

Gender-Related Differences in the Relationships Between Blood Pressure, Age, and Body Size in Prepubertal Children

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BACKGROUND

The blood pressure (BP) increase with age is well documented in adults and children. However, in the pediatric age group, body size is the most important determinant of age-related BP increases. The aim of the present analysis was to investigate the relationships between age, gender, and body size and BP in children.

METHODS

To this purpose, data were analyzed from 4,514 prepubertal children, aged 6–11 years (71% of the eligible sample; boys = 2,283, girls = 2,231) from the ARCA Project, a screening of childhood obesity carried out in southern Italy. Girls who reported the occurrence of menarche were excluded from the analysis. The sample constituted roughly 20% of all the children attending the primary schools in the area. Weight, height, waist circumference, and BP were measured according to standardized procedures.

RESULTS

As expected, both systolic and diastolic BP significantly increased ($P < 0.001$) with age in boys and girls. However, after adjustment for waist circumference (as index of adiposity) and height (as index of body size), BP significantly increased with age only in girls (systolic BP: $F = 4.380$, $P = 0.002$; diastolic BP: $F = 3.093$, $P = 0.01$) but not in boys (systolic BP: $F = 0.711$, $P = 0.55$; diastolic BP: $F = 2.180$, $P = 0.07$). The association, however, was no longer apparent after the exclusion of children aged >10 years.

CONCLUSIONS

In prepubertal girls in the age range 6–11 years, but not in boys, age is significantly associated with BP independently of body size and adiposity.

Am J Hypertens 2008; **21**:1007–1010 © 2008 American Journal of Hypertension, Ltd.

The increase in blood pressure (BP) with age has been extensively documented in adults¹ and children:² in adults, the observed BP increase is associated with ageing¹ but this is not the case of children for whom the increase in BP with age is mainly related with the increase in body size.² However, in prepubertal children, the association between BP and age might also be dependent on the biological (hormonal) changes leading to sexual maturation.²

It is reasonable to hypothesize that the association between age and BP could be different between genders because the progression to puberty occurs at different ages in boys and girls.

To date, only a few studies have investigated the gender-related differences in cardiovascular risk factors in prepubertal children^{3–5} and none, to the best of our knowledge, have evaluated whether differences between sexes exist in the relationships between BP, age, and body size in this age group.

The present study aimed at evaluating this association in a large sample of children aged 6–11 years, screened for overweight and obesity in the framework of the ARCA Project carried out in southern Italy.⁶

METHODS

To investigate this issue, data were analyzed from 4,514 prepubertal children (age 8.7 ± 1.4 , range 6–11 years; boys = 51%; body mass index (BMI) = $19.3 \pm 3.9 \text{ kg/m}^2$; height = $1.33 \pm 0.10 \text{ m}$) who participated in a screening of childhood obesity^{6,7} carried out in the Avellino district, southern Italy, in cooperation with the Agriculture Department of the Campania Region and the local National Health Service Authorities. The eligible sample was composed from all the children enlisted in 19 primary schools, randomly selected from urban, suburban, and rural parts of the Avellino District, that were invited to participate in the study. The population under examination (71% of the eligible sample) represented roughly 20% of the children aged 6–11 years living in the area. Girls who reported the onset of menarche ($n = 117$; age = 9.4 ± 0.9 years; height = $1.37 \pm 0.09 \text{ m}$) were excluded from the analysis as well as those for whom an incomplete dataset was available ($n = 277$; age = 8.1 ± 1.7 years; boys = 52%). Parents, or legal guardians, provided written

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Received 20 February 2008; first decision 3 April 2008; accepted 8 June 2008; advance online publication 10 July 2008. doi:[10.1038/ajh.2008.228](https://doi.org/10.1038/ajh.2008.228)

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informed consent. The local Ethics Committee approved the design of the study.

