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# Size at birth and blood pressure in young adults: findings from a Brazilian birth cohort study

## Tamanho ao nascer e pressão arterial em adultos jovens: achados de uma coorte de nascimentos brasileira

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### ABSTRACT

**OBJECTIVE:** To describe the prevalence of borderline blood pressure (BBP) and hypertension (HT) among young adults and to assess the association between size at birth and BBP/HT.

**METHODS:** Data were collected from the first Ribeirão Preto Birth Cohort Study conducted in the city of Ribeirão Preto, southeastern Brazil, that started in 1978-1979. Of the 6,827 singletons born in hospitals, 2,060 were assessed at 23-25 years of age. Blood samples were collected, an anthropometric assessment was performed, and information was obtained regarding occupation, schooling, life habits and chronic diseases. Blood pressure (BP) was classified as: 1) BBP: systolic BP (SBP)  $\geq 130$  mm Hg and  $< 140$  mm Hg and/or diastolic BP (DBP)  $\geq 85$  mm Hg and  $< 90$  mm Hg; and 2) HT: SBP  $\geq 140$  mm Hg and/or DBP  $\geq 90$  mm Hg. A polytomic logistic regression model was used.

**RESULTS:** BBP prevalence was 13.5% (males: 23.2%) and HT prevalence 9.5% (males: 17.7%). BBP was independently associated with male gender (relative risk [RR] 8.84; 95%CI 6.09;12.82); birth length  $\geq 50$  cm (RR 1.97; 1.04;3.73); body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup> (RR 3.23; 2.02;5.15); and high waist circumference (RR 1.61; 1.13;2.29), while HT was associated with male gender (RR 15.18; 8.92;25.81); BMI  $\geq 30$  kg/m<sup>2</sup> (RR 3.68; 2.23;6.06); high waist circumference (RR 2.68; 1.77;4.05); and elevated blood glucose (RR 2.55; 1.27; 5.10), but not with birth length.

**CONCLUSIONS:** The prevalence of BBP and HT among young adults of this cohort was higher in males than females. Greater birth length was associated with BBP, but not with HT, whereas birth weight was not associated with either BBP or HT. Adult risk factors explained most of the increase in the levels of BBP and HT.

**DESCRIPTORS:** Borderline blood pressure, hypertension, birth weight, birth length, young adults, cohort studies, obesity, abdominal obesity, high blood glucose.

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## RESUMO

**OBJETIVO:** Descrever a prevalência de pressão arterial limítrofe (PAL) e hipertensão (HT) entre adultos jovens e avaliar a associação entre tamanho ao nascer e PAL/HT.

**MÉTODOS:** Dados foram coletados do primeiro estudo brasileiro de coorte de nascimentos em Ribeirão Preto (sudeste do Brasil), iniciado em 1978/79. De 6.827 recém-nascidos de parto único hospitalar, 2.060 foram avaliados aos 23/25 anos. Foram realizadas coleta de sangue, avaliação antropométrica e obtidas informações sobre ocupação, escolaridade, hábitos de vida e doenças crônicas. Pressão arterial (PA) foi classificada em: 1) PAL: PA sistólica (PAS)  $\geq 130$  e  $< 140$  mm Hg e/ou PA diastólica (PAD)  $\geq 85$  e  $< 90$  mmHg; 2) HT: PAS  $\geq 140$  e/ou PAD  $\geq 90$  mm Hg. Foi aplicado modelo de regressão logística polinômica.

**RESULTADOS:** A prevalência de PAL foi de 13,5% (homens 23,2%) e a de HT, 9,5% (homens 17,7%). PAL foi independentemente associada com sexo masculino (RR 8,84; IC95%: 6,09;12,82), comprimento ao nascer  $\geq 50$  cm (RR 1,97; 1,04; 3,73), índice de massa corporal (IMC)  $\geq 30$  kg/m<sup>2</sup> (RR 3,23; 2,02; 5,15) e circunferência de cintura alterada (RR 1,61; 1,13;2,29), enquanto HT associou-se com sexo masculino (RR 15,18; 8,92;25,81), IMC  $\geq 30$  kg/m<sup>2</sup> (RR 3,68; 2,23;6,06), circunferência de cintura alterada (RR 2,68; 1,77;4,05) e glicemia elevada (RR 2,55; 1,27;5,10), mas não com comprimento ao nascer.

**CONCLUSÕES:** As prevalências de PAL e HT entre os adultos jovens dessa coorte foram maiores em homens que em mulheres. Maior comprimento ao nascer foi associado com PAL, mas não com HT, enquanto peso ao nascer não foi associado com PAL ou HT. Fatores de risco do adulto explicaram a maioria dos aumentos de PAL ou HT.

