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PEDIATRIC HIGHLIGHT

Metabolic syndrome in obese Caucasian children: prevalence using WHO-derived criteria and association with nontraditional cardiovascular risk factors

C Invitti[1], C Maffeis[2], L Gilardini[1], B Pontiggia[1], G Mazzilli[3], A Girola[1], A Sartorio[3], F Morabito[3] and GC Viberti[4,1]

[1]*Department of Metabolic Diseases and Diabetes, Istituto Auxologico Italiano, Milan, Italy;* [2]*Department of Pediatrics, University of Verona, Verona, Italy;* [3]*Department of Auxology, Istituto Auxologico Italiano, Verbania, Italy and* [4]*Cardiovascular Division, GKT School of Medicine, Guy's Hospital, King's College London, London, UK*

Objective: Studies on the prevalence of metabolic syndrome (MS) in European obese children using child-based criteria are scanty. Moreover, it is unknown if nontraditional cardiovascular disease (CVD) risk factors are associated with the MS at this early age in these subjects.
Design and subjects: We studied the prevalence of the MS in 588 Caucasian obese children and adolescents by devising a World Health Organization derived definition and child-specific criteria, whose deviation from normalcy was based on an age, sex, and ethnically comparable control group of 1363 subjects. In a subgroup of 206 obese children, we investigated the association of the MS with nontraditional CVD risk factors.
Measurements: Fasting blood samples for glucose and lipids measurements were taken in both control and obese children. In addition, the obese children underwent an oral glucose tolerance test. In the subgroup of 206 obese children, albumin excretion rate , plasma uric acid, fibrinogen, plasminogen activator inhibitor type 1(PAI-1), C-reactive protein, interleukin 6 and white blood cells were also measured.
Results: The prevalence of MS was 23.3%. A similar prevalence of 23% of MS was recorded in the subgroup of 206 obese children in whom measurements of nontraditional CVD risk factors were available. After adjustment for the degree of obesity, subjects with MS had significantly higher uric acid (6.6 ± 0.23 vs 6.1 ± 0.12 mg/dl, $P<0.0001$) and PAI-1 plasma concentrations (231.4 ± 25.50 vs 214.3 ± 12.96 ng/ml, $P<0.05$) and a higher frequency of microalbuminuria (37 vs 20%, $P<0.05$) than those without MS. Microalbuminuria, uric acid and PAI-1 explained 10.6% of the variance of MS.
Conclusion: Approximately, a quarter of Caucasian obese children have the MS. The association of MS with several nontraditional risk factors for CVD early in life suggests a heightened CVD risk in these individuals.
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Keywords: metabolic syndrome; obese children; uric acid; PAI-1; microalbuminuria

Introduction

Obesity is closely associated with cardiovascular disease (CVD) risk factors such as dyslipidemia, hypertension and glucose intolerance. A common denominator of these different clinical and biochemical phenotypes is insulin resistance. The concomitant occurrence of these abnormalities, referred to as metabolic syndrome (MS), predicts mortality for ischemic heart disease and the development of diabetes.[1] As for adults, obesity in children is in rapid expansion across the world[2] with the potential of adding considerably to the future health burden of cardiovascular and metabolic diseases. Coronary risk factors measured in children are associated with the early development of coronary artery calcifications,[3] and obesity in adolescence is related with a significantly increased risk of early death from coronary heart disease during adulthood.[4] For these reasons, the recognition of the MS in obese children, who have not yet developed a metabolic and/or CVD, is of great importance from a clinical and public health perspective. Adult definitions of MS do not apply to children because of the age- and sex- dependent changes in several of the