Body weight, height, waist circumference, and BP were measured according to standardized procedures, as described earlier.^{6,7} Briefly, body weight and height were measured on a standard beam balance scale with an attached ruler, with children wearing indoor clothes, without shoes. BMI was calculated as weight (kg) divided by squared height (m²). Waist circumference was measured at the umbilicus level, at the end of a normal expiration, with a flexible inextensible plastic tape and approximated to the nearest 0.1 cm. BP and heart rate were measured, after the subject had been sitting for at least 10 min, using a cuff appropriate to the size of the child's upper arm.² Systolic and diastolic (phase 5) BP were taken three times, 2 min apart, with a mercury sphygmomanometer. The average of the second and third reading was recorded. Pediatric hypertension was defined as systolic and/or diastolic BP \geq 95th BP percentile for age, sex, and height, according to the cutoff values of the National High Blood Pressure Education Program Working Group on high blood pressure in children and adolescents.² Sex- and age-specific height, BMI, waist, and BP z-scores were available for the population under study.⁷ Anthropometry and BP measurements were taken by trained pediatricians and nurses who underwent dedicated standardization sessions.

Table 1 | Characteristics of the population by gender and age class

	Age class (years)				
	6.0–6.9	7.0–7.9	8.0–8.9	9.0–9.9	10.0–10.9
Boys					
N	355	476	466	468	516
Height (m)	1.21 ± 0.06	1.27 ± 0.06	1.32 ± 0.06	1.38 ± 0.07	1.43 ± 0.07
BMI (kg/m ²)	18.1 ± 3.4	18.5 ± 3.4	19.6 ± 3.7	20.0 ± 4.4	20.8 ± 4.6
Waist (cm)	59.8 ± 8.6	62.4 ± 8.7	65.7 ± 10.0	68.7 ± 11.5	71.6 ± 10.9
SBP (mm Hg)	92.4 ± 12.1	94.3 ± 13.3	97.8 ± 12.9	99.4 ± 12.7	101.3 ± 13.0
DBP (mm Hg)	58.4 ± 8.2	59.4 ± 9.7	62.3 ± 9.0	62.8 ± 8.5	64.0 ± 8.8
Girls					
N	362	451	473	434	512
Height (m)	1.21 ± 0.06	1.26 ± 0.06	1.32 ± 0.06	1.37 ± 0.07	1.43 ± 0.08
BMI (kg/m ²)	18.0 ± 3.3	18.2 ± 3.4	19.0 ± 3.7	19.7 ± 3.8	20.3 ± 3.9
Waist (cm)	59.3 ± 8.3	61.5 ± 9.1	64.5 ± 9.5	66.7 ± 9.7	69.2 ± 9.7
SBP (mm Hg)	91.3 ± 11.8	93.3 ± 13.1	95.9 ± 12.4	96.7 ± 12.3	101.6 ± 12.8
DBP (mm Hg)	57.9 ± 8.4	58.5 ± 9.6	60.8 ± 8.8	60.8 ± 9.9	63.6 ± 9.3

Data are mean ± s.d.; $P < 0.0001$ by ANOVA for all variables.

BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

The child physical activity level (regular practice of sports = at least 1 h, three times/week) was investigated by a questionnaire completed by the parents/legal guardians.^{6,7} Age was calculated as the difference between the date of examination and date of birth. The sample was then divided into 1-year age groups, from 6.0–6.9 to 10.0–10.9 years.

Data are expressed as mean ± s.d. Analysis of covariance (trend analysis) and linear regression analysis (stepwise model) were used to compare BP across age groups controlling for body size (height) and degree of adiposity (waist), i.e., the most important determinants of BP in the age range under examination. Statistical significance was accepted at $P \leq 0.01$.

RESULTS

The study sample comprised a similar proportion of boys and girls (boys = 2,281, girls = 2,233); no statistically significant differences were observed between genders with regard to age (boys = 8.7 ± 1.4 , girls = 8.7 ± 1.4 years) and height (boys = 1.33 ± 0.10 , girls = 1.33 ± 0.10 m). BMI, waist circumference, and BP were significantly higher in boys in comparison with girls (BMI: 19.5 ± 4.0 kg/m² vs. 19.1 ± 3.8 kg/m²; waist: 66.1 ± 10.9 cm vs. 64.5 ± 9.9 cm; systolic/diastolic BP: $97.4/61.6 \pm 13.2/9.1$ mm Hg vs. $96.1/60.5 \pm 13.0/9.4$ mm Hg; boys vs. girls, respectively, $P < 0.001$).

