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Relationship between body composition and dyslipidemia in children and adolescents

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Abstract *We studied the relationship between different anthropometric indexes and plasma lipids. Data were collected from 2014 to 2016 in 854 schoolchildren (6-18 years). Waist circumference (WC), body fat percentage (BFP) by bioimpedance, body mass index (BMI), and waist-to-height ratio (WHtR) were measured. Total cholesterol (TC), HDLc, and triglycerides were measured in fasting blood samples and Non-HDL cholesterol (Non-HDLc) was calculated. Data are presented as mean ± standard deviation, with percentages. Means were compared using the t test or ANOVA followed by Tukey's test. The association between variables was tested by linear regression. The study was approved by the Research Ethics Committee of the Universidade Federal do Espírito Santo. Obese boys had higher TC, non-HDLc, and LDLc than eutrophic boys (p < 0.05). In girls this difference was found only for non-HDLc (p < 0.05). Children with inappropriate BFP and WHtR presented higher LDLc and non-HDLc concentrations (p < 0.001), which showed positive association (p<0.001) with lipid fractions (TC and non-HDLc). Excess body fat increased the probability of cholesterol above the reference value (170 mg/dL) by 21%. Excess body fat was associated with an atherogenic lipid profile (higher non-HDLc), especially in boys.*

Key words *Dyslipidemia, Child, Adolescent, Body composition, Anthropometry*

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Introduction

The prevalence of overweight and obesity in children and adolescents has been increasing in recent decades[1]. A recent national study conducted in Brazil revealed 17.1% of overweight and 8.4% of obesity in schoolchildren 12 to 17 years of age[2]. Increased adiposity in childhood or adolescence is an important risk factor for the development of cardiovascular disease (CVD) in adults[3,4] and alterations in plasma lipids may be important mediators of this process. Thus, preventive measures should be implemented and monitored starting at an early age, by controlling the main risk factors, including cholesterol and its fractions[5,6]. Studies have shown that increased cholesterol in children is associated with thickening of the carotid intima-media complex, a subclinical marker of atherosclerosis in adults[7,8].

Body mass index (BMI) and waist circumference (WC) are associated with higher values for blood pressure, fasting insulinemia, and dyslipidemia in children and adolescents[6]. These factors act synergistically to increase cardiovascular risk[9]. However, body fat percentage (BFP) and waist-to-height ratio (WHtR) appear to be better indicators of total and central body fat accumulation, respectively, suggesting that they would be better predictors of cardiometabolic risk[10,11].

Dyslipidemias may be genetic or multifactorial in nature. The first is rarer. Multifactorial dyslipidemia is more frequent in both children and adults, and arises from changes in lifestyle, including inappropriate diet and physical inactivity[5], factors also strongly associated with excess adiposity; regardless of heredity[10,12,13]. Multifactorial dyslipidemia is a risk factor and not a disease when present in childhood or adolescence[14] and, therefore, should be controlled by adopting healthy lifestyle habits.

The increase in total cholesterol (TC) and low density lipoprotein (LDLc) seems to be associated with the accumulation of visceral fat, since its prevalence increases with the increase in BMI, WC, and BFP[14]. Currently, however, non-high-density lipoprotein cholesterol (Non-HDLc) is being considered a better predictor of cardiovascular disease when compared to LDLc or TC in infant-juvenile populations[15,16].

Considering that nutritional status is one of the risk factors for multifactorial dyslipidemia, this study aimed to verify the relationship between body composition, through different indicators, and alteration in lipid fractions in schoolchildren, in order to quantify the impact of excessive fat accumulation on the alterations in these fractions. In addition, we also verified whether the accumulation of body fat affects plasma lipids in the same way in boys and girls.

Methodology

Study population

This was a quantitative, descriptive and analytical cross-sectional study in children and adolescents enrolled in an institution called the 'Knowledge Station', situated in Serra, Espírito Santo. Data was collected between 2014 and 2016, with around 1,100 individuals eligible in the specified period. Of this contingent, 856 children and adolescents participated in the study as volunteers. Two children were excluded from the analysis because they were <6 years old, thus totaling 854 participants between ages 6 and 18 years. The 'Knowledge Station' is an institution that offers extracurricular activities before and after school hours for children and adolescents regularly enrolled in municipal public schools in Serra, Espírito Santo. Thus, all participants in this research are students enrolled in the public school system and who belong to lower socioeconomic classes and primarily reside near the institution. The present work is part of a broader research project entitled "Determinants of elevated blood pressure in children and adolescents of various ancestries", approved by the Research Ethics Committee of the Health Sciences Center at the Federal University of Espírito Santo (*UFES*).

