Evaluation of cardiovascular risk in obese children and adolescents attended at a Level III hospital in Posadas, Misiones, Argentina

Evaluación del riesgo cardiovascular en niños y adolescentes obesos atendidos en un hospital de Nivel III de Posadas- Misiones

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Abstract

Argentina suffers from an epidemic of non-communicable chronic diseases and a population with cardiovascular risk factors, particularly obesity. In this work, the cardiovascular risk in obese children and adolescents who attended a level III hospital in the city of Posadas, between September 2018 and January 2020, was studied. Eighty-one patients were included, age 10 (2-15) years; 51% female. Body mass index was calculated, blood pressure was measured and serum HDLc, LDLc, triglycerides and glucose were determined. A questionnaire was completed on family history of cardiovascular disease, physical activity, tobacco and alcohol consumption. The presence of metabolic syndrome (SAP) according to Argentine Pediatric Society criteria and cardiovascular risk (Alustiza´s score) were identified and the relationship between them was established. Results: severe obesity: 43 (53%) patients; biochemical or clinical family history 27 individuals (33%); insufficient physical activity: 57 (70%) patients; tobacco and/or alcohol consumption: absent; blood pressure >p95: 11 individuals (14%). Fifty one patients (63%) had some dyslipidemia, 4 (5%) had hyperglycemia; metabolic syndrome was observed in 26 (32%) and 25 (31%) at medium/high cardiovascular (CV) risk. No association was found between CV risk by Alustiza score and metabolic syndrome. Since the pediatric population has cardiovascular risk factors and components of metabolic syndrome, it is important to search for and validate scores to measure this risk.

Key words: Cardiovascular risk; Alustiza score; Metabolic syndrome; Obesity.

Resumen

Argentina, padece una epidemia de enfermedades crónicas no transmisibles y una población con factores de riesgo cardiovascular, particularmente obesidad. En este trabajo se estudió el riesgo cardiovascular en niños y adolescentes obesos que concurrieron a un hospital de nivel III de la ciudad de Posadas, entre septiembre 2018 y enero 2020. Se incluyeron 81 pacientes, edad 10 (2-15) años; 51% mujeres. Se calculó el índice de masa corporal, se midió la presión arterial y se determinaron los niveles de HDLc, LDLc, triglicéridos y glucosa. Se realizó un cuestionario sobre antecedentes familiares de enfermedades cardiovasculares, actividad física, consumo de tabaco y alcohol. Se identificó la presencia de síndrome metabólico (SAP) y el riesgo cardiovascular (puntaje de Alustiza) y se estableció la relación entre ellos. Resultados: obesidad grave: 43 (53%) pacientes; antecedentes familiares bioquímicos o clínicos 27 individuos (33%); actividad física insuficiente: 57 (70%) pacientes; consumo de tabaco y/o alcohol: ausente; presión arterial >p95: 11 individuos (14%). Presentaron alguna dislipidemia 51 pacientes (63%), hiperglucemia 4 (5%), síndrome metabólico 26 (32%) y riesgo cardiovascular medio/alto 25 (31%). No se encontró asociación entre riesgo cardiovascular y síndrome metabólico. Debido a que la población pediátrica posee factores de riesgo cardiovascular y componentes del síndrome metabólico, es importante establecer y validar puntajes para medir dicho riesgo.

Palabras claves: Riesgo cardiovascular; Puntaje de Alustiza, Síndrome metabólico; Obesidad.

Introduction

In western societies, cardiovascular diseases (CVD) are one of the leading causes of death in adults. Argentina, like most countries, suffers from a serious epidemic of chronic noncommunicable diseases (NCDs), particularly CVD (1).

Recent research has shown that the process of atherosclerosis (the anatomopathological substrate of CVD) and the appearance of risk factors associated with its development, begin in childhood and are related early to obesity and MetS (2,3) whose identification and distribution in the population is extremely important given that there is evidence that, by taking actions against them, the risk of CVD can be significantly reduced.

When dealing with pediatric populations, it is essential to be able to detect MetS at the right time, since in this period of development it is possible to implement preventive measures to avoid irreversible consequences (3).

