-30.1) **,##
Waist circumference ###	78.5 (±6.2) **,***,##	82.8 (±6.0) ***,###,##	90.1 (±5.4) **,##	96.0 (±10.2) **,##
Body fat (%) ###	14.4 (±7.7) **,***,##	34.2 (±5.5) ***,###,##	18.8 (±5.8) **,##,###	35.1 (±5.9) ***,###,##
Muscle mass (kg) ###	43.0 (±9.3) **,***,##	34.2 (±5.3) ***,###,##	54.5 (±7.2) **,##,###	46.9 (±10.2) ***,###,##
Level of physical activity §				
Sedentary (%)	32.5	66.7	25.9	38.1
Low (%)	15.0	11.1	6.4	15.8
Moderate (%)	26.0	16.7	35.5	20.7
High (%)	26.5	5.5	32.2	25.4
Total (%)	100.00	100.00	100.00	100.00

MTEs: metabolic task equivalents; Normal weight: adequate BMI and body mass percentage; Normal weight obese: adequate BMI and high body fat percentage; Excess weight and adequate body fat percentage: excess weight by BMI and adequate body fat percentage; Excess weight and high body fat percentage: excess weight by BMI and high body fat percentage.

* Median and interquartile range. Classification of level of physical activity (IPAQ): sedentary (0 MTEs/week), low (1 to < 600 MTEs/week), moderate (600 to < 3,000 MTEs/week), and high (≥ 3,000 MTEs/week);

** p-value < 0.05 when compared to normal weight obese;

*** p-value < 0.05 when compared to excess weight and adequate body fat percentage;

p-value < 0.05 when compared to normal weight;

p-value < 0.05 when compared to excess weight and high body fat percentage.

Mean and standard deviation.

§ p-value = 0.006.

Table 4

Biomarkers in groups classified simultaneously by body mass index (BMI) and body fat percentage in adolescents. São Luís, Maranhão State, Brazil, 2016.

Biomarkers	Normal weight	Normal weight obese	Excess weight and adequate body fat percentage	Excess weight and high body fat percentage
	(n = 403)	(n = 36)	(n = 31)	(n = 63)
Triglycerides (mg/dL) *	81.0 (62.0-108.0) **	83.5 (62.5-105.5) **	91.0 (60.0-126.0)	114.0 (73.0-149.0) ***,#
Total cholesterol (mg/dL) ##	149.6 (±26.5) **,#	172.5 (±29.9) **,***,###	152.8 (±36.1) #	162.0 (±35.0) ***,#
LDL-cholesterol (mg/dL) ##	84.9 (±22.9) **,#	103.5 (±26.8) **,***,###	85.4 (±31.5) **,#	94.5 (±31.6) ***,#,###
HDL-cholesterol (mg/dL) ##	46.9 (±10.9) **,#	49.7 (±11.7) **,#	46.2 (±10.4) **	43.2 (±11.1) ***,#,###
Interleukin-6 (pg/mL) ##	1.5 (1.0-2.7) **,#	2.4 (1.3-3.5) ***	1.5 (1.1-4.1) **	2.7 (1.5-5.3) ***,###
TNF-α (pg/mL) *	5.5 (3.9-8.1)	5.5 (3.7-7.5)	6.5 (3.9-8.5)	5.5 (4.0-8.1)
CRP (ng/mL) *	0.06 (0.02-0.14) **,###	0.10 (0.03-0.15) **	0.14 (0.05-0.19) ***	0.14 (0.08-0.69) **,#
Interleukin-17 (pg/mL) *	2.7 (1.7-4.5)	2.6 (1.7-5.2)	2.4 (1.6-4.5)	2.1 (1.6-4.2)
HGF (pg/mL) *	763.1 (485.3-1,327.0)	792.4 (473.2-1,685.0)	838.61 (450.6-1,113.0)	744.2 (543.4-1,582.0)
VEGF (pg/mL) *	161.8 (12.94-465.1)	97.8 (0.9-335.5)	197.8 (23.9-370.9)	139.1 (6.5-380.4)
IFN-γ (pg/mL) *	7.2 (2.7-17.7)	8.4 (2.8-16.0)	7.2 (2.7-16.2)	5.8 (1.9-19.6)
RANTES (pg/mL) *	1,846.0 (1,223.0-3,307.0)	1,980.5 (1,312.5-3,808.0)	1,552.0 (1,264.0-5,192.0)	1,768.0 (903.3-3,475.0)
Interleukin-4 (pg/mL) *	1.9 (0.6-67.1) **	1.8 (0.6-18.8)	8.1 (0.5-67.1) **	1.1 (0.5-12.5) ***,###

