Birth Weight and its Association with Blood Pressure and Nutritional Status in Adolescents Aged 12 to 18 Years.

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Abbreviated title: Birth weight, blood pressure and nutritional status

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ABSTRACT

Objective: Investigate the association of birth weight with blood pressure and nutritional status in adolescents.

Methods: Cross-sectional study, performed in a Brazilian capital in 2010-2011. 829 adolescents, aged between 12 and 18 years, enrolled in public and private schools, have been studied. Birth weight, blood pressure, through four office measurements and home blood pressure measurements and the nutritional status, through body mass index, height z-score for the age and waist circumference have been assessed.

Results: Odds ratio for low height was 2.4 times higher among adolescents with low birth weight (CI 95%= 1.1-5.1; p=0.027). In the multiple linear regression analysis, for each increase of 100g in birth weight, height increased by 0.28 cm (CI 95%= 0.18-0.37; p<0.01). Birth weight has not influenced blood pressure (office and home measurements) of adolescents (p>0.05). Initially, there has been a positive linear relation of birth weight to body mass index and to waist circumference, however it was not statistically sustained in a significant manner after adjustment for confounding variables.

Conclusion: Birth weight may be a height predictor in adolescence, reinforcing the plausibility of fetal programming.

Keywords: body mass index, waist circumference, height, birth weight, blood pressure.

Keynotes: Low birth weight was a low height mild predictor in adolescence, indicating the influence of fetal programming. On the other hand, the absence of correlation between birth weight and overweight, abdominal adiposity and high blood pressure emphasized the relevance of post-natal factors in the explanation of these outcomes.
INTRODUCTION

Recent studies show that individuals with extreme birth weights, consequence of inadequate intrauterine development, are prone to developing, among other conditions, blood hypertension, obesity and low height in late stages (1,2,3). Barker, in 1990 (4), was the first to suggest the “programming” or hypothesis of fetal origin of diseases, stressing that fetal malnutrition, for which the main biomarker is a low birth weight (LBW), would inalterably modify the physiology or metabolism of an organ, increasing disease susceptibility in adult life. However, this association is controversial and its mechanisms are poorly understood.

Due to the scarcity of studies on fetal programming of diseases in developing countries such as Brazil, mainly in the teenage population, our objective was to investigate the association of birth weight with blood pressure and nutritional status of adolescents in a Brazilian capital.

METHODS

Population and delineation

It is a cross-sectional study, approved by the institution’s ethics committee (protocol nº 017/2010). Population was composed by young individuals, aged between 12 and 18 years, enrolled in public and private schools of Goiânia/Brazil. Exclusion criteria have been chronic disease, use of medication that alters blood pressure (BP), physical disability that does not permit anthropometric evaluation, pregnancy and absence of information concerning birth weight.

In the period between October 2010 and November 2011, 1,221 adolescents had been in the the inclusion criteria and were invited to participate in the study. Forty-eight refused (3.8%), four (0.5%) did not submit to anthropometric measures and 340 parents or legal guardians did not provide information about birth weight (41.0%), resulting in 829 adolescents (67.9% of the participants). In the final sample, 53 young individuals did not
measure office BP (6.4%) and 128 did not perform home blood pressure measurement (HBPM) correctly (15.4%).

By the sample, it was possible to estimate the association of birth weight with anthropometric variables and BP in adolescents, detecting a difference of 15% for boys and girls separately, with a two-tailed $\alpha$ of 0.05 and test power of 80% (5). Schools were selected by probabilistic conglomerate sampling and students’ selection was randomly and stratified by age and gender.

**Method**

The instrument for data collection was a standardized questionnaire, previously tested in a pilot study, with questions regarding the individual's identification, including gender and age, family hypertension and obesity background, as well as socioeconomic classification of the adolescent, defined by school type (public or private) and by the economic scale from the Brazilian Association of Institutes and Market Research (Associação Brasileira de Institutos de Pesquisa de Mercado) (6).

**Anthropometric measures**

Nutritional status was evaluated through weight, height and waist circumference measures, using standardized procedures (7). Weight was measured on a Kratos® electronic scale, with capacity of 150 kg and variation of 50 g and height was assessed with Secca® stadiometer, mounted on the wall and graded to an accuracy of 0.1 cm. Adolescents were classified based on the height z-score for the age: mild low height (-1 <z-score ≤ -2) and normal height (z-score ≥ -1) (8). Body mass index (BMI) was calculated and classified according to the specific reference standard for the age and gender proposed by the World Health Organization (WHO) (2007) (9). Waist circumference measurement (WC) was performed with a Sanny® 200 cm inextensible tape measure with 0.1 cm variation, and the cut off points were utilized according to those proposed by Taylor (10).
Birth weight

It was required from parents or guardians to answer, in the study presentation letter, whether the birth was premature or not and to write the birth weight, according to the data from the Children’s Card. Birth weight was classified in low (PN < 2,500 g), insufficient (2,500 g ≤ PN < 3,000 g), normal (3,000 g ≤ PN < 4,000 g) or high (PN ≥ 4.000 g) (7).

Office blood pressure measurement

Measurements were performed in school, with OMRON® HEM-705CP semiautomatic equipment, and cuffs in three different sizes, according to the right arm circumference. The equipment is validated for adolescents (11). BP was measured in duplicate, according to pre recognized procedures by 4th Task FORCE and in two encounters within one-week intervals, totaling four readings. For the analysis, the two last measurements average were employed. Values equal to or above 95 percentile classified office BP as high (12).