**DESCRIPTORIOS:** Pressão arterial limítrofe, hipertensão, peso ao nascer, comprimento ao nascer, adultos jovens, estudos de coortes, obesidade, obesidade abdominal, glicemia elevada.

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## INTRODUCTION

Essential hypertension is an important risk factor for morbidity and mortality from coronary heart disease, stroke, and renal disease.<sup>26</sup> Although clinical manifestations of hypertension (HT) do not generally emerge until middle age, the pathophysiologic precursors of adult HT are thought to originate very early in life even during fetal development.

Fetal growth disorders are associated with chronic non-communicable diseases in adulthood, among them HT, according to the fetal origins of adult disease hypothesis.<sup>6</sup> However, it is not clear whether early life factors such as weight and length at birth are also associated with borderline blood pressure (BBP).

Prospective studies show that HT is preceded by a prehypertension stage characterized by abnormalities considered as potential metabolic precursors of HT.<sup>14,24</sup>

The course of concurrent development of adverse blood pressure (BP) levels and other risk factors for the metabolic syndrome during childhood, adolescence, and

young adulthood still needs elucidation. BBP, a new risk category for Latin American and European countries, includes a population at high risk of developing HT and in which lifestyle modifications are needed. This might be useful not only in assessing future risk of hypertension but also in prevention and intervention algorithms.<sup>11</sup>

This study aimed to describe the prevalence of BBP and HT among young adults and to assess the association between size at birth and BBP/HT.

## METHODS

Study carried out with data from the first Ribeirão Preto Birth Cohort Study conducted in the city of Ribeirão Preto, southeastern Brazil, that started in 1978-1979. Data were obtained at birth and at young adult age (23 to 25 years). There were recruited 9,067 liveborn infants delivered at the city's eight maternity hospitals from June 1<sup>st</sup>, 1978 to May 31, 1979 (98% of all live births). Infants whose families did not reside in the

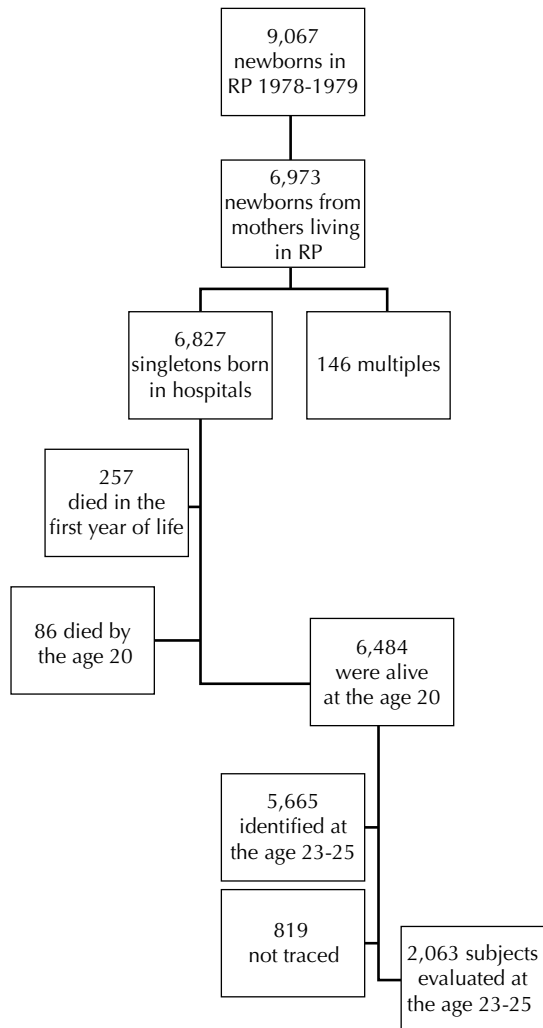
city (2,094) and twins (146) were excluded from the study, remaining 6,827 live births.<sup>9</sup> Information about mother's age, schooling and smoking was obtained through interviews with the mothers after delivery and review of medical records at the maternity hospitals. Birth weight and length were measured within 30 minutes of birth by trained personnel with appropriate devices that were donated by the research team to all hospitals. The infants were weighed naked on scales that were calibrated on a weekly basis with 10-g precision (Filizola, São Paulo, Brazil). Two trained staff members measured length at birth with the infants lying in the supine position on a neonatometer with a fixed vertical headpiece and a smooth sliding vertical foot-piece. Measurements were taken to the nearest 0.5 cm.