As shown in **Table 1**, anthropometric indices (height, BMI, waist) and BP were significantly higher going up across age groups ($P < 0.001$) to a similar extent in boys and girls. Height, age-, and sex-specific z-scores tended to increase across age classes in both boys and girls whereas diastolic BP z-scores

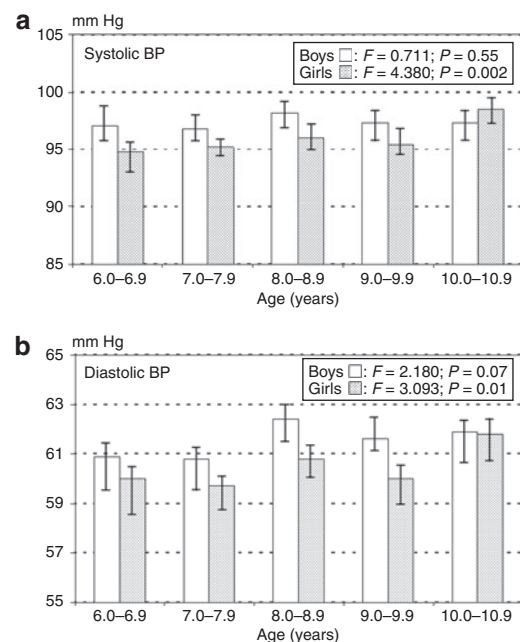


Figure 1 | Height- and waist-adjusted (a) systolic and (b) diastolic blood pressure across 1-year age groups in boys (white bars) and girls (hatched bars). Analysis of covariance: (systolic blood pressure, boys, $F = 0.711$, $P = 0.55$; girls, $F = 4.380$, $P = 0.002$; diastolic blood pressure, boys, $F = 2.180$, $P = 0.07$; girls, $F = 3.093$, $P = 0.01$). Data are expressed as mean and 95% confidence interval.

increased in girls only. BMI and waist *z*-scores did not change with age.

The prevalence of pediatric hypertension² and of high diastolic BP was significantly higher in girls than in boys (hypertension = 13.2% vs. 10.4%; high DBP = 4.7% vs. 3.3%, $P < 0.01$) whereas no differences were observed in the prevalence of high systolic BP (6.0% vs. 5.7%, $P = 0.62$, girls and boys, respectively).

However, following adjustment for height and waist circumference, systolic BP (Figure 1a) was found to increase significantly with age in girls ($F = 4.380$, $P = 0.002$) but not in boys ($F = 0.711$, $P = 0.55$). The same pattern was apparent for diastolic BP (Figure 1b) although to a lesser extent than systolic BP (girls: $F = 3.093$, $P = 0.01$; boys: $F = 2.180$, $P = 0.07$). Linear regression analysis confirmed the independent effect of age on systolic BP in girls (standardized $\beta = 0.083$, $P = 0.004$; adjusted R^2 for the whole model = 0.17) but not in boys ($\beta = 0.008$, $P = 0.78$); the effect of age on diastolic BP was borderline statistically significant in girls (standardized $\beta = 0.063$, $P = 0.03$; adjusted R^2 for the whole model = 0.10), and not significant in boys ($\beta = 0.040$, $P = 0.18$).

The association between BP and age observed in girls (but not boys) after adjustment for body size indices was not influenced by the inclusion of physical activity level in the model as covariate (systolic BP: girls, $F = 4.526$, $P = 0.001$; boys, $F = 1.092$, $P = 0.35$). No association between age and BP was observed for either boys or girls when age- and sex-specific *z*-scores for BP, waist, and height were included in the model.

DISCUSSION

In this study, we investigated the association between age, BP, and body size in a large sample of prepubertal children.

The main finding was that, in prepubertal boys, the BP increase with age was dependent on the concomitant increase in body size; in girls, in contrast, the association between age and BP remained statistically significant after adjustment for height and waist circumference. It appeared from our data that the differences in BP between genders were driven by the upper age group: we could then speculate that, in particular in the period closer to the completion of puberty, the association between age and BP becomes evident in girls.

The association between BP and age is well documented in adults: in this period of life, age is the expression of “ageing of the vascular system,” which explains the increase in BP observed, on average, with increasing age.¹ In healthy pediatric populations, the increase in BP with age is not due to ageing, but rather associated with the increase in body size.² However, in children and adolescents, the relationship between age and BP is more complex because age might have a dual significance. As mentioned above, age is an index of child growth and accordingly it is referred as to “chronological age”; age indeed also expresses the sexual hormones-dependent changes that lead to the completion of sexual maturation, thus referring as to “biological age.”