LDL-cholesterol: low-density lipoprotein cholesterol; HDL-cholesterol: high-density lipoprotein cholesterol; TNF-α: tumor necrosis factor alpha; CRP: C-reactive protein; HGF: hepatocyte growth factor; VEGF: vascular endothelial growth factor; IFN-γ: interferon gamma; RANTES: T cell expressed and secreted; Normal weight: adequate BMI and body fat percentage; Normal weight obese: adequate BMI and high body fat percentage; Excess weight and adequate body fat percentage: excess weight by BMI and adequate body fat percentage; Excess weight and high body fat percentage: excess weight by BMI and high body fat percentage.

* Median and interquartile range;

** p-value < 0.05 compared to excess weight and high body fat percentage;

*** p-value < 0.05 compared to normal weight;

p-value < 0.05 compared to normal weight obese;

Mean and standard deviation;

p-value < 0.05 compared to excess weight and adequate body fat percentage.

Discussion

Adolescents in this study with “excess weight and high body fat percentage” presented four biomarkers with worse values (triglycerides, HDL-cholesterol, IL-6, and CRP), “normal weight obese” had two higher biomarkers (total cholesterol and LDL-cholesterol), and those with “excess weight and adequate body fat percentage” had one elevated biomarker (CRP) compared to their “normal weight” peers. The main result is that adolescents with “excess weight and high body fat percentage” had a worse lipid and inflammatory profile. Some adolescents also showed high body fat percentage despite normal BMI, or so-called “normal weight obese” individuals, with higher values for some lipid markers. Thus, the use of BMI alone has limited capacity to assess obesity and the risk of atherosclerotic and cardiovascular diseases in adolescents.

The study presents some limitations. Loss to follow-up of participants in the cohort was 20.9%. Information was also missing for 126 adolescents, further limiting the study sample. The small numbers of participants in the groups classified as “excess weight and normal body fat percentage” reduced the precision of some estimates. The dosing of inflammatory markers with Milliplex presents some limitations related to stability, specificity, and possible cross reactions between reagents. Since this was a cross-sectional study, it was not possible to establish a causal relationship between the study groups and their biomarkers.

The study's strengths were the use of air displacement plethysmography, one of the most valid methods for measuring adiposity, and the use of various biomarkers to assess cardiovascular and inflammatory risk in adolescents, including biomarkers related to low-grade inflammation, such as IL-6, TNF- α , and CRP¹⁵, and to more intense inflammatory processes, namely IFN- γ , IL-17, IL-4, and RANTES^{16,17,18} and cardiovascular diseases, such as VEGF and HFG^{19,20}.

Few studies were identified that analyzed all the groups considered in the current study. Martinez et al.⁴, in 5,983 American adults 20 to 84 years of age, found the following prevalence rates: "normal weight obesity" 4.5%; "excess weight with adequate body fat percentage", 18%; and "excess weight with high body fat percentage", 45.5%. Berg et al.³, in 3,016 Swedes 25 to 74 years of age, observed the following prevalence rates for men and women, respectively: "normal weight obesity", 10% and 8%; "excess weight with adequate body fat percentage", 5% and 4%; and "excess weight with high body fat percentage", 59% and 44%. In these two studies, the prevalence rates for "excess weight with high body fat percentage" were higher than in our study, which was expected since the populations in those studies were older. However, although our study was done in a younger population, the "normal weight obesity" levels were similar to the prevalence rates in studies done in adults and the elderly.