From the original cohort, 30% of subjects were selected to participate in the adult follow-up (between 2002 and 2004). This sample size was enough to test the study hypothesis. Of 6,827 singleton liveborns, 343 subjects were found to be deceased and 819 could not be traced, leaving 5,665 singletons. Subjects were classified according to the income of the head of the family (geoeconomic classification) to ensure a representative sample of socioeconomic groups. One in every three subjects from the same geographic area was invited to undergo medical examination. The first of every three names was selected from a list sorted by birth date in each geographic area, and if unavailable the next name down was selected. Losses to follow-up ( $n = 705$ ) occurred because of refusal to participate, imprisonment, death after 20 years of age, or failure to show up for the interview. Losses were replaced using the same sampling method, resulting in 2,063 young adults (Figure).<sup>5</sup> Data were obtained by structured questionnaires, physical examination, and blood collection. Anthropometric measurements (weight, height, and waist circumference) were taken according to standardized techniques with subjects barefoot and wearing light clothing. The instruments used were a precision scale periodically calibrated, anthropometers for standing and sitting measurements, a non-extensible metric tape and a caliper. Blood pressure was measured three times using a digital sphygmomanometer with a cuff of the same size which was adjusted to the arm circumference. The measurements were taken by the same examiner at 15-min intervals, with the subject resting in the sitting position with the left arm at the height of his/her heart. The mean of the last two measurements was then calculated.

Three of 2,063 subjects were excluded because of technical difficulties in recording BP (extreme obesity), totaling 2,060 young adults. A sample size of 1,291 was needed to test the study hypothesis assuming the event had a 10% prevalence with a 5% probability of type I error and 1% precision. Details regarding the methodology are available elsewhere.<sup>5,9</sup>

Blood pressure was the primary outcome measure and was classified into three groups: 1) normal blood pressure (NT): systolic BP (SBP) < 130 mm Hg and/or diastolic BP (DBP) < 85 mm Hg; 2) borderline blood pressure (BBP): SBP 130 mm Hg to 139 mm Hg and/or DBP 85 mm Hg to 89 mm Hg; 3) hypertension (HT): SBP  $\geq$  140 mm Hg and/or DBP  $\geq$  90 mm Hg according to Argentinean, Brazilian, and European guidelines.<sup>12,23,25</sup>

Sociodemographic characteristics were evaluated at birth: mother's age (years), maternal schooling (years), occupation of the head of the family according to the International Standard Classification of Occupation<sup>21</sup> and maternal smoking (no smoking; 1-10; > 10 cigarettes). Gender, gestational age, birth weight (BW), length, ponderal index (PI,  $\text{kg}/\text{m}^3$ ), and adverse perinatal outcomes (low birth weight [LBW, < 2,500 g],



RP: Ribeirão Preto

**Figure.** Subjects from the 1978-1979 Ribeirão Preto Birth Cohort Study evaluated at the age of 23-25 years. Ribeirão Preto, Southeastern Brazil, 1978-1979.

small for gestational age [SGA, BW lower than the 10<sup>th</sup> percentile<sup>27</sup>], preterm birth [ $< 37$  completed weeks]) were presented.

Adulthood sociodemographic characteristics evaluated were: occupation of the head of the family; smoking habit (no smoking; 1-10;  $> 10$  cigarettes); physical activity (active, sufficiently active, and inactive according to the International Physical Activity Questionnaire scoring protocol);<sup>a</sup> alcohol consumption (g/day; high  $> 31$  g/day; low  $\leq 31$  g/day).<sup>4</sup>

The recommendation of the World Health Organization (WHO) of a daily intake of  $< 5.0$  g of salt (2,000 mg of sodium) was adopted to define the cut-off of high sodium intake in mg/day.<sup>28</sup>

Obesity in adulthood was defined as BMI  $\geq 30$  kg/m<sup>2</sup>. Abdominal obesity was based on the waist circumference cut-offs proposed for the metabolic syndrome classification by the International Diabetes Federation.<sup>2</sup> Fasting blood glucose was determined by the GOD/PAP human diagnostic colorimetric enzymatic method (Chronolab AG, Zug, Switzerland) and was considered high when  $\geq 100$  mg/dL.<sup>2</sup> Total cholesterol, HDL cholesterol, and triglycerides were determined by an enzymatic colorimetric method using the Dade Behring XPand device (Dade Behring, Liederbach, Germany) and reagents of Dade Behring Dimension clinical chemistry. Insulin resistance was estimated by a so-called surrogate marker,<sup>18</sup> the triglyceride-to-high density lipoprotein (TG/HDL) ratio, which has been proposed as one of the most accurate surrogate markers; optimal cut-off was 2.90 or less.

All variables are presented as proportions (n, %) and the three levels of blood pressure were compared by the chi-square test.

A univariate risk analysis between BBP/HT and covariates was performed. The variables with a  $p < 0.05$  were included in a polytomous logistic regression analysis to evaluate the risk of both BBP and HT; SBP  $< 130$  mm Hg and/or DBP  $< 85$  mm Hg were the reference values. To be consistent with the literature, we opted to keep birth weight as a covariate in the regression models.

