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Original / *Síndrome metabólico*

Metabolic syndrome and associated factors in children and adolescents of a Brazilian municipality

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Abstract

Background: **the risk factors associated to metabolic syndrome (MS) have been extensively studied in adults, but in children and adolescents it is poorly explored.**

Objective: **To identify the prevalence of MS and associated factors in children and adolescents.**

Methods: **A cross-sectional study with 540 children and adolescents from 7 to 14 years of age. The socioeconomic, demographic and lifestyle data and the family history of chronic diseases were reported by the individual and/or guardian and recorded in a structured questionnaire. Biochemical tests (fasting blood glucose, triacylglycerols, reduced high-density lipoprotein, very-low-density lipoprotein, homocysteine and cysteine), an anthropometric assessment and a blood pressure measurement were performed. MS was defined according to the criteria of The National Cholesterol Education Program Adult Treatment Panel III adapted by Ferranti. A Poisson regression was used to identify the factors statistically associated with MS.**

Results: **The MS prevalence was 12.8%, in which the most frequent component was a decreased high-density lipoprotein level (58.2%), followed by hypertriglyceridemia (41.8%), elevated blood pressure (29.1%), increased waist circumference (26.7%) and hyperglycemia (7.2%). Associations between metabolic syndrome and overweight [prevalence ratio (PR): 2.2 (1.22-3.95)], father education [PR: 2.19 (1.10-4.37)], serum very low-density lipoprotein concentration [PR: 1.08 (1.04-1.11)] and concomitantly increased serum homocysteine and cysteine concentrations [PR: 2.58 (1.32-5.04)] were observed.**

Conclusions: **The MS prevalence is high in children and adolescents and it is increased in patients with overweight, higher father education, increased serum very-low-density lipoprotein concentrations and a concomitant serum homocysteine and cysteine high levels.**

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Key words: *Metabolic syndrome X. Obesity. Homocysteine. Cysteine. Children.*

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SÍNDROME METABÓLICO Y FACTORES ASOCIADOS EN NIÑOS Y ADOLESCENTES DE UN MUNICIPIO BRASILEÑO

Resumen

Introducción: **Los factores asociados al Síndrome metabólico (SM) han sido ampliamente estudiados en adultos, pero aún son poco explorado en niños y adolescentes**

Objetivo: **Identificar la superioridad de SM y los factores asociados en niños y adolescentes.**

Métodos: **Se trata de estudio transversal, con 540 niños de 7 a 14 años de edad. Los datos socioeconómicos, demográficos, estilo de vida e historia familiar de enfermedades crónicas fueron informados por la persona y/o responsable y registrados en cuestionario estructurado. Fueron realizadas dosificaciones bioquímicas (glicemia en ayuno, triglicérides, lipoproteína de alta densidad reducida, lipoproteína de muy baja densidad, homocisteina y cisteina), evaluación antropométrica y verificación de la presión arterial. La SM fue definida de acuerdo con los criterios del The National Cholesterol Education Program Adult Treatment Panel III adaptado por Ferranti. Se utilizó regresión de Poisson como técnica estadística para identificar los factores asociados a la SM.**

Resultados: **La superioridad de la SM fue del 12,8%, siendo a lipoproteína de alta densidad reducida (58,2%) el componente más frecuente, seguido por la hipertrigliceridemia (41,8%), presión arterial aumentada (29,1%), circunferencia de la cintura aumentada (26,7%) e hiperglicemia (7,2%). Fue observada asociación entre SM y exceso de peso (RP: 2,2 [1,22-3,95]), escolaridad paterna (RP: 2,19 [1,10-4,37]), concentración sérica de la lipoproteína de muy baja densidad (RP: 1,08 [1,04-1,11]) y concentraciones séricas simultáneamente aumentadas de homocisteina y cisteina (RP: 2,58 [1,32-5,04]).**

Conclusiones: **La superioridad de SM es elevada en niños y adolescentes y se encuentra aumentada en paciente con exceso de peso, mayor escolaridad paterna, concentraciones séricas aumentadas de la lipoproteína de muy baja densidad, y elevación simultánea de los niveles séricos de homocisteína y cisteína.**

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Palabras clave: *Síndrome metabólico X. Obesidad. Homocisteína. Cisteína. Niños.*

Abbreviations

WC: Waist circumference.
TG: Triacylglycerols.
MS: Metabolic syndrome.
BP: Blood pressure.
WHO: World Health Organization.
BMI/A: Body mass index per age.
TC: Total cholesterol.
VLDL-C: Very-low-density lipoprotein cholesterol.
HDL-C: High-density lipoprotein cholesterol.
LDL-C: Low-density lipoprotein cholesterol.
NCEP/ATP III: The National Cholesterol Education Program Adult Treatment Panel III.
AIC: Akaike's information criterion.
NHANES: National Health and Nutrition Examination Surveys.
SE: Standard error.
HCY. Homocysteine.
CYS: Cysteine.