This finding is worrisome, since "normal weight obese" adolescents presented lower mean muscle mass and were more sedentary. Jean et al.²¹ state that "normal weight obesity" is related to reduced muscle mass, leading to lower energy expenditure since there is less metabolically active tissue, besides involving metabolic deregulation and worse aerobic conditioning.

A comparison of our data with the results reported by Berg et al.³ shows that girls presented a higher percentage of "normal weight obesity", while boys had more "excess weight with adequate body fat percentage". Girls tend to exhibit higher body fat percentage due to genetic and hormonal factors²². Meanwhile, boys tend to show a higher proportion of "excess weight with adequate body fat percentage", possibly since they have more muscle mass and practice more physical activity on average²³.

Another relevant result was that "normal weight obese" adolescents showed higher total cholesterol and LDL-cholesterol, and those with "excess weight and high body fat percentage" had worse values for triglycerides and HDL-cholesterol. These findings may be due to excess body fat percentage and the fact that the mean values were similar in the groups with "normal weight obesity" and "excess weight with high body fat percentage". Serrano et al.⁵ studied 113 female schoolchildren 14 to 18 years of age in Minas Gerais, Brazil, and found that adolescents with "normal weight obesity" and "excess weight with high body fat percentage" had a worse lipid profile than their "normal weight" peers. The authors expressed their concern that the pathogenesis of atherosclerosis correlates with lipid levels in this life phase. They further warned that even with adequate BMI, high body fat percentage can contribute to the development of chronic noncommunicable diseases which, if present since adolescence, can be exacerbated in adulthood.

High body fat percentage is also implicated in chronic low-grade inflammation involving an increase in inflammatory cytokines and acute-phase proteins, such as IL-6, TNF- α , and CRP, which are classic inflammatory mediators²⁴.

The current study found a difference between groups in IL-6 and CRP levels, but no difference in TNF- α values. The adolescents did not show differences in IL-6 concentrations between the groups with "excess weight and high body fat percentage" or "normal weight obesity". However, IL-6 was higher in these two groups when compared to "normal weight" individuals, indicating that IL-6 was more related to high body fat percentage. Schlecht et al.²⁵, in 97 Germans 22 to 69 years of age, observed that the associations between visceral adipose tissue and IL-6 were stronger than between BMI and IL-6, indicating that adipose tissue can furnish metabolic information captured by IL-6 that is not captured by BMI.

Adolescents with "excess weight and high body fat percentage" and "excess weight and adequate BFP" showed the same concentrations of CRP, and these concentrations were higher than in "normal weight" individuals. Thus, higher concentrations of CRP in this study were related to obesity indicated by BMI and not to high body fat percentage. Different results appeared in a study of 3,483 individuals 22 years of age in Pelotas in which obese individuals (both according to BMI and high body fat percentage) had higher IL-6 and CRP values²⁶.

Studies have reported a positive correlation between IL-6 and CRP and high body fat percentage. When adipocytes increased, their secretory properties are altered, elevating the levels of circulat-

ing CRP and IL-6. These cytokines are associated with worse cardiovascular outcomes and play an important role in all stages of atherosclerosis, from onset of progression to the rupture of atherosclerotic plaques²⁵.

“Normal weight obese” adolescents showed higher IL-6 levels, but not higher CRP. IL-6 is the principal interleukin that stimulates the CRP release in the liver, which does not rule out the future possibility of higher CRP values in “normal weight obese” adolescents if the same exposure characteristics are maintained, since altered IL-6 occurs first, followed later by altered CRP²⁷.

One intriguing finding was the similar CRP value between adolescents with “excess weight and adequate body fat percentage” and “excess weight and high body fat percentage”. The fact that CRP in this study was related to obesity measured by BMI and not by elevated body fat percentage in these two groups may be because these adolescents presented other risk factors for elevated CRP, such as stress, smoking, medications, alcohol abuse, and inadequate diet, and not necessarily increased adipose tissue²⁸.