Three models were constructed: the first one (1) was adjusted for sociodemographic and clinical conditions at birth; the second one (2) include sociodemographic and clinical conditions and biochemical markers during young adulthood; and the third one (3) was adjusted for variables included in previous models. Interaction terms were tested for significance. The models were tested for collinearity using the “vif” command of the Stata software, version 9.0 (College Station, Texas, USA). Statistically significant difference was set at  $p < 0.05$ .

The study was approved by the Research Ethics Committee of Ribeirão Preto University Hospital, *Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo* (HCFMRP-USP). Confidentiality was ensured.

## RESULTS

The study sample at birth and at 23-25 years of age was comparable with the original population regarding birth variables: birth weight ( $p = 0.618$ ) and length ( $p = 0.507$ ), SGA ( $p = 0.513$ ), and maternal age at delivery ( $p = 0.065$ ). There were slight differences between those followed up and those who did not participate. There was a predominance of women ( $p = 0.004$ ), preterms ( $p = 0.037$ ), belonging to families with more qualified occupations ( $p < 0.001$ ), mothers with five years or more of schooling ( $p < 0.001$ ), married mothers ( $p < 0.001$ ), and who did not smoke at the time of delivery ( $p < 0.001$ ) (data not shown).

Males accounted for 48.2% (95%CI 46.1;50.4) of the sample. The prevalence of BBP was 13.5% ( $n = 279$ , 95%CI 12.1;15.0) and HT 9.5% ( $n = 196$ , 95%CI 8.3;10.8). BBP and HT were significantly higher in males than females (23.2% vs. 4.5% for BBP and 17.7% vs. 1.9% for HT, respectively,  $p < 0.001$ ).

BBP and HT were positively associated with birth length but not with birth weight. Subjects with a birth length of 50 cm or more had significantly greater proportions of BBP and HT. Ponderal index was not associated with blood pressure.

No differences were observed for maternal characteristics at birth, preterm, LBW or BW for gestational age according to blood pressure levels (Table 1).

Occupation of the head of the family and smoking were not significantly associated with BP levels among young adults. A physically active life, high alcohol consumption, and elevated sodium intake per day were significantly higher in BBP/HT. Subjects with BBP and HT tended to have high BMI ( $\geq 30$  kg/m<sup>2</sup>) and abdominal obesity. Similar findings were found for high fasting blood glucose and triglyceride/HDL cholesterol ratio  $> 2.90$  (Table 2).

Male gender showed the strongest association with BP levels in univariate analyses at birth; there was an eight-fold increase in the effect estimate (crude relative risk [RR] 8.18, 95%CI 5.89;11.34) for BBP and a fourteen-fold increase for HT (RR 14.96, 95%CI 9.31;24.02) in males compared to females ( $p < 0.001$ ). Birth length  $> 50$  cm showed a significantly increase only for the risk of BBP (RR 1.92, 95%CI 1.20;3.05,

<sup>a</sup> International Physical Activity Questionnaire. Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ): Short and Long Forms. Stockholm; 2005 [cited 2006 Mar 3]. Available from: <http://www.ipaq.ki.se/scoring.pdf>

**Table 1.** Sociodemographic and clinical characteristics at birth according to blood pressure levels. Ribeirão Preto Birth Cohort Study, Ribeirão Preto, Southeastern Brazil, 1978-1979.<sup>a</sup>