Introduction

The occurrence of obesity in childhood and adolescence has increased in the last 4 decades and has become an important health problem in many regions worldwide[1].

The prevalence of overweight and obesity has increased considerably between the years 1974/75 and 2008/09 in Brazilian children and adolescents. During this period, the occurrence of obesity increased by nearly 6-fold, and overweight tripled in children of both genders. In adolescents, the problem expanded with greater intensity among males[2]. Currently, the prevalences of overweight and obesity in Brazil are 33.5% and 14.3% in children and 20.5% and 4.9% in adolescents, respectively[2].

Excessive weight gain in childhood and adolescence may favor the waist circumference (WC) increase and the development of metabolic disorders such as hypertension, hyperglycemia, elevated serum triacylglycerols (TG) and decreased high-density lipoprotein[1]. The combination of 3 or more of these components constitutes metabolic syndrome (MS), a condition that is well established as an additional complication of obesity in adults and is also currently becoming common among children and adolescents. This syndrome is considered an important risk factor for the development of cardiovascular disease and diabetes in children, adolescents and adults[3,4].

MS is well defined, but there is no global consensus for its diagnosis, making it difficult to compare the prevalence rates of MS between different regions[5]. The criteria used for diagnosis in adults are also being adopted in children and adolescents, after adjusting for the pediatric reference standards[1,5]. However, there is no consensus for the adoption of this practice among all researchers of the subject[1,5].

Although excess weight[6-8] and insulin resistance have often been associated with MS, the broad range of determining factors has hampered a complete understanding of the pathogenesis of MS.

Other factors have been associated with MS in children and adolescents, such as gender[8], low birth weight, fetal macrosomia, low levels of maternal and paternal education[7,9], physical inactivity, the time spent on sedentary activities[7,9], a family history of obesity, diabetes, hypertension and an unhealthy diet[9].

Elevated serum homocysteine concentrations have also recently been associated with MS in adults[10-12]. However, little is known regarding the relationship of these factors with the occurrence of MS in children.

Thus, although the study of the factors associated with MS in adults has raised the interest of Brazilian researchers, few studies have sought to identify the presence of MS and the alterations that may increase the risk of developing the disease in children and adolescents. This article aimed to identify the prevalence and risk factors associated to MS in children and adolescents.

Methods

Study design and sample

This cross-sectional study examined a random sample of 540 children and adolescents aged between 7 and 14 years old from the municipality of Recôncavo Baiano. The data were obtained from a broader study entitled "Strategy to promote a healthy lifestyle and diet at school and at home - an interventional study" and have a power of 80% to identify the prevalence of MS in this population with a significance level of 5%.

Inclusion and exclusion criteria and losses

The study included schoolchildren from 7 to 14 years of age who were enrolled in public or private schools in the urban area of the municipality of Mutuípe, state of Bahia, Brazil, in 2006.

Pregnant adolescents, nursing mothers or schoolchildren with some type of disability or physical trauma that prevented obtaining anthropometric data; those previously diagnosed with diabetes, liver disease or chronic kidney disease; and those using medication to control blood pressure (BP) and lipid profile or medication that alters serum homocysteine and cysteine levels were excluded from the study.

Students from the enrollment list who moved to other municipalities or who were not found were considered losses.

Ethics Statement

The study was approved by the Research Ethics Committee of the School of Nutrition, Federal Univer-

sity of Bahia (number 03/2006). The students' participation in the study was subject to written permission from parents and/or guardians, who signed an informed consent form after being informed about the objectives of the study.

Data collection

The data were collected by nutritionists and by laboratory technicians duly trained in the standard techniques adopted in this study.