The participants were referred for the study by the Knowledge Station Social Service and all exams were conducted at the Cardiovascular Research Clinic (*CIC*), linked to the University Hospital of the *UFES*. The project was announced to parents and guardians through letters and meetings. Parents or guardians signed the consent form and the adolescents (≥12 years) signed the assent form.

Biochemical exams

Participants appeared at the *CIC* on a pre-scheduled morning of fasting for clinical exams and collection of material for biochemical exams. A blood sample was collected by venipuncture in the forearm. Aliquots were sent to a central laboratory for measurement of total cholesterol (TC), HDLc and triglycerides (TG), plus other components. The LDL-c fraction was

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calculated using Friedewald's formula [LDLc = TC - (HDLc + TG/5)]. Non-HDLc was calculated by the formula (TC - HDLc). Reference values for the lipid fractions were obtained according to the National Cholesterol Education Program[17].

Anthropometric measurements

Anthropometry and bioimpedance were done after bladder emptying, with the participant barefoot and wearing only a bathing suit. Height was determined using a wall stadiometer with an accuracy of 0.1 cm. Body weight was obtained on a tetrapolar eight-electrode bioimpedance scale (InBody 230, Korea) with an accuracy of 0.1 kg, which also automatically provided body fat percentage (BFP). An individual was classified by BFP as 'normal' or 'excessive' according to Freedman et al.[18], with the category "excessive" being obtained by combining the classifications "moderate" and "excessive". Waist circumference (WC) was measured midway between the lower costal margin and the iliac crest, and classified according to Taylor et al.[19]. Body mass index (BMI) was calculated as the ratio of body weight (kg) to height (m) squared, and individuals were classified according to percentile (p) (Centers for Disease Control and Prevention[20]) into: underweight (p <5), normal weight (p ≥ 5 and < 85), overweight (p ≥ 85 and < 95), and obesity (p ≥ 95). The classification of the ratio of WC to height (WHtR) was dichotomized into 'appropriate' or 'inappropriate' by the cutoff point established at p90 of the sample itself.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and by frequency. The Kolmogorov-Smirnov test was used to test the normality of the continuous variables. Means were compared using the Student's *t*-test (two groups) or by one-way analysis of variance (ANOVA) with Tukey's post hoc test (three or more groups). The comparison of proportions was obtained using the Chi-square test. The degree of association between continuous variables was obtained using Pearson's coefficient and the fit to the linear model conducted via regression analysis. The *Z* statistic was used to estimate the influence of excessive body fat accumulation on the frequency of high cholesterol. The calculations were done using the Statistical Package for the Social Sciences (SPSS), version 17.0 and the significance level set at $P < 0.05$.

Results

Of the 854 children and adolescents studied, 478 (56%) were boys. Participants were divided into 3 age groups (6 - 9 years, 9 - 15 years, 15 - 19 years) with the highest proportion in the 9 - 15 group (n = 584; 68.4%). The overall average age was 11.9 ± 2.8 years. The mean body weight was 44.3 ± 15.4 kg and 44.4 ± 14.7 kg, in boys and girls, respectively. The distribution of the BMI classification differed between sexes, with more girls (28.2%) being overweight than boys (20.3%) ($P < 0.05$). For the other anthropometric variables, no difference was detected between sexes (Table 1).

The distribution of the lipid profile in the sample was similar in both sexes (Table 1). The most frequently altered lipid fraction was HDLc, which presented low values (< 40 mg/dL) in 20.8% of the sample. Increased TG levels were found more frequently in younger children (6-9 years) compared with older children (11.9% vs. 4.0%; $P < 0.01$).

In associating the classification of nutritional status by BMI with lipid fractions, a progressive increase in TC, LDLc, and Non-HDLc was observed as individuals from the lowest to the highest BMI percentile were compared, both in boys and girls (Table 2). HDLc behaves inversely with total cholesterol and non-HDLc, increasing ($P < 0.001$) progressively from underweight towards obesity, in both sexes.

A similar pattern can be seen when classifying girls and boys in relation to WHtR and BFP. Participants with inappropriate values for these indicators had higher TC, LDLc, and Non-HDLc in both sexes.

