

ORIGINAL ARTICLE

Sympathoadrenergic and metabolic factors are involved in ambulatory blood pressure rise in childhood obesity

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We investigated in a young Italian obese population, the relationship between ambulatory BP (ABP) and several pathophysiological factors linking obesity to hypertension. A total of 89 obese children and adolescents underwent a 24-h ambulatory BP monitoring (ABPM) and an oral glucose tolerance test. The circulating levels of insulin, lipids, uric acid, C-reactive protein, interleukin-6, renin and aldosterone and the 24-h urinary levels of epinephrine, norepinephrine and albumin excretion rate were measured. Nine percent of subjects had daytime sustained hypertension (SH), 26% night-time hypertension and 11% a non-dipping pattern. SH subjects compared to those with sustained normotension (SN) were more obese ($P < 0.05$), with a more frequent family history of hypertension ($P < 0.05$), higher urinary catecholamine ($P < 0.05$) and heart rate values ($P < 0.05$) after adjustment for standard deviation score (SDS) of body mass index (BMI) and sex. Subjects with night-time hypertension compared to those with

night-time normotension were more obese ($P < 0.0001$), with a higher prevalence of impaired glucose tolerance ($P < 0.05$) and metabolic syndrome ($P < 0.05$) and higher 2-h glucose ($P < 0.05$), uric acid ($P < 0.05$) and triglycerides ($P < 0.05$). In multivariate regression analysis, daytime systolic BP (SBP) remained independently correlated with urinary norepinephrine and SDS-BMI ($P < 0.05$ for both), daytime diastolic BP (DBP) with waist circumference ($P < 0.05$) and night-time SBP and DBP with SDS-BMI ($P < 0.01$ for both). The risk of having systolic and diastolic hypertension increased with the increase in SDS-BMI and waist circumference, respectively. In conclusion, in our cohort of obese children and adolescents, daytime and night-time hypertension were associated with activation of the sympathoadrenal system and worst metabolic conditions, respectively.

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Introduction

During the past decade, there has been an increasing interest in childhood and adolescent hypertension. Data from different countries demonstrate that the prevalence of paediatric hypertension ranges between 3 and 11%, and is three times more frequent in obese than in normal-weight children.^{1–4} Using office blood pressure (BP) measurements in a large cohort of Italian obese children and adolescents, we have previously shown that 29% of boys and 14% of girls aged 6–12 years have hypertension and that this percentage increases by three times in adolescents.⁵

The abnormal office BP rise observed in obesity is primarily caused by an increase in peripheral vascular resistance. The latter has been ascribed to different factors such as insulin resistance, activation of the sympathetic nervous system and an abnormal production of substances by adipose tissue.⁶ Several papers have reported that office BP levels correlate with metabolic and inflammatory markers in children as well as in adults;^{7–11} however, the precise mechanisms involved in starting and maintaining childhood obesity-related hypertension in the office environment, and even more so in ambulatory conditions, are still unknown. Further insight into the pathophysiology of hypertension affecting young obese people can be obtained by exploring the relation between BP levels measured with ambulatory BP monitoring (ABPM) and a number of factors that might be involved in their elevation. Use of ABPM in this context appears to be particularly important because in children, as in

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adults, ABPM was shown to be superior to office BP measurements in detecting early BP elevations already associated with hypertension-related organ damage, and in particular, with an increase in left ventricular mass.^{12–14}

The aim of our study was, therefore, to explore the relationship between ABP measurements and several variables linking obesity to hypertension, such as metabolic (insulin, fasting, and 2-h glucose, lipids and albumin excretion rate (AER)), inflammatory (C-reactive protein (CRP) and interleukin-6) and hormonal (epinephrine, norepinephrine, aldosterone and renin) factors.

Materials and methods

Study population

In all, 89 children and adolescents of Caucasian origin, ranging from 7 to 18 years of age, were recruited among obese subjects referred to the Istituto Auxologico Italiano, a national centre for the study of obesity. Patients with secondary obesity and on any drug therapy were excluded from the study. None of the children in this cohort reported to be a smoker, even occasional.