Correspondence: Dr C Invitti, Department of Metabolic Diseases and Diabetes, Istituto Auxologico Italiano, Via Ariosto 13, 20145 Milan, Italy.
E-mail: invitti@auxologico.it
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component variables of the MS, and at present specific definitions of MS for children and adolescents are not available. Using the National Cholesterol Education Program Adult Treatment Panel III (NCEP) criteria adapted to adolescents, two recent papers have shown that from one-third to a half of American overweight and obese children have the MS.[5,6] These criteria, however, do not include a measure of insulin resistance which has been recently shown to provide incremental information in assessing CVD risk in nondiabetic subjects.[7] We therefore devised child-specific criteria derived from the World Health Organization (WHO) definition[8] to estimate the prevalence of MS in a cohort of Caucasian obese children. In addition, in a subgroup of children we assessed the association of MS with nontraditional cardiovascular risk factors. Several lines of evidence support the view that a proinflammatory state may induce insulin resistance leading to clinical and biochemical manifestation of MS.[9,10] This low-grade inflammatory state may be detected systemically by measurement of inflammatory markers, which have been found to be independent risk factors for CVD.

Thus, the aims of this study were to determine: (a) the prevalence of the MS using WHO-derived child-specific criteria among 588 obese children, (b) the association of the MS with several nontraditional CVD risk factors including plasminogen activator inhibitor type 1 (PAI-1), interleukin 6 (IL-6), white blood cells (WBC), uric acid, fibrinogen and C-reactive protein (CRP) among the group of 206 obese children most recently enrolled.

Methods

Study population

We studied 588 obese children (291 males, age range 6–16 years) of Caucasian origin for the prevalence of MS. These obese subjects were referred by their general practitioner or their primary care paediatric consultant to the Istituto Auxologico Italiano, a specialized center for the study of obesity, between 1994 and 2001 for metabolic evaluation and clinical management. Subjects were eligible if their BMI exceeded the age- and sex- adjusted 97th BMI percentile, which defines obesity according to the Italian BMI charts.[11] Exclusion criteria were secondary obesity, known diabetes and the use of any drug. Anthropometric measures, blood pressure (BP) and fasting blood samples for glucose and lipids measurements were taken in both control and obese children. For construction of normal reference ranges, a random sample of 1363 'nonobese' children of the same ethnic and geographical origin was drawn from the school districts of six areas of Northern Italy.[12] They had an age range between 6–16 years, superimposable to that of the obese children and were in good health, as assessed by medical history, physical examination and routine hematological and biochemical tests. They were of normal weight except for 129 subjects who were overweight as defined by a BMI $\geqslant$ 85th and $\leqslant$ 97th percentile for age and sex according to Italian population charts.[11]

In order to investigate the relation between nontraditional CVD risk factors and the MS, in the 206 most recently enrolled obese children, albumin excretion rate (AER), uric acid, PAI-1, fibrinogen, CRP, IL-6 and WBC count were measured.

Procedures

Obese children underwent, after a 12-h overnight fast, an oral glucose tolerance test (1.75 g/kg, up to a maximum of 75-g glucose in 250 ml of water). Plasma samples were drawn at baseline and after 120 min for determination of plasma glucose and insulin concentration. No insulin levels were available in 'non obese' children. The study was approved by the Ethics Committee of the Istituto Auxologico Italiano and informed consent was obtained from all subjects and their parents after full explanation of the study. Family history for obesity and diabetes were obtained by questionnaires filled in by the parents. Body weight was recorded to the nearest 100 g using a standard beam balance scale with the subjects wearing indoor clothing and wearing no shoes. Height was recorded to the nearest 0.5 cm using a standardized wall-mounted height board. The degree of obesity was quantified using BMI and waist circumference, which was measured at the level of the umbilicus and the superior iliac crest at the end of a normal expiration while the subjects were in a standing position. Pubertal development was assessed according to the criteria of Tanner[13] by physical examination by the same observer, a consultant paediatric endocrinologist (F.M.). Diastolic and systolic BP were measured to the nearest 2 mmHg in the supine position after 5 min rest, using a standard mercury sphygmomanometer with an appropriately sized cuff. The average of three measurements obtained on different days during admission was used in the analysis.

