

Metabolic syndrome in a sample of the 6- to 16-year-old overweight or obese pediatric population: a comparison of two definitions

Fatemeh Saffari
Shabnam Jalilolghadr
Neda Esmailzadehha
Peyman Azinfar

Qazvin Children Hospital, Qazvin
University of Medical Sciences,
Qazvin, Iran

Purpose: The purpose of this study was to estimate the presence of metabolic syndrome (MS) in a group of children and adolescents with a body mass index (BMI) above the 85th percentile for their age and sex in Qazvin Province, Iran; to evaluate the relationship between obesity and metabolic abnormalities; and to compare two proposed definitions of MS.

Patients and methods: The study was conducted on 100 healthy subjects aged between 6 and 16 years (average age, 10.52 ± 2.51 years) with a high BMI for their age and sex. Fifty-eight percent of subjects were female. Physical examination including evaluation of weight, height, BMI, and blood pressure measurement was performed (“overweight” was defined as a BMI between the 85th and 95th percentiles for children of the same age and sex; “obese” was defined as a BMI over the 95th percentile for children of the same age and sex). Blood levels of glucose, insulin, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, and uric acid were measured after a 12-hour overnight fast. The authors used and compared two definitions of MS: the National Cholesterol Education Program’s Adult Treatment Panel III (NCEP ATP III) criteria and a modified definition by Weiss et al. Variables were compared using the Student’s *t*-test and chi-square and Mann-Whitney *U* tests, and agreement between the two definitions was analyzed using kappa values.

Results: The subjects had a mean BMI of 26.02 ± 4.38 and 80% had obesity. Insulin resistance was found in 81% of the study population. MS was present in ten (50%) of the overweight and 53 (66.2%) of the obese subjects using the NCEP ATP III criteria. MS was present in five (25%) of the overweight and 34 (42.5%) of the obese subjects using the definition by Weiss et al. The overall kappa value for the two definitions of MS was 0.533. There were no statistically significant differences between the two definitions of MS in participants.

Conclusion: The prevalence of MS in children and adolescents depends on the criteria chosen and their respective cutoff points. The NCEP ATP III criteria, the parameters of which include higher cutoff values for high-density lipoprotein cholesterol and triglycerides, detected the higher prevalence and therefore the NCEP ATP III criteria are able to diagnose a larger number of children and adolescents at metabolic risk.

Keywords: children, adolescents, obesity, body mass index, metabolic syndrome

Correspondence: Shabnam Jalilolghadr
Clinical Research Center, Qazvin
Children’s Hospital, Qazvin University of
Medical Sciences, Qazvin, Iran
Tel +98 912 281 4230
Fax +98 281 334 4088
Email shabnam_jalilolghadr@yahoo.com

Introduction

The prevalence of childhood obesity has more than doubled in the last 2 decades in many countries and it is now considered a serious medical and public health problem globally.¹⁻³ Obesity causes sleep apnea and psychological problems in childhood and it increases the risk of cardiovascular disease, diabetes, hypertension, dyslipidemia, osteoarthritis, and cancer in future life.^{1,4,5}

Hanefeld and Leonhardt⁶ first discussed metabolic syndrome (MS) in 1981. In 1988, Reaven⁷ described it as a link between insulin resistance (IR) and hypertension, dyslipidemia, type 2 diabetes, and other metabolic abnormalities that are associated with an increased risk of atherosclerotic cardiovascular disease in adulthood.⁷

It has been suggested that MS may originate in the uterus.^{8,9} Genetic factors or adverse events in early life or a sedentary lifestyle may cause MS and its complications, especially in non-European populations.^{10–12} IR has been recognized in the pathogenesis of the syndrome, and childhood obesity is the most common feature associated with IR.^{7,13}

Few studies have estimated the prevalence of MS in children and adolescents,¹⁴ and diagnostic criteria have not been standardized.^{15–17} Definitions agree on the essential components of the syndrome but there are differences in some diagnostic criteria.^{13,18} Although, the accuracy of present MS definitions is under debate, it seems that MS screening in the overweight and obese pediatric population and comparison of different suggested criteria is essential.

The aim of this study was to estimate the presence of MS in a group of children and adolescents with a BMI above the 85th percentile for their age and sex in Qazvin Province, Iran, to evaluate the relationship between obesity and metabolic abnormalities, and to compare two proposed definitions of MS.