The term MetS refers to a group of risk factors for CVD, including abdominal obesity, dyslipidemia, glucose intolerance and hypertension (4,5, 6). However, in children, a consensus definition of MetS has not yet been universally accepted (5-7).

Among the risk factors that increase the possibility of having MetS are age (increases with age), ethnic origin, central predominant obesity, diabetes, and insulin resistance, being the child of a diabetic mother or with gestational diabetes, low (<2.5 kg) or high (>4 kg) birth weight, very rapid weight regain in the first months of life, early initiation of complementary feeding (before 6 months of age), feeding with industrialized milk in the first 6 months of life, being the child of parents with obesity, not doing any physical activity, spending more than two hours in sedentary activities, having a family history of T2D, hypertension (HTN), acute myocardial infarction (AMI) or CVD, eating more than twice a week away from home, habituated consumption of drinks with high sugar content and low milk consumption (8).

Children and adolescents have an elevated cardiovascular (CV) risk depending on the level of physical activity performed, age, gender, family history, alcohol and tobacco consumption, body mass index (BMI), blood pressure and/or lipid levels. Alustiza et al. propose to assess this risk by calculating a score that takes these parameters into account and that has been validated in the Chilean population (9,10).

The National Survey of Risk Factors (ENFR) (11) conducted in 2018 in Argentina showed the following results in an adult population: 40.6% presented elevated blood pressure (HTN); obesity increased from 20.8% to 25.4% in just 5 years; low physical activity increased from 54.7% to 64.9%; the prevalence of high blood glucose or diabetes increased from 9.8% to 12.7%, and 30.7% of individuals recorded elevated cholesterol (higher or equal to 200 mg/dL); such data show the importance of identifying at early age individuals with cardiovascular risk factors.

By using appropriate diagnostic criteria, it is possible to detect the presence of MetS in the population and to evaluate CV risk, by calculating the Alustiza score, thus identifying those individuals at greater risk of future health complications. The aim of the study was to analyze cardiovascular risk in obese children and adolescents attending a level III hospital in the city of Posadas between September 2018 to January 2020.

Materials and methods

Type of study

A descriptive crossover study was made.

Population

Eighty-one obese children and adolescents were included without dietary restriction assisted at Outpatient Clinic Service, Nutrition Services, Provincial Pediatric Hospital "Dr. Fernando Barreyro" from September 2018 to January 2020. Patients with endocrinological disorders, neoplasms, renal disease or liver disease, genetic disorders or treated with medication that could affect blood pressure (BP) were excluded.

Doctors filled out an approved form for each patient containing information obtained from the patient anamnesis: personal data such as surname and first name, ID number, gender, age, weight, height, waist circumference (WC), BP, and laboratory data. In order to calculate Alustiza score patients were asked about family history, exercise, smoking and alcohol consumption. Subsequently, obese children were classified according to whether or not they had MetS and the CV risk was calculated.

Obesity: was diagnosed based on the Body Mass Index calculated as BMI = weight (kg) / height^2 (m^2). Weight was obtained from a standing patient, wearing underwear and barefoot, using standing scales with a 0.100 kg resolution. Height was measured with a standing patient, barefoot, Frankfort plane position, using a tape measure attached to the wall. BMI was categorized according to the Z score (12,13): overweight Z between +1 and +2 or percentile 85-96; obese Z ≥ 2 or percentile ≥ 97 and Z ≥ 3 or percentile ≥99: severe obesity.

Cardiovascular risk (CV) score

It was calculated from the Alustiza score using Tables 1 and 2(9).

Table 1: Alustiza's score for the different variables.

Variable	Value	Score
Age	2 – 5 years	0 points
	6 – 12 years	2 points
	>13 years	3 points
Gender	Female	0 points
	Male	2 points
Familiar backround	None	0 points
	(+) Biochemical	2 points
	(+) Clinical	4 points
Exercise	Sufficient > 2 hrs/day & TV < 3 hrs/day	0 points
	Insufficient < 2 hrs/day & TV > 3 hrs/day	1 points
Tobacco / Alcohol	No	0 points
	Yes	1 points
Obesity (BMI)	<Percentile 95	0 points
	>Percentile 95	1 points
Blood Pressure (BP)	<Percentile 95	0 points
	>Percentile 95	1 points
Cholesterol (mg/dL)	TC: 200-220, LDLc 110-130	1 points
	TC: 221-230, LDLc 131-160	2 points
	TC: 231-280, LDLc 161-190	3 points
	TC: > 281, LDLc > 191	6 points

References: TC: total cholesterol; LDLc: low-density lipoprotein cholesterol; BMI: body mass index.