Variable	Normal blood pressure (n = 1,585)	BBP (n = 279)	HT (n = 196)	Total (n = 2,060)	p-value*
Gender					<0.001
Female	998 (93.62)	48 (4.5)	20 (1.88)	1,066 (100)	
Male	587 (59.05)	231 (23.24)	176 (17.71)	994 (100)	
Maternal age (years)					0.141
< 20	208 (81.89)	27 (10.63)	19 (7.48)	254 (100)	
20 to 34	1,246 (76.77)	223 (13.74)	154 (9.49)	1,623 (100)	
≥ 35	122 (71.25)	27 (15.79)	22 (12.87)	171 (100)	
Maternal schooling (years)					0.818
Up to 8	1,146 (77.75)	195 (13.23)	133 (9.02)	1,474 (100)	
9 to 11	249 (75.23)	48 (14.50)	34 (10.27)	331 (100)	
12 or more	162 (75.35)	30 (13.95)	23 (10.70)	215 (100)	
Occupation of the head of the family					0.377
Non-manual	250 (73.96)	46 (13.61)	42 (12.43)	338 (100)	
Manual-skilled	983 (77.77)	170 (13.45)	111 (8.78)	1,264 (100)	
Manual unskilled	306 (76.88)	54 (13.57)	38 (9.55)	398 (100)	
Maternal smoking					0.478
No smoking	1,228 (77.09)	208 (13.06)	157 (9.86)	1,593 (100)	
1 to 10 cigarettes	243 (78.39)	43 (13.87)	24 (7.74)	310 (100)	
+ 10 cigarettes	76 (72.38)	19 (18.10)	10 (9.52)	105 (100)	
Preterm					0.262
No	1,481 (77.26)	259 (13.51)	177 (9.23)	1,917 (100)	
Yes	104 (72.73)	20 (13.99)	19 (13.29)	143 (100)	
LBW					0.838
No	1,483 (76.80)	263 (13.62)	185 (9.58)	1,931 (100)	
Yes	102 (79.07)	16 (12.40)	11 (8.53)	129 (100)	
Birth weight for gestational age					0.366
AGA	1,340 (77.23)	233 (13.43)	162 (9.34)	1,735 (100)	
SGA	158 (78.61)	23 (11.44)	20 (9.95)	201 (100)	
LGA	87 (70.16)	23 (18.55)	14 (11.29)	124 (100)	
Birth length (cm)					<0.001
< 47	185 (81.86)	23 (10.18)	18 (7.96)	226 (100)	
47 to 49.9	695 (80.25)	89 (10.28)	82 (9.47)	866 (100)	
≥ 50	695 (72.62)	166 (17.35)	96 (10.03)	957 (100)	
Birth weight (g)					0.695
≥ 3,000	1,158 (76.18)	215 (14.14)	147 (9.67)	1,520 (100)	
2,500 to 2,999	325 (79.08)	48 (11.68)	38 (9.25)	411 (100)	
< 2,500	102 (79.07)	16 (12.40)	11 (8.53)	129 (100)	
PI (kg/m <sup>3</sup> )					0.053
> 3.0	220 (81.48)	31 (11.48)	19 (7.04)	270 (100)	
> 2.5 a 3.0	1,075 (77.39)	182 (13.10)	132 (9.50)	1,389 (100)	
≤ 2.5	280 (71.79)	65 (16.67)	45 (11.54)	390 (100)	

<sup>a</sup> Values are numbers (percentage).

\* p-values are for the chi-square test

BBP: borderline blood pressure; HT: hypertension; LBW: low birth weight; AGA: adequate for gestational age; SGA: small for gestational age; LGA: large for gestational age (greater than the 90<sup>th</sup> percentile)<sup>25</sup>; PI: ponderal index

$p = 0.006$ ). BW had no effect on blood pressure either BBP or HT, whereas a significant association between ponderal index  $< 2.5 \text{ kg/m}^3$  and blood pressure was seen (RR 1.64, 95%CI 1.03;2.61 and 1.86, 95%CI 1.05;3.27 for BBP and HT, respectively).

The following conditions showed significantly high RR for both BBP and HT, being higher for the latter in young adults: high alcohol consumption (RR 2.09, 95%CI 1.44;3.04 and 3.83, 95%CI 2.46;5.98 for BBP

and HT, respectively); sodium intake  $> 2,000 \text{ mg/day}$  (RR 1.39, 95%CI 1.06;1.82 and 1.65, 95%CI 1.20;2.28 for BBP and HT, respectively); BMI  $\geq 30 \text{ kg/m}^2$  (RR 3.38, 95%CI 2.40;4.74 and 5.62, 95%CI 3.94;8.01 for BBP and HT, respectively); abdominal obesity (RR 2.49, 95%CI 1.92;3.23 and 4.47, 95%CI 3.28;6.09 for BBP and HT); high fasting blood glucose (RR 2.69, 95%CI 1.49;4.85 and 4.49, 95%CI 2.52;7.98 for BBP and HT); and elevated triglyceride/HDL cholesterol

**Table 2.** Sociodemographic, clinical and biochemical characteristics in young adulthood according to blood pressure levels. Ribeirão Preto Birth Cohort Study, Ribeirão Preto, Southeastern Brazil, 1978-1979.<sup>a</sup>