Material and methods

This study was conducted with 100 children and adolescents (calculated sample size was 83 persons, considering $Z = 1.96$, expected prevalence or proportion was 31.9%, and precision was 0.07) living in Qazvin Province. Qazvin is a city located about 150 km west of Tehran, the capital of Iran. Overweight and obese subjects were referred to the authors' pediatric endocrine clinic by their general practitioner or primary care pediatric consultant between 2009 and 2010.

The subjects were healthy, aged between 6 and 16 years old (average age, 10.52 ± 2.51 years), and had a body mass index (BMI) above the 85th percentile for their age and sex. Fifty-eight percent of the subjects were female. "Overweight" was defined as a BMI between the 85th and 95th percentiles for children of the same age and sex; "obese" was defined as a BMI over the 95th percentile for children of the same age and sex.¹⁹ Subjects with diabetes and who were under treatment with medication that influences blood pressure (BP), blood glucose, or lipid metabolism were excluded from the study. Children with secondary obesity due to drugs or endocrine or genetic disorders were also excluded from the study.

The ethics committee of Qazvin University of Medical Sciences approved the study. Written informed consent from both the participants and their parents was obtained.

Demographic characteristics were noted in a questionnaire given to participants. A pediatric endocrinologist performed the physical examination of the subjects, which included an evaluation of weight, height, BMI, and BP measurement, with special attention given to the existence of acanthosis nigricans, defined as the thickening and darkening of the upper layers of the skin of the posterior neck, axilla, elbows, or knees.²⁰

Height was measured twice, while subjects were barefoot, to an accuracy of ± 0.1 cm. Weight was measured twice, while subjects were lightly dressed, to an accuracy of ± 0.1 kg. BMI was calculated by dividing the weight (kg) by the square of the height (m). Waist circumference (WC) was measured to an accuracy of ± 0.2 cm with a nonelastic measuring tape. WC was measured at a point halfway between the lower border of the thorax and the iliac crest at the end of expiration.²¹

BP was measured with a mercury sphygmomanometer after a 5-minute rest. Systolic and diastolic BPs were taken twice, with the patient sitting down. Appropriately sized BP cuffs were used, with the width of the cuff being 40% of the mid-arm circumference, and with cuff bladders covering 80%–100% of the arm circumference and approximately two-thirds of the length of the upper arm, without overlapping. The readings at the first and fifth phases of Korotkoff sounds were considered as the systolic BP and the diastolic BP, respectively.²² Elevated systolic or diastolic BP was defined in two ways, on the basis of the definitions of MS, as a value exceeding the 90th percentile in NCEP ATP III definition or the 95th percentile in Weiss et al's definition¹² for age, sex and height.

Venous blood samples were obtained from subjects after a 12-hour overnight fast. Blood levels of glucose, insulin, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), and uric acid were measured in all patients. All biochemical measurements were performed in one laboratory.

A Selectra E analyzer with photometric assay and reagent (Parsazmun Company, Tehran, Iran) was used to measure fasting blood sugar (FBS); mean intra- and inter-assay coefficients of variation (CVs) were 1.28% and 0.84%, respectively. Impaired glucose tolerance was defined as a glucose level greater than 140 mg/dL but then less than 200 mg/dL at 2 hours. Insulin levels were measured by electrochemiluminescence immunoassay using reagent (Roche Diagnostics GmbH, Germany). A within-run precision CV was 1.9% and total precision CV was 1.45%. The degree of

IR was determined with the use of a homeostatic model, and calculated as the product of the fasting plasma insulin level ($\mu\text{U/mL}$) and the fasting plasma glucose level (mmol/L), divided by 22.5.²³ IR was defined as a homeostasis model of insulin resistance (HOMA-IR) value of more than 1.775.²⁴

A Selectra E analyzer with photometric assay and reagent (Parsazmun Company) was also used to measure cholesterol, HDL-C, LDL-C, TGs, and serum uric acid; mean intra- and interassay CVs for cholesterol were 1.82% and 1.04%, respectively; for HDL-C, they were 0.73% and 1.8%, respectively; for LDL-C, 0.66% and 1.45%, respectively; for TGs, 1.82% and 1.04%, respectively; and for serum uric acid, 1.18% and 1.13%, respectively.