Table 2: Alustiza's score.

Total, points	19
Low Risk	0-6
Medium Risk	7-8
High Risk	9-19

Metabolic syndrome: criteria used for diagnosis of pediatric metabolic syndrome were based on those used for adults (Adult Treatment Panel III, ATP III) and accepted by Argentine Society of Pediatrics (2005) (12) (12): TG ≥110 mg/dL, HDL ≤ 40 mg/dL, WC ≥ p90; glycemia ≥110 mg/dL and blood pressure ≥ p90.

Waist circumference: was measure following World Health Organization (WHO) criteria, using an inextensible flexible millimeter tape measure with standing patient, anatomical position, with both arms down to their sides, after exhalation, bringing the tape all the way around the abdomen at the midpoint between iliac crest and tenth rib (12-14).

Blood pressure: the measurement was performed using an aneroid sphygmomanometer on the right arm, by convention in pediatrics, with an ergonomic cuff appropriate to the size of the arm (covering 80-100% of the arm circumference) (15).

Definition of hypertension: systolic and/or diastolic blood pressure ≥ p95 (for age, gender, and height); prehypertension: systolic and/or diastolic blood pressure ≥ p90 and < p95 (for age, gender, and height) or blood pressure values ≥ 120/80 mmHg measured on three separate occasions (15).

Biochemical determinations

Samples were obtained from patients under basal conditions and fasting for 8 hours. Determinations were made as detailed below:
- Blood glucose (BG): enzymatic method based on the hexokinase/glucose 6-phosphate dehydrogenase reaction. Variation Coefficient, VC 3.72%.
- Total cholesterol (TC): enzymatic method based on cholesterol oxidase/peroxidase reaction. VC 1.89 %.
- Low density lipoprotein cholesterol (LDLc): homogeneous method for direct measurement based on 2 detergents and cholesterol oxidase/peroxidase. VC 3.21 % When triglyceride (TG) levels are < 200 mg/dL, the Friedewald formula is applied: LDLc = TC (mg/dL) - [HDLc (mg/dL) + TG/5 (mg/dL)].
- Triglyceridemia (TG): enzymatic method based on the glycerol kinase/peroxidase reaction. VC 1.87%.
- High density lipoprotein cholesterol (HDLc): direct enzymatic method, VC 2.01%

All determinations were made in Dimension RxL Max-Siemens autoanalyzer.

Dyslipidemia: it was diagnosed when the patient presented one or more of the following alterations of the lipid profile: TC: ≥200mg/dL, LDLc ≥ 130mg/dL, TG: 0 to 9 years old ≥100mg/dL and from 10 to 19 years old ≥130mg/dL and HDLc <40mg/dL (16).

Family history: categorized as absent (no records); biochemical positive (when one or both parents had total cholesterol > 240 mg/dL) and clinical positive (when one or both parents or grandparents aged less than 55 had a history of angor, myocardial infarction or cerebral or peripheral vascular disease.

Statistical analysis

A descriptive analysis of the variables evaluated was performed, expressing the results as proportions and their corresponding 95%CI.

Comparing the proportions between groups, chi-square test of independence was applied using an available free software statistical program and values of $p < 0.05$ were considered statistically significant.

Ethical considerations

This study is part of the research project "Cardiovascular and metabolic risk factors in children and adolescents attending public health services", which protocol was approved by the Research Ethics Committee of Pediatric Hospital Dr. Fernando Barreyro. All the samples were classified with a code to preserve the patient's identity and the information obtained was confidential following the ethical, legal and juridical

regulations established by National Bioethical Standards -Disposition 5330/97 of the National Administration of Drugs, Food and Medical Technology (ANMAT)- and International -Nuremberg Code, Declaration of Helsinki and its modifications.