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. All subjects included were above the age- and sex-adjusted 97th body mass index (BMI) percentile, which defines obesity according to the Italian BMI charts.¹⁵ The degree of obesity was quantified using Cole's LMS method,¹⁶ which normalizes BMI and its skewed distribution, by expressing BMI as a standard deviation score (SDS-BMI). Waist circumference was measured in a standing position, at the level of the umbilicus frontally and of the superior iliac crest laterally, at the end of a normal expiration. Pubertal development was assessed by physical examination according to the Tanner criteria. Family history of hypertension (FH) was defined as hypertension in first-degree relatives and assessed by questionnaires filled in by parents. In addition, parents were asked for their usual BP levels or prescription of antihypertensive compounds.

All subjects underwent a fasting oral glucose tolerance test (1.75 g kg⁻¹ up to a maximum of 75 g glucose in 250 ml of water). Plasma samples were drawn at baseline and after 30 and 120 min for determination of plasma glucose and insulin concentration. Impaired fasting glucose (IFG) was defined as a fasting glycaemia between 5.6 and 7.0 mmol l⁻¹, impaired glucose tolerance (IGT) as 2-h post-load glycaemia between 7.8 and 11.1 mmol l⁻¹ and type II diabetes as fasting glycaemia ≥ 7.0 mmol l⁻¹ or a 2-h post-load glucose value ≥ 11.1 mmol l⁻¹. Insulin resistance was estimated using the homeostasis model assessment insulin resistance (HOMA-IR:

fasting insulin \times fasting glucose/22.5).¹⁷ A blood sample was drawn for lipids, uric acid, CRP and interleukin-6 circulating level assessment. Plasma renin activity and aldosterone levels were measured in recumbent position and after a 2-h walk. All children collected 24-h urine samples on two occasions, 1–2 weeks apart, for the measurement of AER, epinephrine and norepinephrine levels.

Metabolic syndrome (MS) was defined using WHO-derived definition and child-specific criteria as previous described.⁷

The study was approved by the Ethics Committee of the Istituto Auxologico Italiano, and informed consent was obtained from parents and participants after full explanation of the study procedures and aims.

Blood pressure measurements

Office BP was measured to the nearest 2 mm Hg in the seated position three times after 5 min rest, using a standard mercury sphygmomanometer with an appropriately sized cuff on the non-dominant arm. The average of measurements obtained on 3 different days was used in the analysis. Office hypertension was defined as the occurrence of systolic BP (SBP) or diastolic BP (DBP) levels ≥ 95 th percentile of height- and sex-adjusted reference levels.¹⁸

Ambulatory blood pressure monitoring

Measurements were taken with a validated oscillometric device (Profilomat; Disetronic Medical Systems AG, Burgdorf, Switzerland). An appropriately sized cuff was attached to the non-dominant arm. Measurements were obtained every 15 min during the daytime (0600–2200 hours), and every 20 min during the night-time (2200–0600 hours). Children were instructed to relax the arm and keep it still until completion of each automated BP measurement. During ABPM, children were free to perform physical activity according to their usual habits. ABP recording started between 0800 and 0900 hours. The accuracy of automated BP readings in each individual subject was confirmed by comparison of two oscillometric measurements with two auscultatory measurements simultaneously obtained with a mercury sphygmomanometer at the beginning of the recording period.

For data analysis, not only the 24-h period, but also daytime (from 1000 to 2000 hours) and night-time (from midnight to 0600 hours) subperiods, defined according to narrow fixed criteria, that is, by excluding transitional periods between wakefulness and sleep, were separately considered. This method was shown to provide a more reliable definition of the actual awake and asleep BP levels by excluding periods during which individual subjects go to bed or get up at different times.¹⁹

Only ABPM recordings with at least three valid readings per hour during daytime and two valid

readings per hour at night, for a total of at least 75% of valid readings over the whole 24-h period, were accepted. Valid readings were identified according to predefined criteria.²⁰ In 13 children, in whom nocturnal recordings included a very low number of readings to guarantee a reliable evaluation, the night-time subperiod was excluded from the analysis.