Since there is no single internationally accepted definition of MS for children and adolescents, the authors used and compared two definitions. The diagnostic criteria of these definitions are shown in Table 1. The first definition used was similar to de Ferranti et al's¹⁶ definition of MS, which is based on criteria analogous to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III) criteria.²⁵ It should be added that de Ferranti et al¹⁶ used the cutoff of FBS ≥ 110 mg/dL, but the present authors decided to, like recent studies, follow the latest recommendation of the American Diabetes Association.¹¹ The National Heart, Lung, and Blood Institute's recommended cutoff point for BP was used also. The second definition was a modified definition by Weiss et al,¹² in which WC and FBS criteria were similar to the first definition.

Kolmogorov–Smirnov test was used to examine the normality of variables. Data were reported as mean plus or minus standard deviation for normally distributed variables or as median (minimum to maximum) for non-normally distributed variables. Categorical variables were analyzed by chi-square test, continuous variables were compared using Student's *t*-test, and non-normally distributed variables were analyzed by Mann-Whitney *U* test. Agreement between the two MS definitions was analyzed using the kappa value, which was considered excellent for values greater than 0.81, good for values 0.61–0.80, moderate for 0.41–0.60, and

weak for values less than 0.4.²⁶ A *P*-value less than 0.05 was considered statistically significant.

Results

The 100 participants had a mean BMI of 26.02 ± 4.38 . Of the 100 participants, 20 subjects were overweight and 80 were obese. WC in 81 subjects was more than the upper limit of normal, and it ranged from 68 to 118 cm. Waist-to-hip ratio (WHR) was more than the upper limit of normal in all of the females in the study (WHR more than 0.7) and in 40 of the males (WHR more than 0.8). WC and WHR were significantly different between overweight and obese subjects. Eleven overweight subjects and 70 obese subjects had a high WC, and 98 subjects had a high WHR. Forty-eight subjects had acanthosis nigricans. The ratio of LDL-C to HDL-C varied from 1.0 to 10.6 (by a mean value of 2.48 ± 1.30). HOMA-IR values ranged from 1.0 to 20.48. IR was found in 81 subjects. The clinical and biochemical characteristics of the population are shown in Tables 2 and 3. With respect to all biochemical characteristics, the difference between overweight and obese subjects was not significant.

Results by NCEP ATP III criteria

Sixty-three patients met the criteria for MS as defined by the NCEP ATP III. It was present in ten (50%) of the overweight and 53 (66.2%) of the obese subjects. Hypertension was detected in 36% of subjects (34% systolic and 24% diastolic hypertension). Values of every component of the definition other than WC values were significantly different between subjects with and without MS.

The prevalence of each component of MS in both groups of subjects is reported in Table 4. High serum levels of TGs, cholesterol, LDL-C, uric acid, and FBS were reported in 74, 31, 17, eight, and twelve children, respectively. The low level of HDL-C was 70%. The most frequent component of MS was high WC followed by high TGs and low HDL-C. MS was not significantly different between males and females ($P = 0.402$).

Table 1 Diagnostic criteria for two definitions of metabolic syndrome

Component	Weiss et al ¹² (any three of these criteria)	NCEP ATP III (any three of these criteria)
Glucose	FPG ≥ 100 mg/dL	FPG ≥ 100 mg/dL
WC	WC ≥ 75 th percentile for age and sex	WC ≥ 75 th percentile for age and sex
TGs	Fasting TGs \geq fifth percentile for age and sex	Fasting TGs ≥ 100 mg/dL
HDL-C	HDL $<$ fifth percentile for age and sex	HDL < 50 mg/dL (< 45 mg/dL in males over 15 years old)
BP	SBP/DBP $>$ 95th percentile for age and sex	SBP/DBP $>$ 90th percentile for age and sex

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; NCEP ATP III, National Cholesterol Education Program's Adult Treatment Panel III criteria; SBP, systolic blood pressure; TGs, triglycerides; WC, waist circumference.