Results

The median age of the sample was 10 (2-15) years, of which 41 (51%) were women. Family history in parents was distributed as follows: biochemical positive: 13 individuals (16%), clinical positive: 14 (17%) and no history: 54 (67%).

When patients were asked about personal habits, 24 (30%) children and adolescents exercised sufficiently and 57 (70%) insufficiently. No patients with tobacco and/or alcohol consumption were found.

Regarding BMI, 97% of the population sample studied (79 patients) were above the 95th percentile, corresponding to 1 point according to Alustiza score (39 females and 40 males); according to Z score, 38 patients (47%) were obese and 43 (53%) were severely obese.

Abdominal obesity (WC ≥p90) was present in 79 (97%) children and adolescents.

Concerning blood pressure, 11 individuals (14%) presented values above the 95th percentile, corresponding to 1 point of the Alustiza score; according to MetS criteria, 20 individuals (25%) had blood pressure ≥p90.

Referring to lipid abnormalities, according to Alustiza, 56 patients were found with no alterations, 25 children and adolescents (31%) had a score between 1 and 3.

In connection with to dyslipidemia diagnostic criteria 30 (37%) patients were found to have normal values and the rest, (51 patients, 63%) were distributed as follows:
- 14 (17%) patients only with TG elevated for age.
- 16 (19%) patients only with HDLc <40 mg/dL.
- 3 (4%) had both TC ≥200 mg/dL and LDLc ≥130 mg/dL.
- 7 (9%) HDLc <40 mg/dL and elevated TG for age.
- 8 (10%) TC ≥200 mg/dL, LDLc ≥130 mg/dL and TG elevated for age.
- 3 (4%) with the 4 lipid values altered.
- According to MetS criteria:
- 19 (23%) patients have only HDLc ≤ 40 mg/dL.
- 22 (27%) only TG ≥110 mg/dL.
- 13 (16%) HDLc ≤ 40 mg/dL and also TG ≥ 110 mg/dL.

Four patients (5%) were found with hyperglycemia criteria for MetS.

26 (32%) of total obese patients studied presented MetS and 55 (68%) did not meet diagnostic criteria.

Based on the Alustiza score, the classification shown in Table 3 was obtained.

Table 3: Classification of cardiovascular risk according to Alustiza score in obese patients with and without metabolic syndrome (n=81).

Alustiza Score	Obese Patients n	Patients with MetS n (%)	Patients without MetS n (%)
Low	56	16 (29)	40 (71)
Medium	10	3 (30)	7 (70)
High	15	7 (47)	8 (53)
Total	81	26	55

References: MetS: Metabolic Syndrome, Chi-Square 1,800, p =0.4065.

These results indicate that most patients have low CV risk; 29% shown MetS. However, 25 patients with medium/high CV risk, 10 (40%) had MetS. Statistics significant relation between CV risk and MetS (p=0,4065) was not found.

Discussion

Cardiovascular diseases are not one of the leading causes of death in children and adolescents, but it is the leading cause of death in adults in several countries (17). In childhood, general obesity and visceral adiposity are associated with increased cardiovascular and metabolic risk, regardless of the weight the child reaches in adulthood, which makes them one of the most serious public health problems of the 21st century (17,18); for this reason, the obese population was selected for the study. Considering the population studied, 27 patients (33%) had some type of clinical or biochemical family history of CV disease; Balza et al. (19) in a study of 136 Venezuelan adolescents, 20 had overweight or were obese; 37 (27%) had family history of CV diseases. If both parents had CV diseases before 55-year-old, children have 50% more of CV risk. In addition, excess weight is the most prevalent CV risk factor and the one that shows the least improvement when CV disease is already declared (20). Since family history is a nonmodifiable risk factor, individuals with a family predisposition to cardiovascular disease should focus their efforts on controlling the factors on which it is possible to act, such as obesity. In our population, 57 patients (70%) did not engage in sufficient physical activity. In a study carried out to evaluate CV risk in obese Mexican children (17), it was found that none of the patients engaged in physical activity, whereas in Honduran children and adolescents (18), the prevalence of inactivity was 64%. The work of Cárdenas-Cárdenas et al. (22), carried out with 1,309 Mexican participants aged 5 to 17 years who were overweight and obese, reinforces the concept that cardiometabolic risk decreased when physical activity increased from mild to intense. Obesity during childhood is influenced by genetic, epigenetic, behavioral and environmental factors. Among these, behavioral factors such as sedentary lifestyle are more easily modifiable during childhood and adolescence. It has been reported that aerobic exercise helps to reduce obesity levels and

that lifelong exercise habits may be largely determined by childhood experiences (22, 23). The high levels of physical inactivity observed in our population highlight the need to promote sports activities in the pediatric age group to prevent overweight and obesity.

