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Association of Severe Obesity with the Metabolic Profile of Adolescents and Adults

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Abstract

Objective: To evaluate, in adolescents and adults, the association of severe obesity with the extent of the metabolic changes shown.

Methods: This is an observational comparative study with a population consisting of adolescents with severe obesity and adults with class III obesity. The patients underwent anthropometric, biochemical and clinical evaluations. We evaluated the lipid profile (total cholesterol, LDL-c, HDL-c and triglycerides), C-reactive protein (CRP) and fasting glucose. Insulin sensitivity was assessed by calculating the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR). The evaluation of blood pressure was performed and the presence of hepatic steatosis (HS) by total abdomen ultrasound and metabolic syndrome (MS) were verified.

Results: The sample consisted of 128 individuals: 60 adolescents (G1) and 68 adults (G2). There were no significant differences between the groups as regards weight, BMI and WC. HOMA-IR showed significant difference between the groups, with higher means (p = 0.000) and prevalence (p = 0.008) in G2. There was a trend of higher means of blood glucose in adults (p = 0.070). G1 featured larger percentages of all components of the lipid profile with significant differences. High prevalence of HS, MS, blood pressure and CRP were observed in both groups with no statistical differences between them.

Conclusions: Adolescents were similar to adults in relation to the prevalence and severity of the anthropometric, clinical and metabolic changes analyzed. Such findings call attention to the effects of exposure to obesity in the progressive worsening of associated complications which can increase the chances of the emergence of cardiovascular diseases, increasingly early in the lives of individuals.

Keywords

Obesity, Adolescent, Metabolic syndrome, Insulin resistance

Introduction

Obesity stands out in the epidemiological scenario, as it is simultaneously a disease and a risk factor for the development of other diseases, particularly cardiovascular diseases (CVD) [1].

Despite the fact that its increased prevalence is widely distributed in different population segments, regardless of gender and age, in the last 15 years adolescent obesity has more than doubled in various regions of the world [2]. In Brazil, in males and females aged between 10 and 19 years, the frequency of excessive weight in the last 30 years has increased from 3.7% to 21.7% and from 7.6% to 19.4%, respectively [3].

The more intense and the earlier the disease develops, the greater its chances of permanence, with the consequent emergence of associated diseases. Obesity in adolescents is related to significant metabolic effects, dependent on its duration and severity [4].

The most severe class of obesity is associated with the progressive increase of morbidity and mortality and the reduced expectation of life [5]. In adolescents, severe obesity was the sub-group of the disease that showed the highest rise, with a prevalence of approximately 6% [6,7].

It has been recognized that obesity presents itself strongly associated with the development of risk factors for CVD, such as systemic arterial hypertension (SAH) [8]. Hyperinsulinemia is believed to be involved in the genesis of SAH in obese subjects to promote activation of the sympathetic nervous system and tubular reabsorption of sodium, which helps to increase the peripheral vascular resistance and arterial pressure [9].

The prevalence of type 2 diabetes mellitus (DM2) is related to obesity. This relationship leads to the hypothesis that the adipose tissue acts as an endocrine organ in the regulation of glucose metabolism and that insulin resistance (IR) plays an important role in this pathogenesis [10,11].

Obesity can be considered a state of chronic inflammation, with increasing concentrations of interleukin-1, interleukin-6 and tumor necrosis factor, stimulating the production of C-reactive protein (CRP) which in turn promotes the release of additional inflammatory cytokines [12]. The increase of these cytokines may cause the acceleration of atherogenesis and the increase of diseases

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associated with obesity, being visceral fat the biggest contributor to this process [12,13].

Nonalcoholic fatty liver disease (NAFLD) stands out in severe obesity and is quickly becoming one of the most common liver diseases worldwide and the main risk factor for progression to more severe stages of liver disease [14-16]. The prevalence of hepatic steatosis (HS), regarded as the first stage of NAFLD, in patients with severe obesity, ranges from 75% to 100% [17]. HS is strongly associated with metabolic risk factors that reflect metabolic syndrome (MS), obesity, IR and/or dyslipidemia [16,18].

Thus considering the high prevalence of obesity in adolescents and adults, in which severe obesity stands out, and considering that the exposure to this disease increases the chances for the early development of non-transmissible chronic diseases and increased morbidity and mortality, this study had as its objective to evaluate the association of severe obesity with the extent of the metabolic changes presented in these populations.