Table 2 Clinical and laboratory characteristics of subjects

Characteristic	Total	Overweight (n = 20)	Obese (n = 80)	P-value
Sex (M/F)	42/58	4/16	38/42	0.022
Age (years)*	10.52 ± 2.51	11.68 ± 2.90	10.23 ± 2.33	0.020
BMI (kg/m ²)*	26.02 ± 4.38	22.95 ± 2.56	26.72 ± 4.41	<0.001
WC (cm)*	85.82 ± 12.77	79.61 ± 7.75	87.24 ± 13.29	0.021
Hip circumference (cm)*	95.44 ± 11.54	92.20 ± 8.23	96.25 ± 12.13	NS
WHR*	0.898 ± 0.068	0.87 ± 0.056	0.904 ± 0.069	0.047
TGs (mg/dL)**	140 (41–750)	135 (91–750)	146.5 (41–658)	NS
Total cholesterol (mg/dL)*	171.09 ± 45.14	181.75 ± 70.4	168.42 ± 36.4	NS
HDL-C (mg/dL)*	43.462 ± 10.99	43.5 ± 11.36	43.45 ± 10.96	NS
LDL-C (mg/dL)*	100.84 ± 34.07	106.75 ± 51.49	99.36 ± 28.39	NS
SBP (mmHg)*	111.60 ± 12.38	109.20 ± 14.01	112.20 ± 12.54	NS
DBP (mmHg)*	67.26 ± 10.28	65.80 ± 10.98	67.62 ± 10.13	NS
Fasting blood glucose (mg/dL)*	90.65 ± 7.91	89 ± 7.38	91.06 ± 8.03	NS
Blood glucose after 2 hours (mg/dL)*	102.02 ± 22.05	94.5 ± 27.02	103.9 ± 20.4	NS
Fasting insulin (μIU/mL)**	16.3 (5.7–76.8)	15.2 (6.1–48.1)	17.25 (5.7–76.8)	NS
Insulin after 2 hours (μIU/mL)**	58.5 (6.2–351)	55.8 (18.2–248.2)	60.7 (6.2–351)	NS
HOMA-IR**	3.57 (1–20.48)	2.96 (1–10.22)	3.87 (1.05–20.48)	NS
IR (n)	81	16	65	NS
Uric acid (mg/dL)*	5.2 ± 1.17	5.06 ± 1.1	5.24 ± 1.19	NS

Notes: *Data presented as mean plus or minus standard deviation; **data presented as median (minimum to maximum).

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model of insulin resistance; IR, insulin resistance; LDL-C, low-density lipoprotein cholesterol; NS, not significant; SBP, systolic blood pressure; TGs, triglycerides; WC, waist circumference; WHR, waist-to-hip ratio.

In spite of fasting insulin, HOMA-IR was not statistically different between subjects with and subjects without MS. Overall, MS was observed in 64.2% of patients with IR, compared with 57.9% for those without, but the difference was not significant.

Results by Weiss et al's¹² definition

Thirty-nine patients met the criteria for MS as defined by Weiss et al.¹² It was present in five (25%) of the overweight and 34 (42.5%) of the obese subjects. Hypertension was detected in 34% of subjects (33% systolic and 23% diastolic hypertension). Values of every component of the definition between subjects with and without MS were significantly different. In addition, BMI and hip circumference values were statistically different between these two groups.

The most frequent component of MS was high WC, followed by high TGs and then hypertension (see Table 4). MS was not significantly different between males and females ($P = 0.304$). Fasting insulin and HOMA-IR values were statistically different between subjects with and subjects without MS. Overall, MS was observed in 43.6% of patients with IR, as compared with 26.3% for those without, but the difference was not significant.

In both definitions, subjects with MS had lower insulin sensitivity parameters and higher oral glucose tolerance test and uric acid levels than those subjects without MS, but the

difference was not significant. The values of every component of the two MS definitions were compared among subjects diagnosed with MS but no significant differences were found (FBS, 0.22; WC, 0.86; HDL-C, 0.59; TGs, 0.628; BP, 0.103). When the frequency of the different components of MS in overweight and obese patients was compared, there were no significant differences found with respect to hypertension, low HDL-C, high TGs, and FBS.

As expected, abdominal obesity was the most frequent criterion (81%) in overweight and obese children and adolescents, followed by a high TG level.

The overall kappa value for the two definitions of MS was 0.533. To examine possible causes of moderate agreement between the definitions, the authors compared agreement between the criteria of the two MS definitions in the study population. The kappa values were 0.308 and 0.728 for HDL-C and TGs, respectively.