Adolescents with “excess weight and adequate body fat percentage” were also those with the highest muscle mass values and the highest rates of moderate and high physical activity. Kasapis & Thompson²⁹ reported that immediate and short-term physical exercise produces an inflammatory response, since exercise-induced muscle injury causes a repair response, stimulating higher production of CRP. Thus, adolescents with “excess weight and adequate body fat percentage” may have been starting some physical activity program when the data were collected.

This study did not find significant differences between the groups for IFN- γ , IL-17, IL-4, VEGF, HFG, and RANTES. Besides the classic cytokines mediating the inflammatory process in obesity, IFN- γ , IL-17, IL-4, and RANTES also participate in the inflammatory process. However, they have been studied less frequently as possible inflammatory markers of obesity, and generally in older populations. Sumarac-Dumanovic et al.³⁰ studied 46 women 20 to 52 years of age in Serbia, and in keeping with our findings, they did not find higher IFN- γ levels in obese women according to BMI when compared to “normal weight” women. Still, these same authors found that IL-17 concentrations were higher in obese women, independently of the increase in abdominal adiposity, insulin resistance, and leptin.

RANTES is a chemokine related mainly to atherogenesis³¹. Koh et al.³² observed an association between serum RANTES concentrations and cardiovascular risk markers in a case-control study in 302 men 40 to 65 years of age. Records show that this chemokine’s concentrations are elevated in the presence of obesity³³.

Our study did not find a difference between the groups’ VEGF and HFG, which are growth factors secreted by adipose tissue. Contrary to our findings, some epidemiological studies suggest that increased VEGF levels are associated with obesity³⁴. However, a study by Azizian et al.³⁵ (2016) with 242 Iranians did not find a significant difference in VEGF levels between obese and non-obese individuals according to BMI. Rehman et al.³⁶ found that circulating levels of HGF, but not of VEGF, were significantly correlated with BMI in 65 persons 32 to 41 years of age in Indiana, USA. Bell et al.³⁷ observed that increased HGF secretion may result from post-transcriptional events, possibly related to the size of adipocytes and elevated TNF- α stimulus in the adipose tissue in 29 obese individuals 45 to 49 years of age.

The absence of differences between this study’s groups for TNF- α , IFN- γ , IL-17, IL-4, VEGF, HFG, and RANTES may be due to the fact that these biomarkers are not as sensitive to the origins of inflammatory problems, when compared to IL-6 and CRP, as well as to the fact that this study’s population consisted of young people (18-19 years), while the studies assessing the other biomarkers were performed in older populations.

This study found that adolescents with “excess weight and high body fat percentage” had worse lipid and inflammatory profiles. Some adolescents also had high body fat percentage despite normal BMI, with higher levels for some lipid profile parameters. BMI thus exhibits important limitations as a method for assessing obesity status, since it does not distinguish between body compartments, and the use of this indicator alone is insufficient for assessing obesity in adolescents. It is thus pertinent to perform a more precise assessment, including biomarkers, mainly IL-6 and CRP, and considering body fat in order to adequately monitor individuals for health risks or problems related to high body fat percentage and with increased risk of developing inflammatory, atherosclerotic, and cardiovascular diseases.

Contributors

All authors contributed to the study conceptualization and project, data analysis and interpretation, writing of the article, relevant critical revision of the intellectual content, and approval of the final version for publication. They are also responsible for all aspects of the research, guaranteeing the accuracy and integrity of any part of the work.