Material and Methods

This is a comparative observational study. The study population consisted of adolescents with severe obesity (G1), according to WHO estimates (2007) [19] and adults with class III obesity (G2), according to WHO estimates (1998) [20], attended for a first time, in a clinic specialized in the control of obesity, in the municipality of Rio de Janeiro. Data collection was conducted from March 2011 to December 2013.

This was a convenience sampling comprising the overall patients who, in the collection period, met the following inclusion criteria: adolescents aged between 10 and 19 years and 11 months with body mass index (BMI)/age in the percentile higher than 99.9 and adults aged between 20 and 60 years, with a BMI equal to or higher than 40 Kg/m². Exclusion criteria were: having undergone malabsorptive and restrictive surgeries, with malabsorptive intestinal syndromes, neoplasia, use of lipid-lowering drugs, use of hypoglycemic drugs, use of medication or vitamin supplement containing vitamin D, to be pregnant or a nursing mother, with kidney and liver diseases, except for hepatic steatosis.

Patients underwent anthropometric, biochemical and clinical evaluations. For anthropometric evaluation body weight was measured with the aid of an electronic platform scale with a 300 kg capacity with a 100 g variation. Height was obtained through the use of a stadiometer coupled to the scale, up to 200 cm long, with 0.1 cm accuracy, patient standing, barefoot, heels together, back straight position, and arms extended alongside the body. BMI was calculated through the ratio of body weight (kg) and the square of height (m²). Waist circumference (WC) was assessed with a flexible and inelastic measuring tape, 200 cm long and with a 0.1 cm variation. Measurement was carried out in the largest sagittal abdominal diameter, with the individual standing, relaxed abdomen, arms alongside the body, feet together and weight divided into both legs. Measurement was performed at the end of the expiration of the individual [21,22]. For adults, cutoff points were those estimated by WHO (1998) [20]. For adolescents, this cutoff point was based on the 90th percentile proposed by Freedman and co-workers [23].

All measurements were made in duplicate by a single trained evaluator, and 0.5 cm variations were accepted, and mean was calculated between the values. The collection of material for biochemical data analysis was conducted in a specialized laboratory which maintains an agreement with the clinic. The 10 mL blood samples were obtained by venipuncture, after a 12-hour fasting for the assessment of serum concentrations of the lipid profile (total cholesterol, LDL-c, HDL-c and triglycerides), CRP, glycemia, and fasting insulinemia.

The determination of fasting glucose was obtained by the enzymatic colorimetric method and the cutoff point adopted for inadequacy was equal to or higher than 100.0 mg/dL for adults and adolescents, and it was proposed by the International Diabetes Federation (IDF) [24]. Insulin sensitivity was calculated by the Homeostasis Model Assessment - Insulin Resistance (HOMA-IR) formula [25]. The cutoff point adopted for obese adults was higher than 2.9 [26] and higher than 3.16 for adolescents [27].

Serum concentrations of total cholesterol and triglycerides were analyzed using the enzymatic colorimetric method and the LDL-c and HDL-c fractions were analyzed using the selective inhibition method. The reference values adopted for adolescents and adults were in accordance with the V Brazilian Guideline of Dyslipidemia and Atherosclerosis Prevention (*V DiretrizBrasileira de Dislipidemia e Prevenção da Aterosclerose*) (2013) [28].

C-reactive protein (CRP) was dosed by the nephelometry method. The cutoff point adopted for featuring a high cardiovascular risk for adults was higher than 0.3 mg/dL [29], and higher than 0.5 mg/dL for adolescents [30].

For the diagnosis of hepatic steatosis (HS), total abdomen ultrasound was used [31]. The exam was conducted and interpreted by a single specialized doctor. The measurement of blood pressure was performed using the oscillometric technique with a semi-automatic digital arm device, validated and properly calibrated. The measurement was carried out after a 5-minute rest and was repeated twice, with a 1-minute interval between them. The mean of the two measurements was used. The reference adopted for classifying high blood pressure in adolescents and adults was in accordance with the VI Brazilian Guidelines for Hypertension (2010) [32]. For patients making use of antihypertensive drugs, the previous confirmed diagnosis of systemic arterial hypertension (SAH) was used for classification in the study rather than the one-off measurement of blood pressure. For the diagnosis of MS, were used the criteria proposed by the International Diabetes Federation (IDF) for adults [33] and adolescents [34].