Socioeconomic and demographic data, lifestyle and family history of morbidity

The data regarding socioeconomic status, demographic information and lifestyle and the family history of morbidity were reported by the individuals and/or guardians and recorded in a structured questionnaire.

An index was developed to assess the socioeconomic status that considered the number of rooms in the house, the number of people living in the household and the occupation of the household head. Each variable that composed the socioeconomic index comprised answers ranging from 0 (worst condition) to 4 points (best condition). Thus, the index had a minimum score of 0 and a maximum of 12 points. Those who obtained scores above the median were considered to have an adequate socioeconomic status (reference = 0), while the others were deemed to have an inadequate socioeconomic status (risk = 1).

The parental educational level was categorized with regard to years of study (≤ 8 years = 0 and > 8 years = 1).

The variables that characterized alcohol consumption (no = 0, yes = 1), smoking (no = 0, yes = 1), the number of daily hours spent watching TV, playing videogames or using the computer (< 2 hours = 0, ≥ 2 hours = 1) and the practice of regular exercise outside of school (yes = 0, no = 1) were adopted to assess the lifestyle of the participants. The presence (1) of chronic non-communicable diseases such as obesity, dyslipidemia and hypertension in first-degree relatives of the participant, as well as their absence (0), were considered as the family history of morbidity.

Anthropometric data

Weight was measured on a digital scale (Filizola®) with a 150 kg capacity and 100 g precision. Weighing was performed with the participant barefoot, wearing lightweight clothing and with an empty bladder. The individual remained standing on the scale platform with the body weight equally distributed between the feet[13]. Height was measured with a portable stadiometer (Leicester Height Measure). The measurement was performed with the participant barefoot, without accessories or caps on the head, in an upright position with arms hanging at the sides of the body, shoulders relaxed, heels together and with the head positioned in the Frankfort plane[13].

The Waist Circumference (WC) was measured in the horizontal plane at the midpoint between the last right rib and the iliac crest using an inelastic fiberglass tape[14].

All of the anthropometric measurements were repeated by different evaluators, and the maximum acceptable variations between measurements were as follows: weight = 0.1 kg, height = 0.1 cm and WC = 0.5 cm. The mean of the measurements was adopted as the final measure.

Body mass index (BMI)

The anthropometric diagnosis was based on body mass index per age (BMI/A), considering the growth curves for each gender and the cutoff points proposed by the World Health Organization (WHO) (2007)[15]. The student was classified as having excess weight when he/she was overweight (BMI/A ≥ 85th percentile) or obese (BMI/A ≥ 97th percentile).

Blood pressure

The Blood Pressure (BP) was obtained using an aneroid sphygmomanometer with a cuff appropriate for the arm circumference and age of the participant following the techniques proposed by the IV Brazilian Guidelines on Hypertension[16]. The measurements were performed in duplicate, and the mean of the 2 readings was used as the final measure.

The BP was classified according to the criteria proposed by The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents, considering gender, age and height percentile as follows: normal BP (systolic or diastolic BP < 90th percentile), prehypertensive (90th to 95th percentiles), hypertensive (BP ≥ 95th percentile)[17].

Biochemical tests

An 8 ml blood sample was collected after a 12-hour fasting period to determine the lipid profile, the fasting blood glucose level and the levels of homocysteine and cysteine. Total cholesterol (TC), very-low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), triacylglycerols (TG) and fasting blood glucose levels were determined with the enzymatic calorimetric method, while the low-density lipoprotein cholesterol (LDL-C) level was obtained using the Friedewald equation [LDL-C = TC – HDL-C – (TG/5)]. To classify MS, the categorization of the TG, HDL-C and blood glucose levels was

performed according to the cutoff points proposed by Ferranti[18].

Due to the lack of reference values for VLDL-C in children and adolescents, this parameter was included as a continuous variable in the final model.

Serum homocysteine and cysteine levels were measured using high-performance liquid chromatography with an isocratic elution and fluorimetric detection, which is considered the gold standard for this procedure[19]. These analyses were performed at the Laboratory of Inborn Errors of Metabolism of the Federal University of São Paulo. Because the reference values for homocysteine and cysteine in healthy children and adolescents have not been established, the 80th percentile was adopted as a cutoff point based on the values of the sample itself.