	Normal blood pressure (n = 1,585)	BBP (n = 279)	HT (n = 196)	Total (n = 2,060)	P*
Occupation of the head of the family					0.400
Non-manual	518 (74.64)	106 (15.27)	70 (10.09)	694 (100)	
Manual skilled	450 (78.67)	67 (11.71)	55 (9.62)	572 (100)	
Semi-skilled manual	343 (79.21)	57 (13.16)	33 (7.62)	433 (100)	
Unskilled manual	270 (75.84)	49 (13.76)	37 (10.39)	356 (100)	
Smoking habit					0.257
No smoking	1,320 (77.37)	231 (13.54)	155 (9.09)	1,706 (100)	
1 to 10 cigarettes	164 (76.64)	30 (14.02)	20 (9.35)	214 (100)	
>10 cigarettes	101 (72.14)	18 (12.86)	21 (15.00)	140 (100)	
Physical activity					0.002
Sedentary	818 (80.12)	117 (11.46)	86 (8.42)	1,021 (100)	
Sufficiently active	304 (77.16)	54 (13.71)	36 (9.14)	394 (100)	
Active	457 (71.52)	108 (16.90)	74 (11.58)	639 (100)	
Alcohol consumption					< 0.001
None	469 (83.45)	61 (10.85)	32 (5.69)	562 (100)	
Low ( $\leq 31 \text{ g/day}$ )	834 (78.09)	142 (13.30)	92 (8.61)	1,068 (100)	
High ( $> 31 \text{ g/day}$ )	271 (65.14)	74 (17.79)	71 (17.07)	416 (100)	
Sodium intake $< 2,000 \text{ mg/day}$					< 0.001
Yes	651 (81.17)	93 (11.60)	58 (7.23)	802 (100)	
No	934 (74.24)	186 (14.79)	138 (10.97)	1,258 (100)	
BMI $\geq 30 \text{ kg/m}^2$					< 0.001
No	1,461 (80.76)	216 (11.94)	132 (7.30)	1,809 (100)	
Yes	122 (49.80)	61 (24.90)	62 (25.31)	245 (100)	
Abdominal obesity					< 0.001
No	1,174 (83.92)	149 (10.65)	76 (5.46)	1,399 (100)	
Yes	411 (62.27)	130 (19.70)	119 (18.03)	660 (100)	
High fasting glycemia					< 0.001
No	1,531 (77.83)	261 (13.27)	175 (8.90)	1,967 (100)	
Yes	37 (50.68)	17 (23.29)	19 (26.03)	73 (100)	
Triglyceride/HDL cholesterol ratio					< 0.001
Normal ( $\leq 2.90$ )	1,346 (81.58)	189 (11.45)	115 (6.97)	1,650 (100)	
Altered ( $> 2.90$ )	221 (57.55)	86 (22.40)	77 (20.05)	384 (100)	

<sup>a</sup> Values are numbers (percentage)

\* p-values are for the chi-squared test

BBP: borderline blood pressure; HT: hypertension; BMI: body mass index; HDL: high density lipoprotein

Physical activity: Classification based on the *International Physical Activity Questionnaire scoring protocol*; Abdominal obesity: Classification based on the *International Diabetes Federation* (waist circumference altered if  $\geq 90 \text{ cm}$  for male and  $\geq 80 \text{ cm}$  for female)<sup>2</sup>; High fasting glycemia = Glycemia  $\geq 100 \text{ mg/dl}^2$

ratio (RR 2.77, 95%CI 2.06;3.71 and 4.07, 95%CI 2.95;5.62 for BBP and HT, respectively). Smoking was only associated with HT (RR 1.77, 95%CI 1.07;2.91) (data not shown).

In the model 1 (birth) of the polytomic logistic regression analysis, the magnitude of the association of male gender with BBP/HT and birth length with BBP persisted after adjustment. In the model 2 (adulthood), the risk for BBP increased in males. The positive associations between alcohol consumption, sodium intake  $\geq 2,000$  mg/day, smoking, and triglyceride/HDL cholesterol ratio were no longer significant, whereas additional adjustment removed part of the effect of BMI  $\geq 30$  kg/m<sup>2</sup> and central obesity on the risk of BBP and HT. Similarly, the positive association between high fasting blood glucose and HT was reduced but remained significantly associated, while for BBP it was reduced and was no longer significant after adjustment.

The model 3 shows the combined effect of birth plus adulthood variables. For both BBP and HT, the associations were mostly consistent with those observed in previous models for male gender, BMI  $\geq 30$  kg/m<sup>2</sup> and central obesity. Birth length  $\geq 50$  cm remained associated with BBP, while high fasting blood glucose was only associated with HT. BW was not associated with BBP or HT. The replacement of BW and birth length by PI was found to have an inverse association with BBP (adjusted RR [adjRR] 1.91, 95%CI 1.14;3.20) and HT (adjRR 2.29, 95%CI 1.17; 4.4) (Table 3).

There was no evidence of collinearity in the models (Table 3). Interaction terms were tested, but none was significant at the 0.05 level.

## DISCUSSION

One of a few studies conducted in Brazil and Latin American middle-income countries has investigated the suggested association between weight and size at birth and BBP/HT at 23-25 years of age in a population-based sample. Among indicators of size at birth, only birth length was independently associated with BBP at young adulthood. When BBP was replaced by prehypertension (SBP 120 mm Hg to 139 mm Hg or DBP 80 mm Hg to 89 mm Hg according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [JNC 7])<sup>10</sup> in the model 3, birth length showed a significant positive association with BBP but to a lesser extent (RR 1.079, 95%CI 1.002;1.162) while BW was not associated with either prehypertension or HT.