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) for Windows version 17.0. The Kolmogorov-Smirnov test was applied to evaluate the symmetry of the distributions of the continuous variables. For data analysis, the distribution type of the sample was assessed, and later were performed the statistical tests for each type of distribution. When distribution was normal, the following tests were applied: the Student's t test, for comparison between continuous variables; for non-normal distribution, the Mann-Whitney test was used, and the chi-square test was used to assess the association between the categorical variables. The significance level adopted was 5% ($p < 0.05$).

This study was approved by the Research Ethics Committee of the Hospital Universitário Clementino Fraga Filho (Research Protocol n° 011/06). The inclusion of the patients was carried out upon signing of the informed consent either by the patient or his/her legal guardian, in accordance with the resolution n° 196 of the National Health Council (*Conselho Nacional de Saúde*).

Results

The sample consisted of 128 individuals, 60 belonging to the adolescent group (G1), being 63.3% female and 36.7% male, with mean age of 17.32 ± 1.35 years and 68 participants belonging to the adult group (G2), being 75% female and 25% male, with mean age of 39.01 ± 9.45 years.

In table 1 are shown the means and standard deviations of the anthropometric variables in G1 and G2. There were no significant differences between the groups regarding weight, BMI and WC.

Table 2 shows the means of the biochemical variables in G1 and G2. We can notice that the only variable with significant difference between the groups was HOMA-IR, with higher means in adults ($p = 0.000$). All the other assessed variables showed no differences between G1 and G2; however, there was a trend of higher means of glycemia in adults ($p = 0.070$).

In table 3, it can be seen that G2 showed higher prevalence of insulin resistance ($p = 0.008$). G1 showed the highest percentages

Table 1: Mean values of the anthropometric variables of adolescents and adults with severe obesity.

Variables	Adolescents (n = 60)	Adults (n = 68)	
	Mean ± SD	Mean ± SD	p-value
¹Age (years)	17.32 ± 1.35	39.31 ± 9.45	0.000*
Weight (kg)	129.49 ± 22.85	121.68 ± 16.53	0.270
¹BMI (kg/m²)	46.21 ± 7.01	44.66 ± 4.22	0.425
WC (cm)	124.22 ± 14.12	124.26 ± 11.35	0.983

*Values with statistical significance (p ≤ 0.005), T-Student Test, ¹Mann-Whitney Test, SD: Standard Deviation; BMI: Body Mass Index; WC: Waist Circumference.

Table 2: Mean values of biochemical variables in adolescents and adults with severe obesity.

BiochemicalVariables	Adolescents (n = 60)	Adults (n = 68)	p-value
	Mean ± SD	Mean ± SD	
¹Glicemia (mg/dL)	97.08 ± 15.07	107.22 ± 31.08	0.070
¹HOMA-IR	3.41 ± 1.54	5.15 ± 2.45	0.000*
Total cholesterol	199.18 ± 36.87	197.19 ± 35.84	0.757
HDL-c	46.7 ± 9.87	48.25 ± 31.01	0.384
LDL-c	122.47 ± 34.27	118.72 ± 31.01	0.517
¹Triglycerides	128.05 ± 49.15	153.60 ± 75.04	0.117
¹CRP (mg/dL)	1.78 ± 1.16	1.98 ± 1.71	0.843

*Values with statistical significance (p ≤ 0.005), T-Student Test, ¹Mann-Whitney Test, HDL-c: High Density Lipoprotein; HOMA-IR - Homeostasis Model Assessment - Insulin Resistance; LDL-c: Low Density Lipoprotein; CRP-c: Creative Protein.

Table 3: Clinical and laboratorial data according to age group in adolescents and adults with severe obesity.

Variables	Adolescents (n = 60)	Adults (n = 68)	p-value
	% (n)	% (n)	
Hyperglycemia	35 (21)	44.1 (30)	0.293
Insulinresistance	53.3 (32)	76.5 (52)	0.008*
Hypercholesterolemia	88.3 (53)	52.9 (36)	0.000*
High LDL-c	73.3 (44)	42.6 (29)	0.000*
Reduced HDL-c	43.3 (26)	20.6 (14)	0.006*
Hypertriglyceridemia	68.3 (41)	36.8 (25)	0.000*
High CRP	93.3 (56)	94.1 (64)	0.539
Hepatic Steatosis	80 (48)	79.4(54)	0.934
High bloodpressure	65 (39)	60.3 (41)	0.583
Metabolicsyndrome	60 (36)	63.2 (43)	0.707

*Values with statistical significance (p ≤ 0.005)

of changes in the overall components of the lipid profile (total cholesterol, LDL-c, HDL-c and triglycerides) with significant differences. The prevalence of other clinical and biochemical changes showed no significant differences between the groups.