Definition of MS

The criterion proposed by The National Cholesterol Education Program Adult Treatment Panel III (NCEP / ATP III) and adapted by Ferranti et al (2004) was used to characterize the metabolic disorders (MS)[18]. The criterion entails the presence of 3 or more of the following alterations in the same individual: WC ≥ 75th percentile, BP ≥ 90th percentile, TG ≥ 100 mg/dL, HDL-C < 50 mg/dL and blood glucose > 100 mg/dL.

Due to the lack of reference values for the classification of WC in Brazilian children and adolescents, the classification of the participants in this study was performed according to percentile values of the sample, considering gender and age[8,18].

Statistical analysis

The characterization of the study population was conducted through descriptive analysis using prevalence. A Poisson regression was used to identify the factors associated with MS. The variables with a p-value < 0.20 in the bivariate analysis were tested in the multivariate model, and the variables that presented the adopted level of significance of $p < 0.05$ remained in the final model. The Akaike Information Criterio (AIC) and the Pseudo-R^2 were used to evaluate, respectively, the full model adjustment and explanation ability. The analyses were performed using the Stata software (version 12.0).

Results

Characterization of the population, the prevalence of MS and its components

Table I contains the socio-demographic and lifestyle characteristics of the study participants. There was a predominance of females (57.6%) and those who were more than or equal to 10 years old (69.9%). A lower level of education was observed in 91.4% of fathers and 82.8% of mothers.

Table I
Socio-demographic and lifestyle characteristics of the children and adolescents fo the municipality of Mautuipe, state of Bahia, Brazil, 2006

Variables	*Categorization*	*n*	*(%)*
Sex	Females	289	57.6
	Males	213	42.4
Age	< 10 years	151	30.1
	≥ 10 years	351	69.6
Father's educational level	≤ 8 years	380	91.4
	> 8 years	36	8.6
Mother's educational level	≤ 8 years	396	8.28
	> 8 years	82	17.2
Socioeconomic index	Inadequate	243	48.4
	Adequate	259	51.6
Smoking	Yes	40.8	
	No	498	99.2
Alcohol consumption	Yes	64	12.8
	No	438	87.2
Practice of regular exercise	Yes	122	24.3
	No	380	75.7
Time spent TV*, videogames or computer	< 2 hours/day	98	19.9
	≥ 2 hours/day	394	80.1

*Tv: Television.

Regarding the lifestyle of the participants, smoking and alcohol consumption were observed in 0.8% and 12.8% of participants, respectively. Moreover, 24.5% of the students regularly engaged in sports, while 80.1% spent 2 or more hours daily in sedentary activity.

Table II has the clinical and biochemical data of the children and adolescents in the study. Excess weight, hyperhomocysteinemia and hypercysteinemia were identified in 20.5%, 20.5% and 24.7% of the participants, respectively. Among the alterations that compose MS, there was a higher prevalence of low concentrations of HDL-C (58.2%), followed by hypertriglyceridemia (41.8%), elevated BP (29.1%), high WC (26.7%) and hyperglycemia (7.2%).

The prevalence of MS identified among the students in the study was 12.8%. However, the presence of at least 1 component of MS was detected in 85.7% of the participants, and 2 components were found in 32.5% of the students (fig. 1).

Factors associated with MS

Table III has the results of the bivariate analysis of the relationship between MS and the covariates of interest in this study. Statistically significant associations between MS and excess weight ($p < 0.001$), higher father education ($p = 0.01$), hyperhomocys-

Table II
Clinical and biochemical data of the children and adolescents of the municipality of Mutuípe, state of Bahia, Brazil, 2006

Variables	*Categorization*	*n*	*(%)*
BMI/A*	Normal	399	79.5
	Excess weight	103	20.5
Homocysteine	< p 80	379	75.5
	≥ p 80	123	24.5
	> p 80	378	75.3
	≥ p 80	124	24.7
Components of the MS**			
Wasit circumference	< p 75	370	73.7
	≥ p 75	132	26.3
Blood pressure < 90	356	70.9	
	≥ p 90	146	29.1
Fasting glucose	< 100 mg/dl	466	92.8
	≥ 100 mg/dl	36	7.2
HDLc***	< 50 mg/dl	292	58.2
	≥ 60 mg/dl	210	41.8
Triacylglycerols	< 100 mg/dl	292	58.2
	≥ 100 mg/dl	210	41.8

*BMI/A: Body mass indez/age. **MS: Metabolic syndrome. ***HDLc: High density lipoprotein cholesterol.

teinemia ($p < 0.01$), hypercysteinemia ($p < 0.01$), concomitantly elevated serum homocysteine and cysteine concentrations ($p < 0.01$), increased VLDL-C levels ($p < 0.001$) and a family history of obesity ($p = 0.046$) were identified.