In the subgroup of 206 obese children in whom nontraditional CVD risk factors were measured, 24 h urine collections were obtained on two occasions, 1–2 weeks apart. The mean value of AER was used for calculation.

Definitions

Categorization of glucose tolerance status (impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) or diabetes) was made using the WHO definitions.[8] Insulin resistance was measured by homeostasis model assessment for insulin resistance (HOMA-IR: fasting insulin $\times$ fasting glucose/22.5).[14] The adult definition is unlikely to apply to children in that, as we have previously shown, HOMA-IR changes during childhood depending on the pubertal stage.[15] We have considered HOMA-IR values greater than the median value for each of the Tanner stages as an indicator of insulin resistance. This corresponded to values of 2.4, 2.8, 3.0, 4.1 and 3.0, respectively, for stages I, II, III, IV and V.

We derived the child-based definition of MS from the WHO adult definition with the following modifications. Microalbuminuria was omitted from the WHO definition because its significance in children is still uncertain and measurements were available only in a subset of obese subjects. In its place, the elements of dyslipidemia in the WHO definition (i.e. triglycerides and/or HDL cholesterol) were used separately. Waist-hip ratio was replaced with waist circumference because of the unreliability of hip measurements in children.[16] Thus, children and adolescents were classified as having the MS if they had glucose intolerance (IFG or IGT or diabetes) and/or insulin resistance + two or more of the following factors: (1) BMI and waist circumference $\geqslant$97th percentile of controls, (2) HDL cholesterol $\leqslant$5th percentile of controls (3) triglycerides $\geqslant$95th percentile of controls, (4) BP$\geqslant$95th percentile of controls. All the obese children in this study met the criterion for both BMI and waist circumference.

Measurements

Plasma glucose, LDL and HDL cholesterol, triglycerides, uric acid and WBC count were measured using an automated analyzer (Roche Diagnostics, Mannheim, Germany). Serum insulin was measured in duplicates by an immunofluorimetric assay (AIA, TOSOH, Tokyo) from 1994 to 1998 and by a chemiluminescent assay (ICMA, DPC, Los Angeles, USA) from 1999 to 2002. The two methods were highly correlated ($r=0.99$, $P<0.0001$) and AIA measured values were converted using the following formula: ICMA insulin $= 0.879 \times$ A $+ 3.099$, where 0.879 represented the slope and 3.099 the intercept of the regression line and A was the AIA insulin value. CRP concentrations were measured by an ultrasensitive immunoturbidimetric assay (CRP Latex HS, Roche Diagnostics, Mannheim, Germany), with a sensitivity of 0.03 mg/l and intra- and interassay CVs of 1.3 and 5.7%, respectively. Fibrinogen was measured in citrate plasma with a clot-rate assay using the ACL 200/IL instrument (Instrumentation Laboratory, Milan, Italy); the sensitivity of the assay was 7.5 mg/dl and the intra- and interassay CV were 4.8 and 5.2%, respectively. PAI-1 was determined by an enzyme immunoassay (Byk-Sangtec Diagnostica, Diezenbach, Germany) with a sensitivity of 2.9 ng/ml and intra- and interassay CV of 4.5 and 6.7%, respectively. IL-6 was measured by an enzyme immunoassay using a monoclonal antibody (R&D System Inc., Minneapolis, USA) with a sensitivity of 0.7 pg/ml and intra- and interassay CV of 4.2% and 6.4%, respectively. Albumin concentration was determined by immunoturbidimetric assay (Roche Diagnostic, Mannheim, Germany) with a sensitivity of 3 mg/l and intra- and interassay CV of 1.3 and 4.3%, respectively. Microalbuminuria was defined as an AER of 20–200 μg/min.[17]