Sustained normotension (SN) was defined as both office and daytime ABP normotension. Daytime sustained hypertension (SH) was defined as a daytime SBP or DBP level \geq 95th percentile of height- and sex-adjusted reference values,²¹ combined with elevated office BP values (see above).¹⁸ Isolated office hypertension (IOH), also known as white coat hypertension, was defined as office BP hypertension combined with ambulatory daytime normotension (that is, daytime SBP and DBP levels $<$ 95th percentile of ABP reference distribution). Masked hypertension (MH) was defined as office BP normotension (that is, SBP and DBP level $<$ 95th percentile of office BP) combined with daytime ambulatory hypertension. Night-time hypertension was defined as ambulatory SBP or DBP levels \geq 95th percentile of height- and sex-adjusted night-time reference values. The non-dipping status was defined as a night-time/daytime SBP or DBP ratio \geq 100%.²²

Biochemical measurements

Plasma glucose, cholesterol, triglycerides and uric acid concentrations were measured on an automated analyser (Roche Diagnostics, Mannheim, Germany). Serum insulin was measured in duplicate by a chemiluminescent assay (DPC, Los Angeles, CA, USA; sensitivity 14.3 pmol l⁻¹ and intra- and inter-assay coefficients of variation (CVs) 3.7 and 6.7%, respectively).

C-reactive protein concentrations were measured by ultra sensitive immunoturbidimetric assay (CRP Latex HS, Roche Diagnostics; sensitivity 0.03 mg l⁻¹ and intra- and interassay CVs 1.3 and 5.7%, respectively). Interleukin-6 was measured by an enzyme immunoassay using a monoclonal antibody (R&D System Inc., Minneapolis, MN, USA; sensitivity 0.7 pg ml⁻¹ and intra- and interassay CVs 4.2 and 6.4%, respectively). Aldosterone was measured by chemiluminescent assay (Nichols Advantage, San Juan Capistrano, CA, USA; sensitivity 1.5 ng dl⁻¹, intra- and interassay CVs 4.1 and 5.2%, respectively). Renin activity was determined by radioimmunoassay (Techno Genetics, Milan, Italy; sensitivity 0.15 ng ml⁻¹, and intra- and interassay CVs 6 and 7.1%, respectively). AER was determined by immunoturbidimetric assay (Roche Diagnostic; sensitivity 3 mg l⁻¹ and intra- and interassay CVs 1.3 and 4.3%, respectively). Urinary catecholamines were determined by HPLC (Bio-Rad Laboratories, Richmond, CA, USA; sensitivity 2.0 μ g l⁻¹, intra- and interassay CVs 1.1 and 3.2% respectively for

norepinephrine; and 2.2 μ g l⁻¹, 4.8 and 5.2% respectively for epinephrine).

Statistical analysis

Variables that were not normally distributed were log transformed. Group frequencies were compared using a χ^2 test and Fisher's exact test when the expected frequency was less than five. To examine the differences between obese children with and without hypertension, a two-samples *t*-test was used. Pearson correlation analysis was used to analyse bivariate relationship. Multiple regression analysis was performed using variables statistically significant at the 5% level in univariate analysis. Logistic regression analysis was used to estimate odds ratios of having systolic and diastolic hypertension, and the corresponding 95% confidence intervals were calculated for unit increase of SDS-BMI and waist circumference. Data were expressed as means \pm s.d. A *P*-value $<$ 0.05 was considered statistically significant throughout the study. All analyses were performed using SPSS version 14.0 (SPSS, Chicago, IL, USA).

Results

Characteristics of study population

In Table 1, the clinical and biochemical data of the 89 obese children and adolescents included in the analysis are reported. Compared to girls, boys were more obese, more frequently prepubertal and had higher values of triglycerides, uric acid, urinary norepinephrine and office SBP. Daytime and night-time ABP levels and FH were similar in the two genders. Seven subjects (three boys and four girls) had IGT, none had IFG or diabetes. Twenty-seven percent of subjects had MS and 41.6% had microalbuminuria, defined by AER levels between 20 and 200 μ g min⁻¹. FH+ children compared to FH- tended to have higher levels of daytime SBP and DBP (129.9 \pm 12.9 vs 122.2 \pm 9.8 mm Hg, *P* = 0.06 and 84.4 \pm 8.6 vs 79.3 \pm 6.9 mm Hg, *P* = 0.06) and urinary norepinephrine (42.9 \pm 22.3 vs 32.8 \pm 21.2 μ g per 24 h, NS).