The Poisson regression analysis results for MS and the exposure variables are shown in table IV. Excess weight contributed to an increase of 120% in the prevalence of MS compared to the prevalence observed in normal-weight individuals ($p < 0.01$). The prevalence of MS in students whose fathers studied for more than 8 years was 119% ($p = 0.026$) higher than that in children and adolescents whose fathers had a lower education level. An increase of 1 mg/dL in the mean VLDL-C value increased the prevalence of MS by 8% ($p < 0.001$), and the prevalence of MS was 158% higher in students who had serum homocysteine and cysteine concentrations concomitantly elevated compared to that in children and adolescents with adequate concentrations of these biochemical parameters ($p < 0.001$).

This final model fitted well to the data, showing an AIC (Akaike's information criterion) improvement from 373.47 for the reduced model (including the outcome variable MS and the independent variable weight excess) to 287.42 when adjusted by the independents variables father education level, VLDL-c value and homocysteine and cysteine high levels (full model), indicating little loss of information when included all the variables of the full model. This final model tested, containing all the exposure variables associated with MS, demonstrated a good explanatory power, measured by the pseudo-R2, indicating that these variables explain 15% of the cases of MS in the population studied (table IV).

A loss was registered in 38 cases (7.04%), of which 37 were not located and 1 was not tested biochemically.

Discussion

The prevalence of MS in this study was 12.8%, which indicates a clinically relevant condition in the pediatric population. This study also found a higher incidence of MS among children with excess weight, higher paternal education, elevated serum very low-density lipoprotein concentrations and concomitantly elevated serum homocysteine and cysteine levels.

Prevalence of MS and its components

The most frequent component of MS was low HDL-C, followed by hypertriglyceridemia, while hyperglycemia was the least frequent. These results confirm the findings of Kelishadi et al (2008)[9], which are in agreement regarding the ranking of the MS components; however, these authors found a higher prevalence of low HDL-C (72%) and a lower prevalence of elevated BP (7%) and hyperglycemia (4%).

The early identification of abnormal parameters associated with MS is essential to determine the necessary treatment, to prevent the accumulation of MS

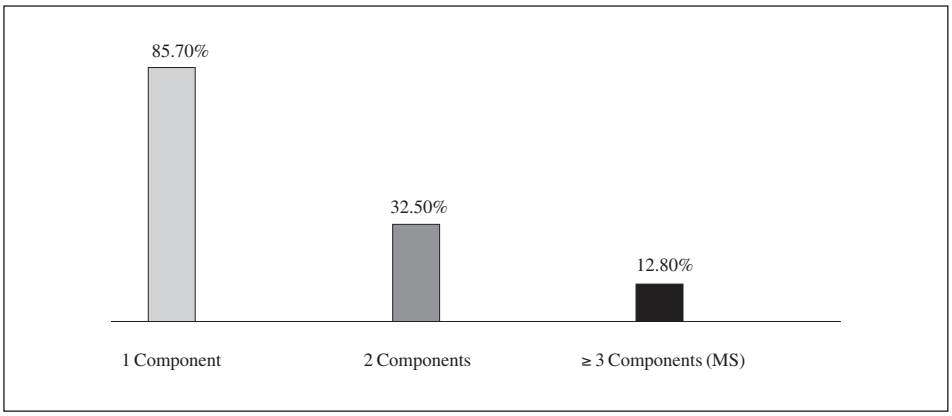

Fig. 1.—Prevalence of metabolic syndrome (MS) and number of components of the MS in children and adolescents.