The high prevalence of changes in CRP, found in over 90% of the individuals in both groups, stands out. HS was present in 80% of the individuals in G1 and 79.4% in G2. Elevated blood pressure values were found in 65% in G1 and 60.3% in G2, with no significant differences between them. Metabolic Syndrome was observed in 60% of adolescents and in 60.3% of adults, and no significant differences were found between the groups as well.

Discussion

In the current study, we observed that the overall adolescents and adults showed mean values of WC related to the classification of very high risk for CVD according to references for each age group, findings shared by other studies with severe obesity in both groups [4,12,35,36].

WC is a good indicator of metabolic disorders, because it seems to better predict the visceral adipose tissue and it strongly correlates with BMI and may be even more sensitive to assess risks associated with obesity [37,38] and, in addition, presents an association with the development of CVD and metabolic diseases [39].

High percentages of the biochemical and clinical changes evaluated were found in both groups. Other studies also found association of severe obesity with changes in lipid and glucose metabolisms and in blood pressure [4,40].

HOMA-IR, which expresses IR, presented 53.3% of inadequacy in obese adolescents, a value lower than the one found by other studies, whose prevalence of inadequacy were 70% [41] and 100% [35]. Another study found HOMA-IR values 11.7 times higher in obese individuals than the average of eutrophic adolescents. According to Bereket and Atay [42], IR is present in approximately 30% of obese adolescents. With respect to G2, high prevalence and mean of HOMA-IR (76.5%; 5.15) were found, which is very similar to the results found by Adams and Hewison, whose mean value was 5.1 [43].

IR and high concentrations of fasting plasma insulin appear to be the early signs for the development of DM2. In obese subjects, due to IR, the pancreatic ß cells increase the production and secretion of insulin as a compensatory mechanism, while glucose tolerance remains normal. This state remains the same for some time, until there is a decline in insulin secretion and, consequently, a decrease in glucose tolerance. Therefore, the increase in the production of endogenous glucose occurs in the late stage of development of DM2 [44].

The mean of blood glucose in G1 was within appropriate values (97.01 ± 15.07 mg/dL), but those values were adjacent, a result similar to that found by Teeple and co-workers (96.4 ± 12.2 mg/dL) [12]. In G2 this mean was above the appropriate value (107.22 ± 31.08 mg/dL), very close to the mean (109.6 ± 20.05 mg/dL) found by Adams and Hewison [43].

Although blood glucose did not present a significant increase in both groups, IR showed high means and high prevalence, demonstrating that individuals who have not yet present DM2 are at an increased risk for the development of this disease. We also observed that HOMA-IR was significantly higher in adults, suggesting a possible progression of this condition according to age. This finding calls attention to adolescents, because the process of the development of DM2 in childhood and adolescence seems to evolve faster than in adults [45].

Abnormalities in lipid profiles are present in significant number of obese individuals, especially in severe obesity [37]. In the present study, the prevalence of elevated total cholesterol was significantly higher in the adolescent group (88.3%), compared to the adult group (52.9%). This prevalence was higher than the prevalence found in other studies such as the study of Faria and co-workers [46] in which 57% of elevated total cholesterol was found in obese adolescents, but the cited study was conducted with all classes of obesity.

There is high correlation between hyperlipidemia and increased cardiovascular risk in adults; however, this association is not clear in adolescentes [47]. Although both groups presented changes in the overall components of the lipid profile, the presence of abnormalities was significantly higher in the adolescent group. Such findings are important if we consider that the normalization of these changes will reduce the risk of CVD in adult life [12].

The systemic inflammation present in obesity suffers a progressive increase from the early stages of the increase in body fatness [48]. Hence, atherogenic, thrombogenic and inflammatory metabolic changes contribute to children and adolescents with abdominal obesity having higher risk for the development of coronary heart disease in adult life [49].

The mean of CRP in this study was 1.78 ± 1.16 mg/dL in G1, higher than the mean found by Holterman and co-workers in adolescents with severe obesity (1.02 mg/dL) [35]. Similarly, G2 presented mean of CRP (1.98 ± 1.71 mg/dL) higher than the one found in another study with adults with class III obesity (1.29 mg/dL) [13]. In addition, it is worth highlighting that a large percentage of individuals showed CRP value above the reference values, according to the age group studied (93.3% in G1 and 94.1% in G2), who were

classified as presenting high cardiovascular risk. The current study shows that severe obesity, regardless of age, is associated with a component having a significant systemic inflammation, with mean values slightly higher in obese adults.