Prevalence of hypertensive subjects

Fifty-nine (62.9%) obese children and adolescents had SN, 5 (16.9%) MH, 10 (11.2%) IOH and 8 (9%) daytime SH. Isolated systolic hypertension accounted for 87 and 25% of SH, based on the use of office or ABPM, respectively. The frequency of SH was similar in the two sexes, that of IOH was more frequent in boys and that of MH in girls (Figure 1).

Night-time hypertension was detected in 19 out of 74 (25.6%) subjects: 7 of them had SH, 5 MH, 2 IOH and 5 SN.

A non-dipping pattern was observed in 8/74 (10.8%) obese children.

Table 1 Demographic, clinical and biochemical characteristics of study population

	Boys (n = 38)	Girls (n = 51)
Age, year	8–18 (mean 14.6)	7–18 (mean 14.5)
Pubertal, %	68.4	45.1
Family history of hypertension, %	36.8	23.3
Height, cm	163.6 ± 11.3*	156.9 ± 9.4
Weight, kg	105.1 ± 26.5**	90.1 ± 16.3
BMI, kg m ⁻²	36.7 ± 6.4	36.6 ± 4.9
SDS-BMI, score	4.2 ± 0.7**	3.6 ± 0.6
Waist circumference, cm	116.6 ± 14.4**	106.1 ± 12.3
SBP, mm Hg	126.4 ± 13.9*	118.7 ± 9.8
DBP, mm Hg	74.5 ± 10.6	71.7 ± 8.0
Heart rate, beats per min	83.3 ± 9.6	83.6 ± 7.1
Fasting glucose, mmol l ⁻¹	4.3 ± 0.3	4.1 ± 0.3
2-h glucose, mmol l ⁻¹	6.3 ± 1.1	6.0 ± 1.3
Fasting insulin, pmol l ⁻¹	100.4 ± 90.4	86.1 ± 40.2
HOMA-IR, score	2.6 ± 2.2	2.2 ± 1.1
LDL cholesterol, mmol l ⁻¹	2.5 ± 0.7	2.7 ± 0.6
HDL cholesterol, mmol l ⁻¹	1.1 ± 0.2	1.2 ± 0.2
Triglycerides, mmol l ⁻¹	2.6 ± 0.9*	2.1 ± 0.7
Uric acid, μmol l ⁻¹	410.4 ± 107.1*	344.9 ± 83.3
CRP, mg dl ⁻¹	0.7 ± 0.7	0.5 ± 0.4
IL-6, pg ml ⁻¹	2.5 ± 1.8	2.7 ± 1.8
Renin supine, ng ml ⁻¹ h ⁻¹	0.8 ± 0.6	0.7 ± 0.4
Renin upright, ng ml ⁻¹ h ⁻¹	1.4 ± 0.8	1.2 ± 0.8
Aldosterone supine, ng l ⁻¹	87.9 ± 52.2	74.8 ± 62.5
Aldosterone upright, ng l ⁻¹	157.6 ± 78.3	148.9 ± 82.3
Albumin excretion rate, μg min ⁻¹	22.1 ± 21.7	27.7 ± 25.5
Urinary epinephrine, μg per 24 h	5.9 ± 2.6	4.9 ± 2.1
Urinary norepinephrine, μg per 24 h	50.9 ± 25.4**	38.4 ± 17.7

Abbreviations: BMI, body mass index; BP, blood pressure; CRP, C-reactive protein; DBP, diastolic BP; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment insulin resistance; SBP, systolic BP; SDS-BMI, standard deviation score of BMI. * $P < 0.01$, ** $P < 0.0001$.