Tabla III
Bivariate analysis of the Poisson regression for metabolic syndrome and the covariates of interest. Mutuípe, state of Bahia, Brazil, 2006

Variables	*Categorization*	*PR*	*SE**	*CI 95%*	*p*
Sex	Females	1	–	–	–
	Males	1.2	0.30	(0,73-1,96)	0,472
Age	< 10 years	1	–	–	–
	≥ 10 years	1.29	0.37	(0.73-2.27)	0.377
Father's educational level	≥ 8 years	1	–	–	–
	> 8 years	3.09	1.01	(1.62-5.88)	0.001
Mother's educationa l level	≥ 8 years	1	–	–	–
	> 8 years	1.51	0.45	(0.84-2.69)	0.164
Socioeconomic index	Adequate	1	–	–	–
	Inadequate	0.83	0.21	(0.51-1.35)	0.451
Alcohol consumption	No	1	–	–	–
	Yes	1.42	0.47	(0.74-2.72)	0.290
Practice of regular exercise	Yes	1	–	–	–
	No	1.39	0.44	(0.74-2.61)	0.303
Time TV** and videogames	< 2 hours/day	1	–	–	–
	≥ 2 hours/day	1.15	0.38	(0.60-2.21)	0.668
BMI/A***	Normal	1	–	–	–
	Excess weight	3.42	0.86	(2.09-5.58)	0.000
HCY†	< p 80	1	–	–	–
	≥ p 80	2.25	0.57	(1.37-3.69)	0.000
CYS††	< p 80	1	–	–	–
	≥ p 80	2.08	0.53	(1.27-3.43)	0.004
HCY + CYS	Normal	1	–	–	–
	HCY ou CYS ≥ p 80	1.99	0.61	(1.10-3.63)	0.024
	HCY + CYS ≥ p 80	2.73	0.82	(1.52-4.92)	0.001
VLDLc†††	Continuous variable	1.08	0.01	(1.05-1.10)	0.000
Family history of obesity	No	1	–	–	–
	Yes	1.67	0.43	(1.01-2.77)	0.046
Family history dyslipidemia	No	1	–	–	–
	Yes	0.99	0.26	(0.59-1.67)	0.98
Family history of hypertension	No	1	–	–	–
	Yes	1.39	0.45	(0.74-2.61)	0.304

*SE: standard error. **TV: Television. ***BMI/A: Body mass index/age. †HCY: Homocysteine. ††CYS: Cysteine. †††VLDLc: Very low density lipoprotein cholesterol.

Tabla IV
*Factors associated with metabolic syndrome in children and adolescents of the municipality of Mutuípe, state of Bahia, Brazil, 2006**

Variables	*PR*	*SE**	*CI 95%*	*p*
Weight excess	2.2	0.66	(1.22-3.95)	0.009
Father's educational level (> 8 years)	2.19	0.77	(1.10-4.37)	0.026
VLDLc*** (continuous variable)	1.08	0.02	(1.04-1.11)	0.000
Homocysteine ou cysteine ≥ p80	1.74	0.60	(0.89-3.42)	0.107
Homocysteine e cysteine ≥ p 80	2.58	0.88	(1.32-5.04)	0.000

*Poisson regression analysis; **SE: Standard Error. ***VLDLc: Very low density lipoprotein cholesterol. AIC (Akaike's information criterion) of the reduced models (excesso weight = 373.47, excesso weight + father's educational level 0 306.8; excesso weight + father's educational level + VLDLc = 291.13); AIC of full model = 287.42; Pseudo R2 of the full model = 0.15.

components and consequently to prevent the development of MS in childhood. The presence of at least 1 of the identified components among schoolchildren in this study was greater than that found in other regions of the world[9,20,21], while the presence of 2 components occurred less frequently than that observed in children and adolescents from Portugal[20] and more frequently that that observed in Chinese children[21].

The prevalence of MS in children and adolescents (12.8%) found in this study was similar to that recorded

by researchers who adopted the same classification criteria in the United States (12.7%)[22], Korea (13.4%)[1] and Iran (14.1%)[9]. In the studies performed in Brazil [23] and in Portugal[20], the occurrence of MS was higher (22.6% and 34.9%, respectively) than that observed in the present study, however, the majority of participants in those studies were obese, which may have favored these results. Notably, lower frequencies (6.6% and 2.6%) of MS have been reported in China[4,21].

Ferranti et al (2006)[22] determined that the prevalence of MS in American adolescents increased from 9.2% to 12.7% in the period from 1988-94 to 1999/2000 according to the National Health and Nutrition Examination Surveys (NHANES) and that this growth is partly related to the higher occurrence of abdominal obesity. The prevalence of MS has remained stable in normal-weight individuals but has grown considerably among those with excess weight (31.2% to 38.6%) in the same period. Thus, these results indicate that the increases in overweight and obesity in children observed in recent years may favor the development of MS in children and adolescents and, therefore, the earlier onset of cardiovascular disease and diabetes.