Statistical analysis

The group frequencies were compared by χ^2 test. Differences between groups were calculated, in the whole cohort of obese children, using a Student's *t*-test for independent samples. Variables that were not normally distributed (HOMA-IR, triglycerides and CRP) were log-transformed. In order to calculate the impact of obesity on the frequency of MS, we quantified the degree of obesity using Cole's least mean square method which normalizes the BMI skewed distribution and expresses BMI as standard deviation score (SDS-BMI).[18] To assess if the aggregation of the components of MS occurred randomly, the Wald–Wolfowitz runs test was used. The Wald–Wolfowitz runs test compares distribution locations and shapes for two groups by combining the two groups and ranking the data. Sum of the four components of MS (glucose intolerance and/or insulin resistance; low HDL cholesterol; hypertryglyceridemia; hypertension) were compared between subjects with MS and without MS. *Z*-scores and corresponding levels of statistical significance were computed assuming that if the two groups were different, the number of ranks were smaller than random scatter, and *z*-scores are statistically significant. To establish differences in nontraditional CVD risk factors between subjects with and without MS and across groups that had 1, 2, 3 and $\geqslant$4 components of MS after adjustment for SDS-BMI, we performed an analysis of covariance. Logistic regression analysis was used to establish the proportion of the variance of MS explained by the classical components of MS (glucose intolerance and/or insulin resistance; low HDL cholesterol; hypertryglyceridemia; hypertension) and by nontraditional components of MS (microalbuminuria, uric acid and PAI-1). Data were expressed as mean $\pm$ s.d. unless otherwise stated. A *P*-value <0.05 was considered statistically significant. All analyses were performed using SPSS version 11.0 (Statistical Package for Social Science Inc., Chicago, IL, USA).

Results

Prevalence of metabolic syndrome in European obese Caucasian children

The age range was the same in control and obese children, but mean age was higher in the obese cohort. Obese subjects were taller, had higher BP and serum triglycerides and lower HDL cholesterol. After age adjustment these differences remained significant (Table 1). In the obese cohort, the overall median (interquartile range) of HOMA-IR was 2.8 (1.9–4.4) with no difference between sexes. IFG was present in 0.3%, IGT in 4.1% and diabetes in 0.2% of the subjects. The prevalence of MS in obese children was 23.3%. Table 2 shows the clinical features of obese children with and without the MS. Children with MS were older, more often pubertal, more obese, had more frequent IGT and, as expected, had higher values of HOMA-IR, fasting and 2-h glucose, BP, triglycerides and LDL cholesterol and lower values of HDL cholesterol. The frequency of MS significantly increased across the tertiles of SDS-BMI (16 vs 23 vs 31% in tertile I (2–3.5), II (3.6–4.1) and III (4.2–6.2) of SDS-BMI, $P<0.005$). Sex distribution and family history of diabetes

Table 1 Demographic, anthropometric, clinical and biochemical features of Caucasian obese and control children

	Obese			*Nonobese controls*		
	Whole group (n = 588)	*Boys (n = 291)*	*Girls (n = 297)*	*Whole group (n = 1363)*	*Boys (n = 651)*	*Girls (n = 712)*
Age (years)	13 (6–16)*	13 (6–16)	13 (7–16)	10 (6–16)	10 (6–16)	10 (6–16)
Height (cm)	156.5±11.3*†	158.0±11.7‡	155.0±10.7	143.1±13.8	142.8±13.9	143.8±13.6
Weight (kg)	84.5±21.6	86.7±22.7	82.5±20.3	38.2±11.2	37.8±11.4	38.2±11.4
BMI (kg/m^2)	33.9±5.5	34.0±5.5	33.7±5.6	19.1±3.2	18.9±2.8	19.8±2.9
Waist (cm)	102.6±12.5	105.1±12.5	100.8±12.2	61.7±7.8	62.0±7.8‡	61.0±7.3
FPG (mmol/l)	4.5±0.4	4.5±0.4	4.4±0.5	4.9±0.6	4.9±0.4	4.9±0.5
HDL (mmol/l)	1.2±0.3*	1.2±0.3	1.2±0.3	1.5±0.7	1.6±0.6‡	1.5±0.5
LDL (nmol/l)	2.9±0.7	2.9±0.8	2.9±0.7	3.1±0.8	3.0±0.9	3.1±0.7
Triglycerides (mmol/l)	0.9 (0.7–1.3)*	0.9 (0.7–1.3)	1.0 (0.7–1.3)	0.7 (0.5–0.9)	0.6 (0.5–0.8)§	0.7 (0.5–0.9)
Systolic BP (mmHg)	124±13.4*	126±13.5§	122±13.1	111±12.9	112±12.8	110±12.8
Diastolic BP (mmHg)	76±9.3*	76±9.4	75±9.3	66±10.6	67±10.7	66±10.3