Consistent with the Barker hypothesis, low birth weight is related to higher blood pressure later in life in prospective cohort studies. However, other studies have not been able to support this association.<sup>13,20</sup>

The prevalence of HT between 18 and 39 years of age was 7.2% in The National Health and Nutrition Examination Survey (NHANES) III,<sup>15</sup> a proportion that is close to that seen in our study (9.5%).

The higher prevalence of HT among men compared to women is noteworthy but at a lesser rate compared with similar studies.<sup>22,8</sup> This may be attributable to a protective effect of estrogen,<sup>19</sup> higher smoking rates among men (most of the female subjects were non-smokers), higher male height (1.76; standard deviation [SD] 6.48 m for men vs. 1.62; SD 6.45 m for women,  $p < 0.001$ ), elevated sodium intake  $\geq 2,000$  mg/day (70 vs. 52%,  $p < 0.001$ ) and abnormal triglyceride/HDL cholesterol ratio (27% vs. 11%,  $p < 0.001$ ) in males compared to females (data not shown).

There was a lower risk of central obesity (RR 0.78 [95%CI 0.69;0.89],  $p < 0.001$ ) and biochemical markers among women compared to men (data not shown). Increases in body fat may have different effects in women than men, and that a greater degree of adiposity must be achieved in women to obtain a significant rise in blood pressure and an increase in a lipid risk profile comparable with that of men.

Birth length was positively associated with BBP at the age of 23-25 years. The association between birth length and blood pressure is controversial. Studies from high-income countries, where intrauterine growth restriction is rare, have either failed to report an association or found inverse associations.<sup>3,17</sup> On the other hand, studies from low- and middle-income settings have reported positive associations in accordance with the present findings and a previous Brazilian study.<sup>20</sup> This is in agreement with a recent systematic review which showed that the association between birth size and later blood pressure varies according to the level of economic development of the country of birth.<sup>1</sup>

The biological mechanisms by which birth length may influence blood pressure are not yet clear. High blood pressure seen in individuals with higher birth length could be associated to greater height in adulthood.

This was confirmed in a subsequent analysis in which height above the mean of this population (169.0 cm, SD 9.3 cm) was statistically associated with an increase in the risk of either BBP (OR 6.01, 95%CI 4.37;8.27,  $p < 0.001$ ) or HT (OR 6.84, 95%CI 4.63;10.14,  $p < 0.001$ ) compared with those at or below 169.0 cm (data not shown).

Further studies are needed to confirm this association and to clarify potential biological mechanisms.

Subjects with BBP and hypertension showed as young adults an increased prevalence of cardiovascular risk factors for the metabolic syndrome, such as measures

**Table 3.** Risk of borderline blood pressure and hypertension in young adults, adjusted by socio-demographic characteristics, clinical conditions and biochemical markers by polytomic logistic regression analysis in three models. Ribeirão Preto Birth Cohort Study, Ribeirão Preto, Southeastern Brazil, 1978-1979.

	Model 1 – birth <sup>a</sup>		Model 2 – adulthood <sup>a</sup>		Model 3 – birth and adulthood <sup>a</sup>	
	BBP	HT	BBP	HT	BBP	HT
	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)
Sex						
Female	1	1	1	1	1	1
Male	7.64 (5.49;10.65)	14.97 (9.28;24.15)	9.21 (6.38;13.29)	15.05 (8.89;25.49)	8.84 (6.09;12.82)	15.18 (8.92;25.81)
Length (cm)						
< 47	1	1			1	1
47 to 49.9	1.28 (0.72;2.27)	1.37 (0.73;2.56)			1.22 (0.67;2.20)	1.25 (0.63;2.47)
≥ 50	2.02 (1.09;3.75)	1.21 (0.61;2.39)			1.97 (1.04;3.73)	1.06 (0.51;2.22)
Birth weight (g)						
≥ 3,000	1	1			1	1
2,500 to 2,999	1.29 (0.85;1.97)	1.07 (0.67;1.70)			1.49 (0.96;2.31)	1.20 (0.72;1.98)
< 2,500	1.44 (0.70;2.96)	0.92 (0.40;2.13)			1.63 (0.77;3.48)	0.88 (0.35;2.23)
Alcohol consumption						
None			1	1	1	1
Low			1.18 (0.83;1.69)	1.29 (0.81;2.05)	1.17 (0.82;1.68)	1.29 (0.81;2.06)
High			1.07 (0.70;1.64)	1.62 (0.97;2.70)	1.05 (0.68;1.62)	1.62 (0.97;2.71)
Sodium intake < 2,000 mg/day						
Yes			1	1	1	1
No			0.97 (0.72;1.31)	1.04 (0.72;1.50)	0.97 (0.72;1.32)	1.04 (0.72;1.51)
Smoking habit						
No smoking			1	1	1	1
1 to 10 cigarettes			0.88 (0.55;1.39)	0.77 (0.44;1.35)	0.85 (0.54;1.36)	0.77 (0.44;1.35)
> 10 cigarettes			0.61 (0.34;1.09)	0.90 (0.50;1.62)	0.59 (0.33;1.07)	0.90 (0.50;1.63)
BMI ≥ 30 kg/m <sup>2</sup>						
No			1	1	1	1
Yes			3.16 (1.98;5.03)	3.78 (2.30;6.22)	3.23 (2.02;5.15)	3.68 (2.23;6.06)
Abdominal obesity						
No			1	1	1	1
Yes			1.62 (1.14;2.30)	2.58 (1.71;3.88)	1.61 (1.13;2.29)	2.68 (1.77;4.05)
High fasting glycemia						
No			1	1	1	1
Yes			1.88 (0.98;3.62)	2.63 (1.32;5.23)	1.85 (0.95;3.59)	2.55 (1.27;5.10)
Triglyceride/HDL cholesterol ratio						
Normal (≤ 2.90)			1	1	1	1
Altered (> 2.90)			1.33 (0.94;1.88)	1.37 (0.92;2.04)	1.30 (0.91;1.84)	1.37 (0.92;2.05)