Factors associated with MS

Other studies[4,6-8,21] have also reported an association between excess weight and MS in children and adolescents. MS was 5.1 and 11.1 times more prevalent among adolescents who were overweight and obese, respectively, than those with a normal weight for their height, as reported by Stabelini et al (2012)[8]. These results indicate that MS may be associated with excess weight in children and adolescents.

The results of several studies conducted to date have not provided consistent evidence of the association of MS with an individual's life situation. In that context, a higher parental education level was associated with MS, unlike other studies that found no association[9] or that found an association between MS and less education[7,24]. Regarding these results, it is possible to believe that the higher father education level can indicate a better acquisitive power and, consequently, an easier access to industrialized foods at home and at scholar environment and to consumer goods (television, electronics products) which favor a sedentary lifestyle.

This study is one of the few that evaluates the relationship between MS and VLDL-C. From the results, it can be postulated that high serum VLDL-C concentrations lead to hypertriglyceridemia, which results from the increased synthesis of VLDL-C or from reduced triglyceride lipolysis[25,26]. Consequently, the high levels of VLDL-C also favor a reduction in serum HDL-C levels, which favors the development of MS[26,27].

Finally, it is worth mentioning that this study breaks new ground by seeking to identify the relationship between MS and serum homocysteine and cysteine concentrations in children and adolescents. Although few studies have been performed with this age group, recent studies have reported the association between concomitantly elevated serum homocysteine and cysteine concentrations and obesity[28,29] and increased WC[28] in children and adolescents. The concomitant elevation of serum homocysteine and cysteine levels was also associated with reduced HDL-C levels in adults[30].

Therefore, homocysteine and cysteine high levels may enhance the MS development in children and adolescents. Although this study did not observe a significant association between MS and serum homocysteine and cysteine concentrations alone, hyperhomocysteinemia was found to be associated with hypertension and weight gain in children and adolescents by Ganji and Kafai (2003)[31] and with increased WC[32], hypertension[31], low HDL-C [30] and hyperglycemia[32] in adults. Recent studies[10-12] were also able to identify the occurrence of MS in adults with elevated serum homocysteine concentrations.

Although the causal mechanism between hyperhomocisteinemia, hypercysteinemia and MS is not completely clarified, some pathophysiological mechanisms have been suggested to explain the role of these parameters in the onset of the metabolic disorders that compose the SM. The causal relation between hyperhomocisteinemia and hypertension have been associated to the arterial stiffening, endothelial dysfunction due the nitric oxide decreased action, serum folate decrease and insulin resistance[33]. Hyperhomocysteinemia may also promote the HDL-c reduction[34] and the tryacilglycerol increase[35], because it seems to be responsible for the Apolipoprotein AI factor transcription inhibition involved in the HDL-c synthesis and for the SREBP-1 (sterol regulatory element-binding protein 1) expression increase which is important to the TG synthesis[34, 35].

The association between hypercysteinemia and overweight and increased WC may be explained by the fatty acid stimulation synthesis promoted by the cysteine high levels, resulting in adipose tissue accumulation, mainly in the abdominal region. Furthermore, in adipocytes, the cysteine suffers autoxidation and liberates hydrogen peroxide, which acts as a lipolysis inhibitor[29]. The results indicate that the combination of both elevated parameters may promote an increase in the prevalence of MS in children and adolescents.

One of the limitations of the present study can be attributed, in particular, to the nature of its design, which does not allow assessing causality. However, statistical analyses that are appropriate for the study design were adopted as an initial step to identify the factors associated with MS in children and adolescents. Another limitation is related to the absence of an international consensus for classifying MS, which restricts comparison of the results between studies that adopt different criteria. Therefore, one of the most commonly used criteria to diagnose MS was selected[20], using cutoff points adapted to the age group studied.

The prevalence of MS is high in children and adolescents and is increased in patients with excess weight, higher father education, increased serum concentrations of very low-density lipoprotein and a concomitant elevation of serum homocysteine and cysteine levels. These findings highlight the need to identify the components of MS and the factors associated with this disease early and, thereby, to control existing alterations and prevent the development of MS in the pediatric population.

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