*$P<0.0001$; †$P<0.05$ vs controls; age adjustment did not change the level of significance for the differences in lipids and BP; ‡$P<0.05$, §$P<0.0001$ vs. girls in the same group. Data are expressed as mean (range) and mean±s.d. triglycerides are expressed as median (interquartile range). FPG = fasting glucose.

Table 2 Clinical characteristics of 588 Caucasian obese children with and without metabolic syndrome

	With metabolic syndrome	*Without metabolic syndrome*
Subject number (M%)	137 (48.2%)	451 (50%)
Age (years)†	13.5 (7–16)	13.0 (6–16)
Family history of obesity/ diabetes (%)	67/60	61/54
Pubertal (%)*	44	34
BMI (kg/m^2)**	36.2±5.53	33.1±5.3
Standard deviation score BMI**	4.0±0.7	3.7±0.7
Waist (cm)*	106.7±11.7	101.5±12.5
Insulin resistance (%)	95	38
IGT or IFG or diabetes (%)	10.3/0.7/0.7	1.9/0/0
HOMA-IR**	4.5 (3.6–5.8)	2.5 (1.7–3.7)
Fasting glucose (mmol/l)**	4.6±0.04	4.4±0.02
2-h glucose (mmol/l)**	6.3±1.2	5.8±0.9
Triglycerides ⩾95th percentile (%)	44.2	3.8
Triglycerides (mmol/l)**	1.4 (0.9–1.7)	0.8 (0.7–1.1)
HDL ⩽5th percentile (%)	69.3	15.1
HDL (mmol/l)**	1.0±0.2	1.3±0.2
LDL (mmol/l)*	2.8±0.8	2.7±0.7
Blood pressure ⩾95th percentile (%)	19.0	5.7
Systolic BP (mmHg)**	129±13.3	123±13.1
Diastolic BP (mmHg)**	79±10.2	75±8.9

*$P<0.05$, †$P<0.01$, **$P<0.0001$. Data are expressed as mean (range), %, mean±s.d. and for HOMA-IR and triglycerides as median (interquartile range). The frequency of insulin resistance, IGT, triglycerides and BP⩾95th percentile and HDL cholesterol⩽5th percentile was significantly higher ($P<0.0001$) in subjects with metabolic syndrome than in those without the metabolic syndrome.

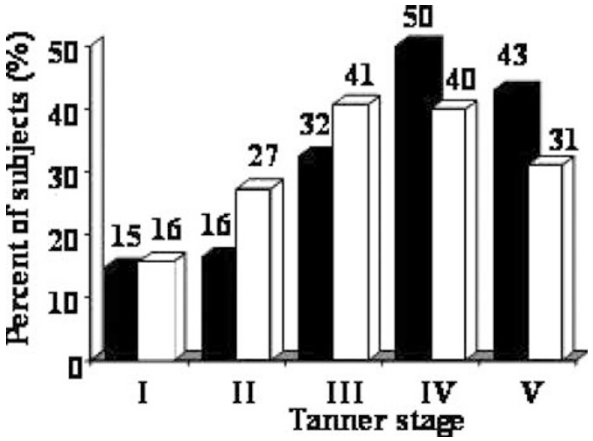

Figure 1 Frequency of WHO-derived child-based MS in 588 obese Caucasian children (boys, $n=291$, black column; girls, $n=297$, white column) according to Tanner pubertal stages. Figures at the top of the columns represent actual percentage of subjects.