Discussion

MS is one of the most important and serious challenges in global health in the modern world. The authors found a high prevalence of MS (42.5%) in the obese children, while prevalence was 25% in the overweight children. Abdominal obesity, a criterion of MS, also presented in a significant portion of the obese and overweight children. Among children and adolescents of Caucasian origin in Italy, the prevalence

Table 3 Clinical and laboratory characteristics of subjects for each group of criteria

Characteristic	NCEP ATP III			Weiss et al ¹²		
	MS (n = 63)	No MS (n = 37)	P-value	MS (n = 39)	No MS (n = 61)	P-value
Sex (M/F)	24/39	18/19	NS	19/20	24/37	NS
Age (year)*	10.72 ± 2.49	10.19 ± 2.50	NS	11.06 ± 2.19	10.07 ± 2.58	NS
BMI (kg/m ²)*	26.43 ± 3.81	25.27 ± 5.24	NS	27.45 ± 3.77	25.06 ± 4.51	0.008
WC (cm)*	87.31 ± 10.17	83.07 ± 16.37	NS	89.80 ± 9.92	83.15 ± 13.82	0.011
Hip circumference (cm)*	0.90 ± 0.05	0.93 ± 0.05	NS	0.90 ± 0.05	0.92 ± 0.05	0.007
WHR*	0.902 ± 0.069	0.89 ± 0.08	NS	0.90 ± 0.05	0.893 ± 0.075	NS
TGs (mg/dL)**	175 (91–750)	92 (41–177)	<0.001	184 (110–750)	118.5 (41–259)	<0.001
Total cholesterol (mg/dL)*	180.06 ± 48.47	154.79 ± 35.22	0.009	183.79 ± 52.92	162.74 ± 38.38	0.025
HDL-C (mg/dL)*	40.67 ± 9.16	48.91 ± 12.32	0.001	39.59 ± 11.02	46.22 ± 10.31	0.003
LDL-C (mg/dL)*	105.77 ± 37.28	92.22 ± 27.01	NS	107.82 ± 40.78	96.45 ± 29.4	NS
SBP (mmHg)	31 (49.2)	3 (8.1)	0.000	25 (64.1)	8 (13.8)	0.000
DBP (mmHg)	23 (36.5)	1 (2.27)	0.000	19 (48.7)	4 (6.9)	0.000
Hypertension (n)	33 (52.4)	3 (8.1)	0.000	27 (69.2)	8 (12)	0.000
Fasting blood glucose (mg/dL)*	91.98 ± 7.66	88.35 ± 8.20	0.032	93.89 ± 7.52	88.56 ± 7.66	0.001
Blood glucose after 2 hours (mg/dL)*	104.65 ± 17.11	97.54 ± 28.29	NS	105.38 ± 18.76	99.68 ± 24.30	NS
Fasting insulin (μIU/mL)**	19.1 (6.1–76.8)	11.8 (5.7–60)	0.048	21.5 (6.1–76.8)	12.6 (5.7–60)	0.001
Insulin after 2 hours (μIU/mL)**	67.15 (9.2–351)	44 (6.2–138.7)	0.001	62 (9.2–351)	56.9 (6.2–211.3)	NS
HOMA-IR**	4.28 (1–20.48)	2.96 (1.05–19.77)	NS	4.88 (1–20.48)	3.11 (1.05–19.77)	0.004
IR (n)	52	29	NS	34	47	NS
Uric acid (mg/dL)*	5.33 ± 1.18	4.93 ± 1.12	NS	5.44 ± 1.10	5.01 ± 1.19	NS

Notes: *Data presented as mean plus or minus standard deviation; **data presented as median (minimum to maximum).

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model of insulin resistance; IR, insulin resistance; LDL-C, low-density lipoprotein cholesterol; MS, metabolic syndrome; NCEP ATP III, National Cholesterol Education Program's Adult Treatment Panel III criteria; NS, not significant; SBP, systolic blood pressure; TGs, triglycerides; WC, waist circumference; WHR, waist-to-hip ratio.

of MS has been reported to be higher in severely obese subjects (31.1%) than moderately obese subjects (12.0%), and none of the overweight or normal-weight children studied had MS.²⁷ Weiss et al¹² also stated that risk of MS increases with the degree of obesity.