<sup>a</sup> Normotension as reference value. All models were adjusted for gestational age

BBP: borderline blood pressure; HT: hypertension; Physical activity: Classification based on the International Physical Activity Questionnaire scoring protocol; Alcohol consumption = low: ≤ 31 g/day, high: > 31 g/day; Abdominal obesity: Classification based on the International Diabetes Federation (waist circumference altered if ≥ 90 cm for male and ≥ 80 cm for female)<sup>2</sup>; High fasting glycemia = Glycemia ≥ 100 mg/dl<sup>2</sup>



of generalized and visceral obesity, adverse glucose homeostasis, and dyslipidemia (Table 2).

Near fifty percent of these young adults lead a sedentary life, which could contribute to higher adiposity and impaired cardiovascular health later in life, in accordance with similar studies.<sup>13</sup>

Our study agrees with Bergvall et al<sup>7</sup> findings that the association of size at birth and blood pressure appears not to be confounded by socioeconomic or family effects.

Subjects with hypertension during young adulthood showed high alcohol consumption, sodium intake  $\geq 2,000$  mg/day, and components of the metabolic syndrome (Tables 2-3). These results are consistent with the tracking concept (persistence) that risk factors remain relatively constant over time. Persistence of high blood pressure over time has been demonstrated in both pediatric and adult populations. This is an important public health issue because of the morbidity and mortality related to HT. Monitoring of BP in these individuals is recommended.

Some of the mechanisms underlying the associations in this study are unclear. Nevertheless, several recognized mechanisms could be postulated such as obesity, hyperinsulinemia/insulin resistance, high sodium intake, and inflammatory markers.<sup>11</sup>

This is the first study that included BBP, a new category of blood pressure classification in Latin American countries. The sample followed up from birth to young adulthood showed better sociodemographic conditions than the original population.

The results of the present study expand a limited body of evidence supporting the hypothesis that BBP increases the risk of progression to full-blown hypertension in young adults.

To the extent that unmeasured risk factors present at baseline may be positively correlated with BBP, there is a chance that BBP was overestimated. Previous observational studies<sup>10,25</sup> have reported that the average

BP in the second visit may be lower than in the initial visit due to regression to the mean or the familiarization of the participants to the clinic setting (white coat effect). Consequently, the prevalence of BBP/HT may be overestimated.

Our control variables have other shortcomings mainly because this study started collecting data more than 30 years ago when risk factors and levels of risk factors were less well established. Misreporting of alcohol consumption may have occurred.

The validity of associations between birth weight and health in later life might be due in part to inappropriate statistical adjustment for variables on the causal pathway which creates an artifactual statistical effect, known as the reversal paradox.<sup>16</sup>

The data obtained for this large community-based birth cohort support the hypothesis that birth length is positively and independently related to blood pressure in early adulthood but do not support an inverse association between birth weight and blood pressure. Adult risk factors explained most of the increase in the levels of BBP and HT.

Moreover, the simultaneous inclusion of current BMI with weight and length at birth in the regression model (indicating an effect of postnatal growth) did not substantially change the effect on the risk of BBP.

Young adults with either BBP or HT showed excess adiposity. These results, when analyzed in the context of the upward secular trends in adiposity and blood pressure in Brazilian youth, underscore the importance of controlling excess adiposity early in life in the general population.

Investigation of causative and synergistic interactions of high blood pressure and other cardiovascular risk factors and of precise physiologic mechanisms associated with early onset of high blood pressure is warranted.

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