and obesity were similar in the two subsets. Obese children without MS had lipids and BP values intermediate between those of children in the control group and obese children with MS. In both sexes, the frequency of MS gradually increased from Tanner stage I to stage IV and declined at stage V (Figure 1). The Wald–Wolfowitz test demonstrated that the components of MS were independently distributed in obese children with and without MS (z score for minimum possible number of runs −23.93; $P<0.0001$; z score for maximum possible number of runs −19.77; $P<0.0001$) and excluded that clustering of risk factors in the children with MS did occur by chance.

In the logistic regression analysis, glucose intolerance and/or insulin resistance explained 30.2%, low HDL cholesterol and high triglycerides 21.7 and 12.8%, respectively, and high BP values 3.5% of the total variance of MS.

Nontraditional CVD risk factors and metabolic syndrome

In the 206 obese children in whom AER and nontraditional CVD risk factors were measured, the prevalence of MS was similar (23%) to that recorded in the whole group of 588 obese children. The children with MS were more obese than those without MS (SDS-BMI 4.13±0.6 vs 3.70±0.7, $P<0.001$). After adjustment for SDS-BMI, the obese children with MS had significantly higher levels of uric acid and PAI-1

Table 3 Levels of nontraditional CV risk factors after adjustment for SDS-BMI in 206 obese children with and without metabolic syndrome

	With metabolic syndrome (n = *47*)	*Without metabolic syndrome* (n = *159*)
Microalbuminuria (%)	37*	20
Uric acid (mg/dl)	6.6 ± 0.23#	6.1 ± 0.12
PAI-1 antigen (ng/ml)*	231.4 ± 25.50*	214.3 ± 12.96
IL6 (pg/ml)	3.1 ± 0.45	2.6 ± 0.20
CRP (mg/dl)	0.5 (0.2–0.8)	0.5 (0.2–0.9)
Fibrinogen (mg/dl)	372.5 ± 10.60	400.5 ± 5.75
WBC (10^9/l)	8.2 ± 0.31	7.6 ± 0.16

*$P<0.05$, #$P<0.0001$. Data are expressed as %, mean ± s.e. and as median (interquartile range).

and a higher frequency of microalbuminuria (Table 3). After adjustment for SDS-BMI, the concentrations of uric acid, PAI-1 and IL-6 increased with the number of the components of MS (mean ± s.e.; uric acid: 5.9 ± 0.21 vs 6.3 ± 0.26 vs 6.5 ± 0.23 vs 7.5 ± 0.42 mg/dl, PAI-1: 169.7 ± 19.5 vs 242.3 ± 17.6 vs 232.7 ± 24.5 vs 277.9 ± 43.4 ng/dl; IL-6: 2.2 ± 0.27 vs 3.2 ± 0.30 vs 3.0 ± 0.47 vs 4.5 ± 0.87 pg/ml in subjects with 1, 2, 3 and ⩾4 components of the MS, $P<0.05$ for trend in all). In the logistic regression analysis, the traditional components of the MS explained 47.2% of the total variance of MS while microalbuminuria, uric acid and PAI-1 together explained 10.6%.

Discussion

Several studies have addressed the issue of the prevalence of the MS in childhood using criteria specific for children and adolescents,[5,6,19–22] however, limited data are available in Caucasian children.[20] We included a measure of insulin resistance among the criteria of MS to increase, over and above the NCEP criteria, the sensitivity for identifying insulin resistance with dyslipidemia in young nondiabetic subjects.[23] To define insulin resistance in this group of obese children, we used HOMA-IR values above the median for pubertal age because there is no definition of insulin resistance for the age range considered in this study and reference range charts for HOMA-IR in normal weight children are not available. This procedure, though reasonable, may be conservative and has underestimated the true prevalence of the phenomenon. In addition, for lipids and BP, we used values ⩾95th percentile (⩽5th percentile for HDL cholesterol) of a control group of children from the same geographical area matched for age, sex and ethnicity. It is indeed still untested how the American criteria adapted for adolescents would apply to other populations who may have different normal reference ranges for some of the criteria of the definition.[24–27] Moreover the use, as in the NCEP definition adapted to adolescents, of a unique cutoff value for triglycerides and HDL cholesterol during childhood may lead to misclassification of dyslipidemia. This life period is characterized by age and sex-specific fluctuation in lipid values.[24–26]