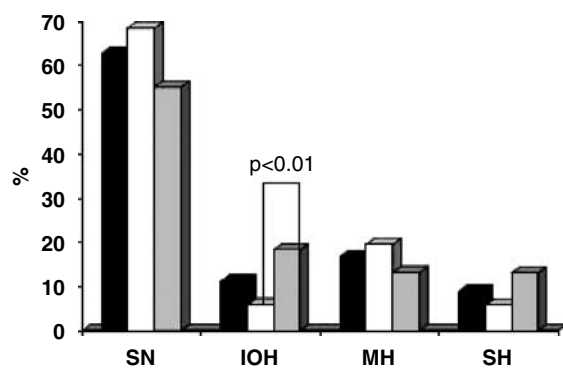


Figure 1 Prevalence of sustained normotension (SN), isolated office hypertension (IOH), masked hypertension (MH) and sustained hypertension (SH) in the whole group of 89 obese children and adolescents (black columns), and separately in boys (grey columns) and in girls (white columns).

Characteristics of hypertensive subjects

Obese children with daytime SH compared to those with daytime SN were more obese (SDS-BMI: 4.2 ± 0.4 vs 3.7 ± 0.7 , $P < 0.05$; waist circumference: 116.7 ± 16.9 vs 108.7 ± 13.9 cm, $P = 0.05$), had a higher frequency of FH (20.1 vs 14.3%, $P < 0.05$), and after adjustment for SDS BMI and sex, higher levels of urinary epinephrine (7.4 ± 0.9 vs 5.1 ± 2.3 μg per 24 h, $P < 0.05$), norepinephrine (56.7 ± 14.6 vs 41.6 ± 21.6 μg per 24 h, $P = 0.05$) and heart rate

(HR; 93.2 ± 13.1 vs 86.7 ± 6.8 beats per min, $P < 0.05$). The proportion of males, pubertal, IGT and MS subjects as well as absolute values of all the other metabolic, hormonal and inflammatory variables were similar in the two groups.

Subjects with night-time hypertension compared to those with normal night-time ABPM values were more obese (SDS-BMI: 4.2 ± 0.4 vs 3.6 ± 0.7 , $P < 0.0001$; waist circumference: 114.2 ± 13.0 vs 107.4 ± 11.9 cm, $P < 0.05$) and had higher percentage of subjects with IGT (21 vs 5%, $P < 0.05$) and MS (42 vs 22%, $P < 0.05$) and higher 2-h glucose (6.9 ± 1.5 vs 5.9 ± 1.1 mmol l⁻¹, $P < 0.05$), uric acid (6.9 ± 1.5 vs 5.9 ± 1.7 μmol l⁻¹, $P < 0.05$) and triglycerides (1.1 ± 0.4 vs 0.9 ± 0.4 mmol l⁻¹, $P < 0.05$) levels.

Non-dipping subjects differed from those with a normal-dipping pattern because of a higher SDS-BMI only (4.3 ± 0.5 vs 3.7 ± 0.7 , $P < 0.05$).

Relations between ABPM parameters, obesity, metabolic and inflammatory variables and renin/aldosterone system

In the univariate correlations, all ABPM parameters were correlated with SDS-BMI, waist circumference and uric acid levels. The 24-h and daytime BPs were correlated with urinary norepinephrine and epinephrine levels and night-time BP with 2-h glucose (Table 2). The adjustment for height did not change

Table 2 Univariate correlations of ABPM values with obesity, uric acid, 2-h glucose and urinary epinephrine and norepinephrine levels

	24-h BP		Daytime BP		Night-time BP	
	SBP	DBP	SBP	DBP	SBP	DBP
SDS-BMI	$r=0.312^{**}$	$r=0.258^{**}$	$r=0.208^*$	$r=0.223^*$	$r=0.429^{***}$	$r=0.402^{***}$
Waist circumference, cm	$r=0.370^{**}$	$r=0.407^{**}$	$r=0.266^*$	$r=0.301^*$	$r=0.320^{**}$	$r=0.251^{**}$
Uric acid	$r=0.278^*$	$r=0.245^*$	$r=0.265^*$	$r=0.284^*$	$r=0.269^*$	$r=0.257^*$
Urinary epinephrine	$r=0.285^*$	$r=0.300^*$	$r=0.285^*$	$r=0.261^*$	—	—
Urinary norepinephrine	$r=0.293^*$	$r=0.284^*$	$r=0.274^*$	$r=0.258^*$	—	—
2-h glucose	—	—	—	—	$r=0.229^*$	$r=0.274^*$