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Resumo

O objetivo do trabalho foi comparar biomarcadores em grupos de adolescentes classificados simultaneamente pelo índice de massa corporal (IMC) e percentual de gordura corporal, mensurados por meio da pletismografia por deslocamento de ar. Estudo transversal com 533 adolescentes de 18 e 19 anos de São Luís, Maranhão, Brasil. O IMC foi classificado em adequado ($< 25\text{kg}/\text{m}^2$) e excesso de peso ($\geq 25\text{kg}/\text{m}^2$). Definiu-se percentual de gordura corporal elevado $\geq 25\%$ para o sexo masculino e $\geq 30\%$ para o feminino. Os adolescentes foram classificados em quatro grupos: “eutrófico” (IMC e percentual de gordura corporal adequados), “obeso de peso normal” (IMC adequado com percentual de gordura corporal elevado), “excesso de peso com percentual de gordura corporal adequado” e “excesso de peso com percentual de gordura corporal elevado”. As meninas registraram maiores valores de “obesidade de peso normal” (15,6%) e “excesso de peso com percentual de gordura corporal elevado” (17,1%). Os adolescentes “obesos de peso normal” apresentaram maiores médias para colesterol total (172,5mg/dL) e LDL-colesterol (103,5mg/dL). Aqueles com “excesso de peso e percentual de gordura corporal elevado” registraram a menor média para HDL-colesterol (43,2mg/dL) em relação aos outros grupos; maior média para interleucina-6 (2,7pg/mL) em relação aos “eutróficos” e “excesso de peso e percentual de gordura corporal adequado”; e maiores medianas para triglicérides (114,0mg/dL) e proteína C reativa (0,14ng/mL) em relação aos “eutróficos” e “obesos de peso normal”. Os com “excesso de peso e percentual de gordura corporal adequado” apresentaram proteína C reativa igual aos com “excesso de peso e percentual de gordura corporal elevado”. A avaliação do estado nutricional pelo IMC é limitada, pois 6,8% dos adolescentes registraram percentual de gordura corporal elevado apesar do IMC normal, além disto, os “obesos de peso normal” apresentaram dois biomarcadores piores que os adolescentes com “excesso de peso e percentual de gordura corporal elevado”.

Índice de Massa Corporal; Adiposidade;
Biomarcadores; Interleucina-6

Resumen

El objetivo del estudio fue comparar biomarcadores en grupos de adolescentes, clasificados simultáneamente por el índice de masa corporal (IMC) y porcentaje de grasa corporal (PGC), medido mediante pletismografía por desplazamiento de aire. Estudio transversal con 533 adolescentes de 18 y 19 años de São Luís, Maranhão, Brasil. El IMC fue clasificado en adecuado ($< 25\text{kg}/\text{m}^2$) y exceso de peso ($\geq 25\text{kg}/\text{m}^2$). Se definió el porcentaje de grasa corporal elevado $\geq 25\%$ para el sexo masculino, y $\geq 30\%$ para el femenino. Los adolescentes se clasificaron en cuatro grupos: “eutrófico” (IMC y porcentaje de grasa corporal adecuados), “obeso de peso normal” (IMC adecuado con porcentaje de grasa corporal elevado), “exceso de peso con porcentaje de grasa corporal adecuado” y “exceso de peso con porcentaje de grasa corporal elevado”. Las niñas tuvieron mayores valores de “obesidad de peso normal” (15,6%) y “exceso de peso con porcentaje de grasa corporal elevado” (17,1%). Los adolescentes “obesos de peso normal” presentaron mayores medias para colesterol total (172,5mg/dL) y LDL-colesterol (103,5mg/dL). Aquellos con “exceso de peso y porcentaje de grasa corporal elevado” tuvieron una media menor para HDL-colesterol (43,2mg/dL), en relación con los otros grupos; mayor media para interleucina-6 (2,7pg/mL), en relación a los “eutróficos” y “exceso de peso y porcentaje de grasa corporal adecuado”; y mayores medianas para triglicéridos (114,0mg/dL) y proteína C reactiva (0,14ng/mL), en relación a los “eutróficos” y “obesos de peso normal”. Quienes tenían “exceso de peso y porcentaje de grasa corporal adecuado” presentaron proteína C reactiva igual a los de “exceso de peso y porcentaje de grasa corporal elevado”. La evaluación del estado nutricional por el IMC es limitada, puesto que un 6,8% de los adolescentes presentaron porcentaje de grasa corporal elevado, a pesar del IMC normal, asimismo los “obesos de peso normal” tuvieron dos biomarcadores peores que los adolescentes con “exceso de peso y porcentaje de grasa corporal elevado”.

Índice de Masa Corporal; Adiposidad.
Biomarcadores; Interleucina-6

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