The prevalence of MS in the present study is higher than reported in European countries.^{18,28–31} The overall prevalence of MS in obese children and adolescents has been reported as 18% in Spain,¹³ 13.9% in Italy,²⁷ 33% in the United Kingdom,³⁰ 30% in Hispanic children in North America,³¹ 27.2% in Turkey,³² 17.3% in Brazil,³³ 15.9% in France,³⁴ and 8.9% in Hungary.³⁵

The differences among studies can originate from the different definitions used for childhood MS. In an article on obese French children, the frequency of MS was found to be 15.9% when using the NCEP ATP III criteria; however, the frequency reached 42.5% when using the World Health Organization's insulin resistance syndrome definition.³⁶ In the present study, the frequency of MS was 63% when using the NCEP ATP III; however, the frequency changed to 39% when using Weiss et al's¹² definition. Agreement between the definitions used was moderate.

Males usually present higher frequencies of MS.^{28,37} In a large US population study concerning adolescents aged

12–19 years, MS was found to be about three times more prevalent in males.³⁷ Other studies have reported a slightly higher prevalence of MS in females than males.^{38,39} However, a significant difference in the prevalence of MS according to sex was not found in the present study.

Childhood obesity is associated with cardiovascular and metabolic disturbances.⁴⁰ In the present study, several parameters failed to present a significant difference between overweight and obese children, except for significantly higher WCs in the obese group.

Elevated BP was detected in about one-third of the sample. The frequency of elevated BP reported in obese children from several European countries (38%)⁴¹ and from the United States⁴² is similar to that found in the present study, but a higher frequency has been reported in 7- to 9-year-old Portuguese schoolchildren.²⁸ High BP has been reported to be responsible for MS in 44.7% of Italians and in 66.1% of Germans.²⁹ The differences found may be attributable to different dietary habits, such as sodium intake, in populations.

The present authors observed that children with MS presented a higher BMI and significant differences in clinical and biochemical characteristics than those children without MS. The reason why some obese children develop MS while others do not is still unclear.⁴²

Table 4 Prevalence of each component of metabolic syndrome in 20 overweight and 80 obese children and adolescents

Component	NCEP ATP III						Weiss et al ¹²						
	Total (n)	Overweight	Obese	P-value	Males (n)	Females (n)	Total (n)	Overweight	Obese	P-value	Males (n)	Females (n)	P-value
High TGs	74	16/20	58/80	NS	29	45	65	11/20	54/80	NS	28	37	NS
Low HDL-C	70	15/20	55/80	NS	28	42	30	6/20	24/80	NS	12	18	NS
High WVC	81	11/20	70/80	0.002	33	48	81	11/20	70/80	0.002	33	48	NS
High SBP/DBP	36	8/20	28/80	NS	13	23	34	8/20	28/80	NS	12	22	NS
High FBS	12	1/20	11/80	NS	7	5	12	1/20	11/80	NS	7	5	NS

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; IR, insulin resistance; LDL-C, low-density lipoprotein cholesterol; NCEP ATP III, National Cholesterol Education Program's Adult Treatment Panel III criteria; NS, not significant; SBP, systolic blood pressure; TGs, triglycerides; WVC, waist circumference.

It is well discussed that atherosclerosis begins in childhood and is associated with several MS risk factors. High TG and LDL levels and low HDL levels are the most important atherogenic factors in children with MS.^{13,28} In the present study, the children with MS presented acanthosis, elevated insulin levels, and increased HOMA-IR values. Acanthosis nigricans is associated in some cases with hyperinsulinemia.²⁰ Children with this characteristic are 1.6 times⁴³ to 4.2 times⁴⁴ more prone to having hyperinsulinemia. Typical areas of involvement include the posterior neck, the axilla, the elbows, and the knees.

In the current study the difference of insulin level when using Weiss et al's¹² definition was significant. IR was found in 81% of the study population, while high fasting glycemia was 12%. However, high fasting glycemia was not common in the subjects. This suggests that an impaired glucose level develops later than the other MS components, while IR is the earlier abnormality of glucose metabolism in obesity.⁴⁵ Actually, excess weight in children and adolescents may serve as an accelerator for the onset of type 2 diabetes in childhood.^{28,46} IR seems to be an important pathophysiologic factor for MS, becoming more important than overall adiposity in the development of the syndrome.^{28,47} In a recent publication, Voss et al⁴⁸ showed that discrimination between overweight and obesity using BMI in young children was not a good marker for the prediction of IR or, therefore, for the prediction of metabolic risk.