The sexual dimorphism of cardiovascular risk factors has been well documented in adults: the prevalence of hypertension

is higher in men than in age-matched premenopausal women,⁸ similarly, in a cohort of adolescents followed up from 12 to 18 years of age,⁹ the risk of developing high systolic BP was higher in boys than in girls. However, differences between genders are no longer apparent at older age: the prevalence of hypertension is rather higher in postmenopausal women than in age-matched men.¹⁰ It has been therefore proposed that sex steroids may impact BP levels.¹¹ Hence, the hormonal-dependent growth that takes place just before puberty may represent a critical phase for the emergence of such gender-related differences in cardiovascular risk.¹² We confirmed with the present analysis, as previously reported,⁶ that the prevalence of pediatric hypertension in 6–11-year-old children is higher in girls than in boys with a significantly higher prevalence of high diastolic BP in female participants. Our findings were in line with those by Genovesi *et al.* who showed, in a large sample of children in the same age range in northern Italy, that the prevalence of high BP was significantly higher in girls than in boys.¹³

The significant association, independent of height and adiposity, between age and BP we observed in girls but not in boys, may suggest that girls were in earlier stages of puberty than age-matched boys: repeating the trend analysis after excluding children aged ≥ 10 years (i.e., those probably in the period closer to the completion of puberty) and controlling for body size, we found that age was no longer an independent predictor of BP in both genders. However, it remains a speculation because, without objective assessment of pubertal status, no firm conclusions can be drawn on this issue.

In addition, the tendency to central fat deposition (higher waist circumference) observed in the boys of the population under study, might affect the relationships between age and BP in this gender, possibly diminishing the relevance of age in the multivariate analysis.

The differences in pubertal stage occurring at any given age between boys and girls would explain the previously mentioned observations of increased prevalence of hypertension—or higher BP—in 6–11-year-old girls in comparison with boys.^{6,13} However, after sexual maturity is achieved, i.e., during adolescence, these differences are no longer apparent or even reverted.⁹ Accordingly, Ahimastos *et al.*⁵ documented that the increase in large artery stiffness with age started earlier in girls than in boys, during prepuberty: however, the changes over time in artery stiffness were such that no gender-differences were observed in the postpuberty.

During the progression to the achievement of sexual maturity, differences between genders become apparent at different ages: body fat mass deposition starts earlier in girls than in boys,¹⁴ independently of the age of onset of puberty.¹⁵ Differences also exist between genders during puberty progression in plasma levels of adiponectin, an adipocytokine with antidiabetic and antiatherogenic effects, that decrease from childhood to adolescence in boys whereas remain stable over time in girls.¹⁶ In addition, it has been also documented that girls are more insulin resistant at the age of 5 years than age-matched male pairs^{17,18} and thus they might be differently—or at least in an earlier phase—exposed to cardiovascular risk than boys. Taken together, these

findings^{14–18} may constitute a theoretical basis to support that functional, biological, differences between genders may exist also in the period of life preceding the onset of puberty, possibly modulating the exposure to cardiovascular risk factors.

A limitation of the study was that pubertal age was not directly estimated and we referred to “prepubertal children” according to age and having excluded girls who reported at the time of the screening the occurrence of the menarche. According to the most updated data from southern Italy, the mean age of menarche is 12.55 years¹⁹ whereas among boys >90% achieved sexual maturity at the age of 13 years.²⁰ A possible weakness is the cross-sectional, rather than longitudinal, design of the study; its strength, however, is the large sample size. In addition, a restrictive statistical significance criterion was adopted to reduce the likelihood of chance-events to be observed.

Although further studies are required on this topic,²¹ our findings suggest that gender might influence the association between BP and age in an early phase of life, possibly even during the prepubertal age, in particular in populations with high prevalence of overweight and obesity.⁷

Acknowledgment: The ARCA Project was partly funded by the Agriculture Department of the Campania Region, Italy. Part of the study data have been presented at the 2006 Meeting of the Italian Society of Hypertension and at the British Pharmacological Society Winter Meeting 2006.

Disclosure: The authors declared no conflict of interest.

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