In the population studied there were no patients with tobacco and alcohol consumption, similar to what was found by Escudero-Lourdes et al. in Mexico (17). This is important because currently a large proportion of preschoolers and schoolchildren present polyconsumption behaviors which are usually added to sedentary lifestyles (24). Tobacco and alcohol consumption before reaching physical, psychological and social maturity, called early consumption, is a particularly harmful behavior for the individual and, consequently, represents a serious problem for health systems worldwide (25, 26).

According to the Alustiza score for obesity, 79 individuals (97 %) were classified with score 1 (BMI> p95); this is in agreement with the findings of Escudero et al (17) in a Mexican population. Applying the Z-score, we found 43 (53 %) severely obese. In a study conducted in Ontario, Canada, in the period 2004 to 2015 (27), according to Z-score, of a total of 2,063 obese children and adolescents evaluated, 24 % presented severe obesity, while another study conducted in Buenos Aires, Argentina (28) and applying the same score, of 197 prepubertal obese children, 17.8 % possessed its severe classification. Our population presents a high percentage of severe obesity, which emphasizes the importance of early medical consultation when children gain weight, in order to determine if they are within an unhealthy range. Obesity could cause cardiovascular disease through mechanisms such as subclinical inflammation, endothelial dysfunction, increased sympathetic tone, atherogenic profile, thrombogenic factors and obstructive sleep apnea (8).

Abdominal waist circumference has been recognized as the best clinical indicator of visceral fat accumulation and thus WC may be a more appropriate measure in terms of MetS and cardiometabolic risk (14). The prevalence of patients with WC ≥ p90 in the present study (97%) was similar to that found by Armoa et al. (94.1%) (29) and higher than that found by Burrows et al. (76.3%) (30).

Another parameter that is altered in pediatric obesity is blood pressure. A study with 1,555 children aged 6 to 9 years in Portugal (31), showed that the prevalence of normal-high BP and HTN was positively associated with the increase in body weight. Ochoa-Avilés et al (32), in Ecuadorian adolescents, found that the most prevalent CV risk factors were dyslipidemia (34.2 %), abdominal obesity (19.7 %), overweight (18.0 %), HTN (6.2 %) and obesity (2.1 %), which led them to consider HTN as an important risk factor linking obesity with the development of CV disease in adults. In the present study, according to the Alustiza score, 11 patients (14%) presented BP> p95, results that agree with those obtained

by Escudero et al (17). These patients are classified as hypertensive according to the Consensus on risk factors for cardiovascular disease in pediatrics (15). Our values differ from those of a study performed in the province of Corrientes, Argentina (33), with 112 obese children, in which a prevalence of 32.1% was found. Sorof et al (34), in a population of 5,120 children aged 13.5 ± 1.7 years, of different ethnicities, found a prevalence of HTN of 4.5%, which was clearly and strongly determined by higher BMI percentiles in the population studied. The application of the criteria for MetS made it possible to identify 9 children and adolescents (11%) with prehypertension, a category at risk of developing HTN in adulthood (15).