Figure 1 shows the association between BFP and WHtR and lipid fractions. Both TC and Non-HDLc increase with increasing BFP, with this increase being more intense in males. Cholesterol increase per percentage unit of body fat increase was higher ($P < 0.05$) in boys than in girls (0.812 ± 2.85 mg/dL and 0.332 ± 3.48 mg/dL, respectively). The association between BFP and Non-HDLc was stronger than in relation to total cholesterol, being significant in both sexes.

Figure 1 also shows the associations between lipid fractions and WHtR. Both TC and Non-HDLc showed significant correlation with WHtR in boys and girls, with no difference between the slope coefficients of the regression lines ($p = 0.164$ and $p = 0.205$, respectively).

To estimate the impact of excess body fat on the likelihood of finding cholesterol greater than

Table 1. Characterization of the sample, stratified by gender, according to developmental aspects, nutritional status, and lipid fractions (Serra, ES, 2014-2016).

Variables	Female		Male		All		
	n	%	‘n	%	n	%	p-value*
Age							0.797
6⊢ 9 years	64	17.0	79	16.5	143	16.7	
9⊢ 15 years	253	67.3	331	69.2	584	68.4	
15⊢ 19 years	59	15.7	68	14.2	127	14.9	
Waist Circumference (cm)							0.113
Appropriate (< p80)	299	81.0	401	85.1	700	83.3	
Inappropriate (≥ p80)	70	19.0	70	14.9	140	16.7	
Waist-to-Height Ratio (cm)							0.513
Appropriate (p < 90)	322	87.0	416	88.5	738	87.9	
Inappropriate (p ≥ 90)	48	13.0	54	11.5	102	12.1	
Body Fat Percentage (%)							0.603
Appropriate	261	70.9	341	72.6	602	71.8	
Inappropriate	107	29.1	129	27.4	236	28.2	
Total Cholesterol (mg/dL)							0.666
Desirable (< 170)	300	82.2	395	84.4	695	83.4	
Borderline (170-199)	54	14.8	62	13.2	116	13.9	
Altered (≥ 200)	11	3.0	11	2.4	22	2.6	
LDLc (mg/dL)							0.893
Desirable (< 110)	331	90.4	424	90.8	755	90.6	
Borderline (110-129)	26	7.1	30	6.4	56	6.7	
Altered (≥ 130)	9	2.5	13	2.8	22	2.6	
HDLc (mg/dL)							0.297
Desirable (> 45)	216	58.7	259	55.3	475	56.8	
Borderline (40-45)	73	19.8	114	24.4	187	22.4	
Altered (< 40)	79	21.5	95	20.3	174	20.8	
Triglycerides (mg/dL)							
0-9 years							0.767
Desirable (< 75)	64	64.0	81	68.6	145	66.5	
Borderline (75-99)	23	23.0	24	20.6	47	21.6	
Altered (≥ 100)	13	13.0	13	11.0	26	11.9	0.506
10-19 years							
Desirable (< 90)	215	80.2	277	79.1	492	79.6	
Borderline (90-129)	40	14.9	61	17.4	101	16.3	
Altered (≥ 130)	13	4.9	12	3.4	25	4.0	
Non-HDLc (mg/dL)							0.195
Desirable (< 120)	294	80.5	399	85.3	693	83.2	
Borderline (120-144)	56	15.3	55	11.8	111	13.3	
Altered (≥ 145)	15	4.1	14	3.0	29	3.5	

*Chi square. Significance $p < 0.05$. 1 The cutoff points for classifying individuals were obtained from the Centers for Disease Control and Prevention (CDC, 2000). Age: n = 854; Waist Circumference (WC): n = 840; Body Fat Percentage (BFP): n = 838; Nutritional Status: n = 854; Waist-to-Height Ratio (WHtR): n = 840; HDLc (mg/dL): High density lipoprotein, n = 836; LDLc (mg/dL): Low density lipoprotein, n = 833; Non-HDLc (mg/dL): Total Cholesterol minus HDLc, n = 833; Total Cholesterol (mg/dL): n = 833; Triglycerides (mg/dL), n = 836

170 mg/dL, the sample was dichotomized by BFP into ‘appropriate’ and ‘excessive’ or high (Table 1). In both groups, cholesterol presented a Gaussian distribution (Figure 2) with a mean of 139.8 ± 27.9 mg/dL in the group with appropriate BFP and 144.9 ± 26.5 mg/dL in the group with excess body fat. Using the cutoff value of 170 mg/dL for high cholesterol, excess fat was associated with a three percentage point increase (from 14% to 17%) in the prevalence of high cholesterol in the study group.