It is recognized that MS in a person's youth can increase risk of developing type 2 diabetes and cardiovascular disease in adulthood.⁴⁹ It is not clear which set of metabolic abnormalities will evolve toward a more serious sequel of MS or, conversely, which one is potentially more reversible by treatment in the future.²⁹ However, it is obvious that treatment and prevention of MS in obese youth is necessary. In spite of the high prevalence of MS observed in obese youth from different studies, there are reports that lifestyle modification for young people has led to changes in single components and reduction of MS prevalence.^{50,51} Early diagnosis and treatment of weight excess in overweight subjects would prevent the health complications of obesity in adulthood.

There is no consensus about the definition of MS in children.⁵² Different MS criteria have been employed for different studies in children and adolescents, and the components and cutoffs used to diagnose the syndrome have varied among the various definitions.^{12,37,52} Because of the age- and sex-dependent changes in several components of MS, adult definitions of MS do not apply to children.⁵³ Growth and developmental effects during childhood and adolescence

make it difficult to choose a distinct cutoff for risk factors.⁵⁴ As a result, the prevalence varies according to the definition used.⁵² This point is corroborated by the present study, as the authors found a wide range of prevalence between the two definitions used.

The major criteria of MS came from the NCEP ATP III in 2001. Weiss et al's¹² definition is a slightly modified version of the NCEP ATP III criteria. The cutoff values for TGs and HDL-C are the main difference between the NCEP ATP III and Weiss et al's¹² definition. Results of this study demonstrated that the prevalence of MS found when using the NCEP ATP III definition was higher than when using the definition by Weiss et al.¹² One of the reasons for these differences could be that lipid profile and BP criteria are higher in the NCEP ATP III definition than in the definition by Weiss et al.¹²

NCEP ATP III criteria do not include a measure of IR, which has been shown to provide incremental information in assessing cardiovascular disease risk in the nondiabetic population.⁵⁵ NCEP ATP III criteria have been adapted for US children and adolescents; other populations may have different normal reference ranges for criteria of the definition.^{56–59} In the NCEP ATP III definition, a unique cutoff value for TGs and HDL-C is used that may lead to misclassification of dyslipidemia. Age- and sex-specific fluctuation in lipid values is a characterization of this life period^{56–58} that has been less valued in NCEP ATP III criteria than other criteria. In the present study the largest disagreement between the two definitions used was found for HDL-C.

As there is not a standardized and internationally accepted definition for pediatric MS, it is difficult to compare the pediatric and adolescent MS frequencies reported in different countries.¹³ Not only discrepancies in the definition of individual components of the syndrome but also normal thresholds used in different studies can have an impact on the identification of MS prevalence.¹⁵

The evaluation of risk factors is more complicated in children, because of the requirement for age- and sex-appropriate values that may lead to less frequent identification of the syndrome.¹⁷ The literature is limited with regard to the usefulness of the identification of MS in adolescents, as the diagnosis of MS is more complicated in this age group.

The most important limitation of the present study is its cross-sectional design. The selection of cases was based on referred children and adolescents, which appears as a limitation but, with respect to an increasing prevalence of obesity, as it highlights the importance of screening of metabolic risk factors in this population it also becomes a strength of the study.

Doubts and discussions exist about which criteria to use. The prevalence of MS varied according to the diagnostic criteria used. The higher prevalence was detected by the NCEP ATP III criteria, the parameters of which include higher cutoff values for HDL and TGs, and therefore the NCEP ATP III criteria are able to diagnose a larger number of children and adolescents at metabolic risk.

Conclusion

The prevalence of MS in children and adolescents depends on the criteria chosen and their respective cutoff points. To avoid possible under- or overestimation of the prevalence of MS, the use of nationwide specific cutoff values would be helpful and seems likely to give more reliable results. The samples in this study were from clinic-based series of overweight and obese children and adolescents seeking medical care; a survey with comparable methodology on national populations, in order to assess obesity and MS prevalence in youth, should be taken.

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The authors report no conflicts of interest in this work.

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