It is especially important to detect alterations in blood lipid levels in childhood and adolescence, since dyslipidemias constitute an important risk factor for cardiovascular pathologies, especially in patients whose clinical history indicates that they are susceptible to higher risk, such as a family history of parents with total cholesterol levels above 240 mg/dL or the presence of arteriosclerosis at an early age in first-degree blood relatives; it is also considered that the child or adolescent increases the risk if he/she is obese (16, 35). Dyslipidemias are lipoprotein disorders characterized by abnormal values of some of the lipid fractions in the blood as a result of genetic and/or environmental alterations such as diet and physical activity (16). In a study carried out in Buenos Aires, Argentina (36), out of 139 overweight or obese children and adolescents, 11.5% presented hypercholesterolemia and 10.1% elevated LDLc. In our work, only 3 (4%) were found with hypercholesterolemia and high LDLc; however, 11 (14%) patients had 3 or 4 lipidic values altered, probably because our patients were obese. The Alustiza score only considers TC and LDLc; however, Escudero et al (17) in their work in Mexican children observed HDLc levels below what is considered normal, as well as altered triglyceride levels. In our population, 16 (19 %) patients had HDL≤ 40 mg/dL, 14 (17%) elevated TG for their age, and 7 (9%) both parameters altered; dyslipidemia was found in the sample.

Avila Flores and Nava Uribe (37) found in overweight and obese Mexican children that dyslipidemia, appeared in 52,6 % of them, especially with hypertriglyceridemia (46,4%) and in a study performed in Buenos Aires, Argentina (36), from 139 children and adolescents, 108 with obesity, a frequency of dyslipidemia of 52.3 % was found. According to MetS criteria, 22 (27 %) had TG ≥ 110 mg/dL, 19 (23 %) HDL≤ 40 mg/dL, and 13 (16%) HDLc decreased and also TG elevated, similar to what was found by Armoa et al. (29) in the same population in 2010.

Impaired fasting blood glucose as a component of MetS in this study has a low frequency of occurrence (5 %); similar to that reported by Armoa et al. (3.9 %) and Hirschler et al. (6 %) in Argentina (30, 38), Burrows et al. in Chile (3.7 %) (30) and Cáceres et al. (8.2 %) in

Bolivian children (39). In a study carried out in Misiones, Argentina (40) on 153 obese children and adolescents, 7.8 % presented hyperglycemia. These children and adolescents who present hyperglycemic states should have a continuous follow-up to evaluate the appearance and development of type 2 diabetes in the future, since one of the major complications associated with childhood obesity is the presence of this disease (41).

As a recommendation for reducing the modifiable factors that influence obesity and therefore cardiovascular risk, the study "Identification and prevention of diet and lifestyle-induced health effects in children"- IDEFICS recommends increasing daily levels of physical activity, reducing the time spent watching television, increasing the consumption of fruits, vegetables and water, strengthening the parents-child relationship and establishing adequate sleep duration patterns (41).

The parameters waist circumference, glycemia, blood pressure, triglycerides and HDL-cholesterol altered individually represent a health problem by themselves, but the grouping or association of their alterations is identified as metabolic syndrome (MetS), a name established by the World Health Organization (WHO) in 1998 based on the premise that the grouping of these risk factors is predictive of cardiovascular disease (8).

The population studied had some component of MetS, so the prevalence was calculated by applying the diagnostic criteria accepted by the SAP; the prevalence of MetS obtained was 32%, similar to that reported by Armoa et al (35.3%) in Misiones (29). Hirschler et al. (38) in obese children and adolescents in the city of Buenos Aires, obtained a prevalence of 21.9%. Using another diagnostic criterion (Cook's criterion), there are data on the prevalence of MetS in obese Chilean children and adolescents (26.8%), obtained by Burrows et al. (30) and in the town of Campo Quijano-Salta, the prevalence was 57% (2). The results obtained by means of the Alustiza score in our study have shown that 25 children and adolescents (31 %) have a medium/high cardiovascular risk, 40% with MetS. However, it could not be demonstrated in this population that MetS meant a higher CV risk. Escudero-Lourdes et al (17), in a study in which 100 records of obese Mexican children were reviewed, found moderate and high CV risk in 74 (74%) of them. Arnaiz et al (10) applying the same score in 209 Chilean schoolchildren (61 obese), found medium/high cardiovascular risk in 36 children (17%). In agreement with the present study, no significant association was found between the CV risk score applied and the markers of subclinical atherosclerosis measured in this study.

Conclusions

Since the population studied has cardiovascular risk factors and metabolic syndrome components, it is important to search for and validate scores to measure this risk in the pediatric population and carry out interventions through the implementation of healthy lifestyles to prevent and/or reverse the appearance of cardiometabolic pathologies in adulthood.

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