Abbreviations: ABPM, ambulatory BP monitoring; BMI, body mass index; BP, blood pressure; DBP, diastolic BP; LDL, low-density lipoprotein; HDL, high-density lipoprotein; SBP, systolic BP; SDS-BMI, standard deviation score of BMI.

* $P<0.05$, ** $P<0.001$, *** $P<0.0001$.

the significance of these relations. Urinary epinephrine and norepinephrine levels were correlated with each other ($r=0.719$, $P<0.0001$) and with waist circumference ($r=0.280$ and 0.332 , $P<0.01$ for both) and uric acid levels ($r=0.310$ and 0.310 , $P<0.01$ for both), but not with HR. Correlations between ABPM and uric acid levels were no longer significant after adjustment for SDS-BMI and waist circumference.

Albumin excretion rates were correlated with fasting insulin ($r=0.278$, $P<0.05$) and HOMA-IR ($r=0.282$, $P<0.01$) but not with BP levels. No relations were found between ABPM values, inflammatory markers and renin/aldosterone levels.

In univariate analysis, night-time SBP and DBP fall was significantly correlated with SDS-BMI ($r=0.346$, $P<0.001$ and 0.362 , $P<0.001$, respectively) only.

In the multivariate analysis with ABPM parameters as dependent variables and SDS-BMI, waist circumference, height, urinary norepinephrine and epinephrine, 2-h glucose and uric acid as independent variables, daytime SBP remained independently correlated with urinary norepinephrine ($\beta=0.274$, $P<0.05$) and SDS-BMI ($\beta=0.209$, $P<0.05$) and daytime DBP with waist circumference ($\beta=0.286$, $P<0.05$). Night-time SBP and DBP remained independently related to SDS-BMI ($\beta=0.434$ and 0.397 , $P<0.01$ for both).

Using logistic regression analysis, each unit increase in SDS-BMI was responsible for a 5-to 4-fold increase, respectively, in the risk of having systolic daytime and night-time hypertension (ORs 4.1 (95% CI 1.2–14.7, $P<0.05$) and 5.0 (95% CI 1.3–19.9, $P<0.05$), respectively). The ORs of having diastolic daytime and night-time hypertension for unit increase in waist circumference were 1.04 (95% CI 1.0–1.1, $P<0.01$) and 1.0 (95% CI 1.0–1.1, $P<0.05$), respectively.

Discussion

Our study provides new information on a few important issues concerning obesity-related hyper-

tension in children. Overall, 9% of the Italian obese children and adolescents included in our study had SH. This proportion is definitely lower than that found by us⁵ and other groups in obese children using office BP.²³ This was particularly the case in boys, given the higher prevalence of IOH in boys than in girls. Similarly, among SH subjects, the prevalence of isolated systolic hypertension, which affects 94% of American obese hypertensive children using office BP,¹⁴ definitely decreased when considering ABP values. This means that the latter condition, which is a major risk factor for cardiovascular morbidity and mortality in adults,²⁴ is rare in children in whom it seems to be linked to BP reactivity to the clinical environment.

Subjects with daytime SH had a higher proportion of FH, were more obese and had higher urinary catecholamine levels. Obesity and FH might have contributed to the increase of sympathetic activity in these subjects. The association between norepinephrine and obesity is supported by our results and by previous studies in young people demonstrating that elevated plasma norepinephrine levels increase with the increase in BMI predicting the development of hypertension.²⁵ Moreover, subjects with a family history of obesity have been shown to be characterized by higher plasma norepinephrine and BP levels.²⁶ In the present study, subjects with daytime SH had higher urinary epinephrine levels, suggesting that adrenal medulla and peripheral sympathetic nervous system hyperactivities are associated with early BP elevations. In this context, other studies reported that adrenergic activity is an important determinant of SBP in a young population and in men with high-normal BP levels.^{27,28}

With respect to the influence of FH in increasing sympathetic activity, a 10-year longitudinal study demonstrated that norepinephrine and BP levels were greater at any time in FH+ than in FH- non-obese young normotensive men.²⁹ In the present study, the adjustment for obesity did not eliminate the difference in urinary norepinephrine levels between SH and SN subjects, supporting the concept that in obese children, activation of the

sympathoadrenal system, obesity and genetic factors act together to promote a daytime BP rise.