Table 2. Lipid fractions of children and adolescents according to nutritional status, stratified by gender (Serra, ES, 2014-2016).

Variables	Nutritional Status [1]				
	Underweight	**Eutrophic**	**Overweight**	**Obesity**	**p-value**
Total Cholesterol					
Female	129.2 ± 24.7	144.0 ± 28.1	149.9 ± 28.8*	151.5 ± 26.7*	0.027
Male	134.0 ± 22.8	141.5 ± 27.3	145.9 ± 29.8	151.2 ± 30.0*┼╪	0.032
LDLc					
Female	62.4 ± 21.1	77.1 ± 24.3	86.2 ± 24.1*┼	88.0 ± 24.6*	0.000
Male	67.0 ± 18.6	76.4 ± 23.6	81.4 ± 25.7	88.6 ± 28.2*┼	0.001
Non-HDLc					
Female	78.8 ± 20.7	95.38 ± 26.0	104.1 ± 25.8*	108.1 ± 26.0*┼	0.000
Male	83.3 ± 21.0	93.48 ± 24.3	100.7 ± 27.1*	108.4 ± 27.6*┼	0.000
HDLc					
Female	50.3 ± 7.9	48.7 ± 9.7	45.8 ± 9.4	43.4 ± 9.8*┼	0.000
Male	50.7 ± 9.3	48.1 ± 9.1	45.3 ± 9.9	42.8 ± 9.4*┼	0.000

Test: One-way ANOVA followed by Tukey's test with a significance of $p < 0.05$, data are expressed as mean ± standard deviation (SD). 1 - Nutritional Status was given according to the Centers for Disease Control and Prevention 20. LDLc (mg/dL): Low density lipoprotein, n = 833; Non-HDLc (mg/dL): Total Cholesterol minus HDLc, n = 833; Total Cholesterol (mg/dL): n = 833, HDL (mg/dL): High density lipoprotein, n = 819. *p <0.05 vs. underweight; ┼p < 0.05 vs. eutrophy; ╪p < 0.05 vs. overweight.

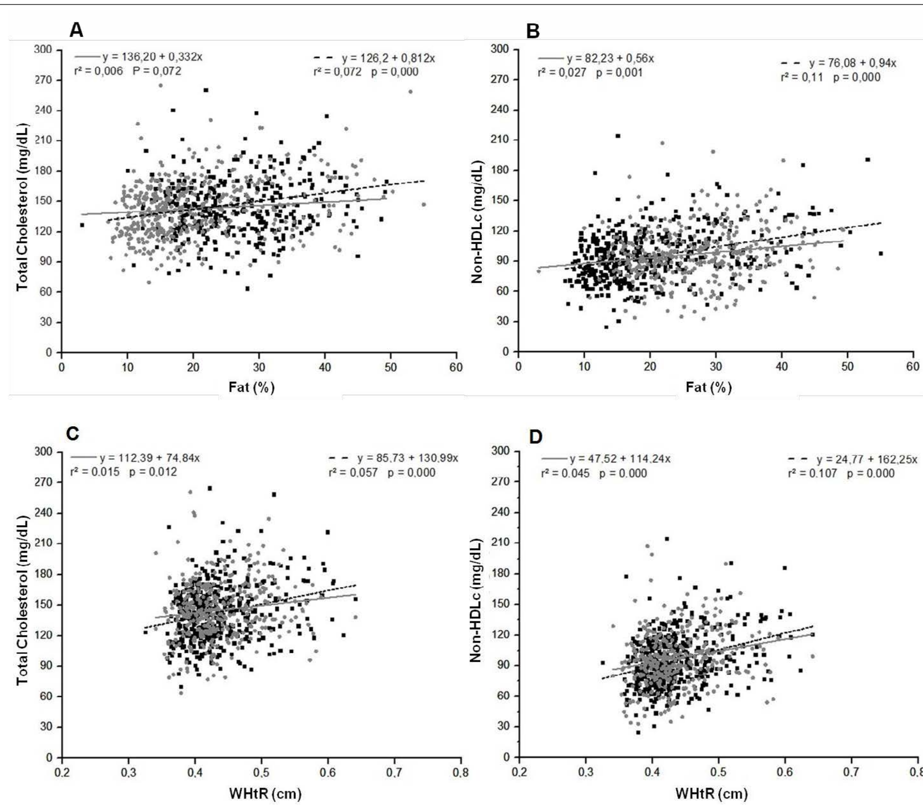

Figure 1. Association of the concentration of total cholesterol and non-HDL cholesterol with body fat percentage (BFP) and waist-to-height ratio (WHtR), stratified by gender.