We found that 23.3% of obese children had the MS. The prevalence of MS in our cohort of all Caucasian children was lower compared to the 29–50% previously reported in cohorts of American multiethnic and Hispanic obese children[5,6,19] using NCEP criteria adapted to adolescents. The frequency of MS among our obese children was also somewhat lower than the 26% recently reported in 268 Mexican obese children[22] using a definition which included the presence of positive family history for obesity and type 2 diabetes. Those factors in our cohort did not differ between children with and without MS. The higher prevalence reported in the American and Hispanic cohorts of obese children and adolescents may be related to ethnic, cultural and social differences. White children and adolescents, for instance, have more often dyslipidemia than black subjects. These latter, by contrast, have higher BP levels than white subjects. Hispanic individuals compared to the other two groups appear to have greater visceral fat distribution and a higher prevalence of IGT and family history of diabetes.[5,6,19] These findings highlight the importance of local, ethnically, culturally and socially compatible representative control groups for investigations of this kind. To define the prevalence of MS even within one of the manifestations of the definition, such as obesity in this case, is important. It has recently been reported, for instance, that in diabetic patients the presence of MS increases the risk for coronary heart diseases.[28] In the present cohort, the prevalence of MS increased with the increasing degree of obesity even within a population of all obese subjects. Similar findings were reported in an American cohort.[6]

A high proportion of nondiabetic obese children had microalbuminuria. Indeed, the frequency of microalbuminuria in the general population has been shown to increase with the degree of obesity.[29] Its frequency was significantly higher in subjects with MS than in those without MS suggesting that in children, as in adults,[30] microalbuminuria is associated with MS. Obese children with MS also had higher concentrations of PAI-1 and uric acid which together with microalbuminuria explained 10.6% of the variance of the MS. This proportion is similar to the 7.4% of the total variance of MS explained by an 'inflammatory factor' in nondiabetic individuals participating in the Insulin Resistance Atherosclerosis Study.[9] The strong association in obese children between uric acid and MS, independent of the degree of obesity, supports the notion of a possible role for uric acid as an independent risk factor for CVD.[31] In this context, the recent observation that allopurinol decreases BP values in hypertensive children is of interest.[32] This suggests that uric acid may be a therapeutic target to reduce CVD risk.

Finally, the present data confirmed that in children, unlike in adults,[33] CRP levels are not related to the MS[6,34,35] and that in children the only variable independently associated with CRP is the degree of obesity.[15,35] If CRP levels are

obesity-driven, MS might fail to influence CRP in the context of an all obesity cohort.

This paper has several limitations. Our cohort, is not a population-based sample and might not reflect the Italian obese child population. However, it is representative of a large proportion of Italian obese children as there were no filters to their referral except for the restriction we applied in the exclusion criteria. We recognize that the WHO-derived criteria adapted to children may not be practical in as much as normal standards of HOMA-IR and lipids are currently not available. Population studies would be required for developing appropriate charts. The prevalence nature of the present study does not estabilish a superiority of our definition of MS in predicting clinical outcomes. Only prospective studies in children will answer this question.

In conclusion, we demonstrated that approximately a quarter of obese children of Caucasian origin in Italy have the MS. We also showed that in children the MS clusters with several nontraditional CVD risk factors supporting the view that chronic subclinical inflammation may be part of the MS. The finding of this aggregation of risk for CVD at this very young age adds further significance to strategies aimed at preventing weight gain and insulin resistance early in life.

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