In our cohort, daytime DBP was independently associated with central distribution of fat. The impact of the degree of obesity on BP rise has been widely demonstrated in children^{1,4,5,9,12,26,30,31} in whom, however, the role of body fat distribution was poorly investigated. This was because waist circumference was considered for a long time a doubtful index of visceral accumulation of fat in children.³² However, the present results as well as the demonstration that waist circumference is the strongest determinant of the increase in office BP in a population survey of children in southern Italy³¹ emphasize the adverse effects of central obesity in children. Interestingly, waist circumference was correlated more with office DBP than SBP in the paper by Barba *et al.*,³¹ in line with what is observed by us using ABPM.

Night-time BP levels were elevated in about a quarter of obese children in our cohort. The group of night-time hypertensive obese children included subjects normotensive during the day and identified subjects in worst metabolic conditions such as those with IGT and MS. These results support the role of insulin resistance in the development of hypertension, previously suggested by cross-sectional and longitudinal studies in childhood.^{33,34} In the present study, however, insulin resistance had not an independent effect on BP, because obesity acted as a proxy for the relation between night-time BP and metabolic disorders. Consistent with this finding, the Heart Health and Nutrition Survey conducted among Quebecers has recently demonstrated that the association between insulin sensitivity and BP is almost entirely explained by the increase in the amount of abdominal fat.³⁵ Along the same line and in contrast with studies on adults³⁶ and children,³⁷ the positive relation we observed between uric acid levels and BP was also dependent of the degree of obesity.

In agreement with our previous report that non-diabetic obese children had a high prevalence of microalbuminuria, which was strongly related to the presence of MS,³⁸ in this cohort a high proportion of subjects had elevated AER levels. AER was associated with insulin resistance rather than with ABP levels as observed in adults,³⁹ suggesting that microalbuminuria precedes BP elevations in non-diabetic obese children.

An additional interesting finding of our study is that obesity was responsible for the decrease in nocturnal SBP and DBP fall. This is in agreement with what was observed in adult obese subjects,⁴⁰ but disagrees with the recent finding of a similar nocturnal BP fall in overweight and in normal-weight children.¹²

Finally, our study demonstrates that the increase in SDS-BMI and waist circumference increased the risk of systolic and diastolic hypertension, respectively. Cross-sectional population study demonstrated that in children, office SBP progressively

increases along BMI percentiles (4–30). Our results support and expand the available data on the role of worsening obesity in increasing the risk of hypertension in obese children.

We acknowledge that data in our study were collected from a relatively small and non-population-based sample of obese children. This sample, however, may be considered representative of the obese children population because we did not apply any filter to their referral. In conclusion, our study showed that in obese children and adolescents, daytime BP elevation appears to be accounted for by the degree of obesity together with an activation of the sympathoadrenal nervous system and genetic factors. In contrast, night-time BP rise is associated with worsening of metabolic conditions. The implications of our findings for the future development of adult hypertension deserve further investigation by long-term longitudinal studies.

What is known about this topic

- The prevalence of hypertension is higher in obese than in normal-weight children.
- The office SBP increases along BMI percentiles in obese children.

What this study adds

In obese children and adolescents

- The activation of sympathoadrenal system, together with obesity and genetic factors, contributes to promote daytime BP rise, while worst metabolic conditions contribute in inducing night-time BP elevation.
 - The risk of diastolic hypertension increases with the increase in waist circumference.
 - AER, CRP, IL-6, aldosterone and renin do not seem to be related to the ABP levels.
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