Test: Linear Regression. TC: total cholesterol; Non-HDLc: Total cholesterol minus cholesterol associated with high density lipoprotein. The dashed line and the square symbol in black represent males; The smooth line and the round symbol in gray represent females.

Discussion

The development of obesity and the onset of dyslipidemia depend on both genetic predisposition and lifestyle habits, including diet, caloric expenditure with physical activity, among others. Increased incidence of obesity has been observed in practically all countries, including Brazil. Since obesity and dyslipidemia depend on common factors, the aim of this study was to quantify the impact of obesity on the occurrence of dyslipidemia in children and adolescents. For this, a study with a robust sample of schoolchildren covering the age group from 6 to 18 years was done. Data showed that inappropriate anthropometric measurements (WHtR and BMI) or excess body fat assessed by bioimpedance were positively associated with higher TC and Non-HDLc values, and negatively so with HDLc, in both boys and girls. This confirmed previous data in which it was observed that overweight/obese children who did not engage in physical activity had higher levels of TC[21]. It is important to stress that in this study, most of the children and adolescents engaged in physical activity at the Knowledge Station itself.

Our study also showed that among the three indicators of fat accumulation tested (BMI, WHtR, and BFP), the BFP estimated from bioimpedance showed the highest internal consistency, constituting the best predictor for identifying children and adolescents with an altered lipid profile. Similar results were found by other authors[1,11,22].

The present study showed an association between BFP and elevation of lipid fractions (TC and Non-HDLc), and this association was slightly stronger in males. The increase in non-HDLc in boys could be explained at an 11% level by the increase in BFP and 10.7% by the increase in WHtR. MiyazakiI et al.[23] showed that Non-HDLc has a higher sensitivity than LDLc in predicting cardiovascular risk in schoolchildren, and is also a better predictor of cardiovascular disease in adults. This better prediction stems from the fact that the LDLc and HDLc lipoprotein fractions have opposite effects on the deposition of cholesterol in the subintimal space of arteries and the generation of atherosclerotic plaques. Thus, non-HDLc would more strongly express the increased risk of atherosclerosis than would TC or the LDLc lipoprotein fraction.

Anthropometric changes, mainly visceral fat accumulation, may be early indicators of lipid profile alterations, according to Garcez et al.[12],

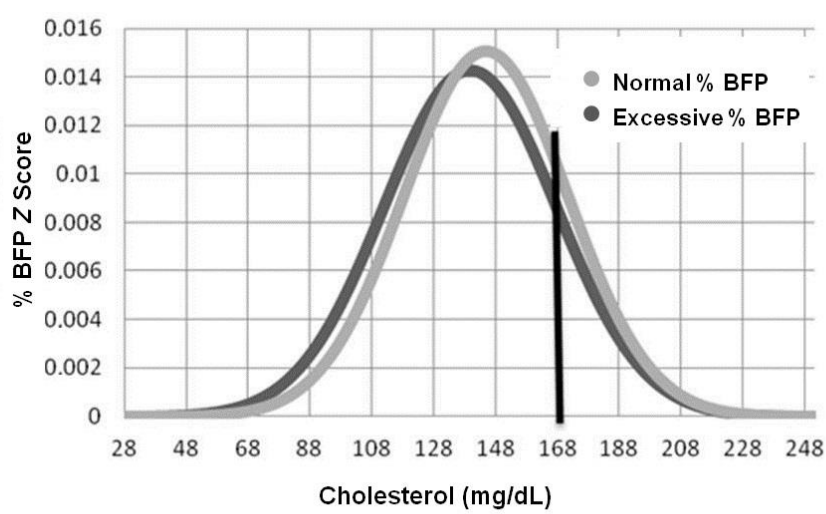

Figure 2. Cholesterol distribution in children and adolescents according to the Z score of normal (appropriate) or excessive (inappropriate) body fat percentage (BFP).

Density curves (adjusted for normal curves accepted by the Kolmogorov-Smirnov test) for individuals with normal (Normal BFP) or increased (Excessive BFP) body fat. The BFP Z score indicates the likelihood of the normal pattern being associated with each point in the cholesterol level. The vertical line indicates the cutoff point of 170 mg/dL (upper limit of normal for total cholesterol in children and adolescents).