A high prevalence of HS was found in G1 (80%) and in G2 (79.4%). Fish and co-workers [50] found prevalence ranging between 74 and 90% in adults with class III obesity. In adolescents with severe obesity, a study found 53% of HS [42]. As reported by literature, it is known that HS is strongly associated with obesity, IR and dyslipidemia [16,18]. In situations of IR, fat cells and muscle show preference for lipid oxidation and a high proportion of concentrations of free fatty acids, released from fat cells, is captured by the liver, promoting HS [51]. In addition, evidence indicates that HS is not just a simple consequence of IR, but also plays a causal role in its genesis and progression. The intracellular lipid content in the liver reduces the clearance of insulin, resulting in hyperinsulinemia [52]. In obese adolescents, HS is considered the most common cause of liver disease [35]. IR, evaluated by the HOMA-IR, which also featured high percentage of change in the present study, is considered a predictor of the progression of this disease [38].

HS can be asymptomatic; however, it has the potential to progress to hepatitis, cirrhosis and hepatocellular carcinoma, with consequent increased mortality [35,42]. We could not assess the degree of this steatosis, which can be considered a limitation of the present study, as the onset of the disease and the maintenance of obesity may be predictors of its progression. Therefore, even having found high prevalence of HS among the group of adolescents in our study, one should consider that adults may show greater severity of this disease, as it has a progressive nature.

High blood pressure was identified in 60.3% of adults, a value similar to that found by Nordstrand and co-workers [36] (68%). One study showed that over 75% of SAH cases are assigned directly to obesity [47]. This comorbidity is considered rare in adolescents, but it has been increasing continuously. Moreover, a three times higher risk of SAH has been observed in overweight and obese children and adolescents, compared to eutrophic individuals [53]. Literature presents a few reports regarding the presence of SAH in adolescents. Possibly this is due to the fact that the studies do not discriminate the degree of obesity found. The present study showed prevalence of high blood pressure changes in this population (65%), and it must be considered that, in the presence of obesity, changes in blood pressure tend to remain and worsen in adulthood.

The use of different criteria for the diagnosis of MS makes difficult the comparison of prevalence between different studies. Even so, approximately 1/4 of the adult world population presents MS [54-56].

Visceral obesity and IR seem to be the most important factors for the development of MS. The accumulation of visceral fat is related to the progression of atherosclerosis and to the increased secretion of pro-inflammatory cytokines from the adipose tissue [57]. One study showed that CRP values are higher in individuals with MS in comparison to individuals without this syndrome (1.0 mg/dL × 0.3 mg/dL), independent of BMI values [58].

In a study conducted with obese adolescents, using the same diagnostic criteria of this study for MS, a prevalence of 50% was observed in the sample evaluated [59]. Considering that MS is an association of metabolic changes related to several adverse health outcomes, including DM2, CVD and different types of cancer, among other diseases, the equally high prevalence both in G1 (60.0%) and G2 (63.2%) presented by the current study, should be valued, in view of the consequences of MS for the health of individuals, especially in the early stages of life.

In the present study, we highlight the fact that the adolescents showed severe metabolic changes, similar to those observed in obese adults. Considering that for 2035 it is estimated an increased prevalence of coronary diseases ranging from 5 to 16%, with over 100,000 cases attributed to the increase of obesity in adolescents of today [42], we point out the need for early intervention, focusing on prevention, in order to minimize its progression and the emergence of adverse results arising from excessive adiposity.

Conclusion

The analysis of the most severe class of obesity showed that adolescents were similar to obese adults with respect to the prevalence and severity of anthropometric, clinical and metabolic changes studied. Such findings call attention and warn of the effects of exposure to obesity in the progressive worsening of the associated complications, which can increase the chances of the emergence of CVD, increasingly early in the lives of individuals.

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Ethical Statement

This study was approved by the Research Ethics Committee of the Hospital Universitário Clementino Fraga Filho (Research Protocol n° 011/06). The inclusion of the patients was carried out upon signing of the informed consent either by the patient or his/her legal guardian, in accordance with the resolution n° 196 of the National Health Council (*Conselho Nacional de Saúde*).

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