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who found a positive correlation of body weight, WC, and BMI with the presence of dyslipidemia in adolescents and adults in São Paulo. These findings were similar to ours, verifying a positive correlation of the lipid variables LDL-c, TC, Non-HDLc with BMI and WC. In our study, however, we showed that this association was stronger with BFP calculated by bioimpedance and WHtR. Nevertheless, other studies have not found the same associations. Almeida et al.[24], studying students from Vitória (ES), did not detect significant associations between anthropometric measurements (WC and skinfold sum) and TC. One possible explanation for this finding would be the fact that the study was conducted on a narrower age range including children from 6 to 9 years old.

Inappropriate eating habits (high consumption of fast food, high fat and high sugar products), as well as low caloric expenditure in physical activity, contribute to fat accumulation and consequent weight gain. Thus, there is evidence of the beneficial effects of healthy lifestyle habits, including physical activity, on cardiovascular health. On the other hand, physical inactivity and inappropriate diet affect the overall health not only of adults but also of children and adolescents. Thus, excess body fat at this stage of life constitutes a risk factor for coronary disease in adulthood [5].

Regarding BFP, a study by Krielmler et al.[25] and a review by Jensen et al. [26] show that bioimpedance is a reliable, practical, and reproducible method for assessing body composition in children and adolescents, when compared to DEXA, considered the gold standard for this measure. Bioimpedance was also used and compared with DEXA by Lim et al.[27]. In this study, it was found that eight-electrode tetrapolar bioimpedance is more appropriate for this age group, compared to four-electrode tetrapolar bioimpedance, since the body compartments of children and adolescents are in modification. Thus, the eight-electrode bioimpedance yields results with good accuracy compared to other methods of measuring body fat.

Comparative studies of the association between body composition and plasma lipids between genders are scarce. Most studies only investigate the influence of gender on the distribution of the prevalence of dyslipidemia[21,28]. In our study we investigated not only the prevalence but also the association between different indicators of obesity and blood lipid values. This made it possible to detect small differences in the influence of fat accumulation on plasma lipids in boys and girls. Our data revealed that fat accumulation in boys has a greater impact on the appearance of a pro-atherogenic lipid profile compared to girls. One possible explanation for this finding would be the sexual dimorphism in body fat distribution. Wells[29] indicated that sexual dimorphism in body composition is evident starting from fetal life, persisting during childhood and increasing with puberty, and then with gender differences decreasing starting with the eighth decade of life. Fat distribution as a characteristic of gender was found by Neduhgadi and Clegg[30], showing that girls had higher concentration of body fat distributed in the subcutaneous space, while boys had more fat in the visceral region. These data coincide with our findings of a stronger association between changes in lipid profile associated with body fat in boys compared to girls.

Finally, our data showed that plasma cholesterol concentration follows a Gaussian distribution and that fat accumulation shifts the curve to the right, leaving the standard deviation virtually unchanged. Although the differences between curve areas (Figure 2) are relatively small (only 3% on the *Z* curves), our data indicate that excess fat would increase the likelihood of a child having cholesterol above the reference value (170 mg/dL) by 21%.

One of the limitations of this study pertains to the use of a non-representative sample of the student population, which would be essential in prevalence studies. However, in association studies it is unlikely that findings in non-representative samples will not be obtained in random samples. In addition, it is important to highlight the fact that the children and adolescents enrolled in the 'Knowledge Station' generally engage in regular physical activity because this strategy is adopted by the institution as a health promotion tool.

Conclusions

Considering the above limitations, it can be concluded that the BFP measured by octopolar bioimpedance proved to be the best anthropometric predictor of elevated total cholesterol and non-HDLc in children and adolescents, with this association being stronger in males. Thus, fat accumulation in this age group would lead to a more characteristic pro-atherogenic profile in boys, demonstrating the importance of monitoring body weight in childhood and adolescence as a mechanism for preventing cardiovascular disease in adulthood.

Collaborations

Contribution by each author: PR Oliosa participated in the data collection, analysis, interpretation, and writing of the work; DA Zaniqueli participated in the data collection, interpretation, and writing of the work; MCR Barbosa participated in the critical analysis of the data and the final revision of the manuscript; JG Mill participated in the conceptualization, planning, interpretation, and revision of the manuscript.

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