Home blood pressure measurement

Regarding HBPM the same equipment and cuffs for office BP were utilized. They were given to the adolescent along with instructions on their use. We requested that two right arm measurements should be performed, in sitting position, after 5 min of rest and interval, in the morning (between 6 and 10 a.m.) and in the evening (between 6 and 10 p.m.), for 6 consecutive days (total of 24 readings) (13).

Home measurements saved in the memory of the equipment were printed and compared to those referred in the home blood pressure form filled by the adolescent. When there was a discrepancy between measures or when the adolescent reported not being the only person to have used the equipment, the exam was excluded from the analysis. Exams were considered valid with at least 12 measurements (50%) performed according to 4th Task FORCE protocol (12,14). HBPM was classified as high when the systolic and/or diastolic pressure average of the six days was equal to or higher than the 95 percentile for the respective age, gender and height (15).
**Statistical analysis**

Data were tabulated in double entry with *Epi-Info* software (version 6.04). It was employed a STATA software (version 8.0) for the categorization of variable and statistical analysis. *Kolmogorov-Smirnov’s test* evaluated whether continuous variables presented normal a distribution and Pearson’s chi-square compared birth weight, BP and nutritional status between genders. The birth weight relation with the outcomes (BP, height, BMI and WC) was studied through a simple and multiple linear regression analysis. Variables that presented p value < 0.20 in the univariate analysis and absence of colinearity between independent variables (Pearson’s correlation coefficient < 0.80) were included in the multiple model. A 5% significance level was considered.

**RESULTS**

Table 1 describes birth weight, anthropometric variables and blood pressure of this population, according to gender. High and low birth weight prevalence has been 8.7% and 9.0%, respectively. Current low weight affected less than 4% of adolescents. Current weight excess (overweight and obesity) presented high prevalence in both genders (22.9%), more sharply in boys (29.2%), when compared to girls (18.1%) (p<0.01).

Low height occurred in approximately 6% of the young individuals, with considerable predominance in the female gender (7.9%), in relation to males (3.9%) (p<0.018). Approximately 15% of adolescents presented abdominal obesity. A higher frequency of high office BP was observed in boys when compared to girls (p=0.029). Alterations (≥ 95 percentile) in HBPM (3.8%) were much below those observed for office BP (8.5%).
Table 1. Characteristics of the sample. Goiânia/GO/Brazil, 2010-2011.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Males (n=359)</th>
<th>Females (n=470)</th>
<th>Total sample (n=829)</th>
<th>P value¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Birthweight</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>31 (8.6)</td>
<td>41 (8.7)</td>
<td>72 (8.7)</td>
<td>0.079</td>
</tr>
<tr>
<td>Insufficient</td>
<td>58 (16.2)</td>
<td>100 (21.3)</td>
<td>158 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>229 (63.8)</td>
<td>295 (62.8)</td>
<td>524 (63.2)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>41 (11.4)</td>
<td>34 (7.2)</td>
<td>75 (9.0)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Low</td>
<td>12 (3.3)</td>
<td>18 (3.8)</td>
<td>30 (3.6)</td>
<td></td>
</tr>
<tr>
<td>Normal weight</td>
<td>242 (67.4)</td>
<td>367 (78.1)</td>
<td>609 (73.5)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>75 (20.9)</td>
<td>52 (11.1)</td>
<td>127 (15.3)</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>30 (8.4)</td>
<td>33 (7.0)</td>
<td>63 (7.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Height</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.018</td>
</tr>
<tr>
<td>Normal</td>
<td>345 (96.1)</td>
<td>432 (92.1)</td>
<td>777 (93.8)</td>
<td></td>
</tr>
<tr>
<td>Mild low</td>
<td>14 (3.9)</td>
<td>37 (7.9)</td>
<td>51 (6.2)</td>
<td></td>
</tr>
<tr>
<td><strong>WC</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.138</td>
</tr>
<tr>
<td>Normal</td>
<td>295 (82.2)</td>
<td>404 (86.0)</td>
<td>699 (84.3)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>64 (17.8)</td>
<td>66 (14.0)</td>
<td>130 (15.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Office BP²</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.029</td>
</tr>
<tr>
<td>&lt; Percentile 95</td>
<td>299 (89.0)</td>
<td>411 (93.4)</td>
<td>710 (91.5)</td>
<td></td>
</tr>
<tr>
<td>≥ Percentile 95</td>
<td>37 (11.0)</td>
<td>29 (6.6)</td>
<td>66 (8.5)</td>
<td></td>
</tr>
<tr>
<td><strong>HBPM³</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.598</td>
</tr>
<tr>
<td>&lt; Percentile 95</td>
<td>290 (95.7)</td>
<td>384 (96.5)</td>
<td>674 (96.1)</td>
<td></td>
</tr>
<tr>
<td>≥ Percentile 95</td>
<td>13 (4.3)</td>
<td>14 (3.5)</td>
<td>27 (3.8)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Pearson’s chi-square test; ²n= 776; ³n= 701. 
BMI - body mass index; WC - waist circumference; BP – blood pressure; HBPM - home blood pressure measurement.

LBW has proven to be associated to mild low height, once 12.5% of the exposed adolescents presented linear growth deficit, compared to 5.7% of those not exposed to low weight at birth (p=0.023). The chance of presenting low height was two times higher among individuals with birth weight < 2.5 kg (Odds Ratio= 2.4; CI 95%= 1.1-5.1; p=0.027).

Birth weight has not influenced office BP and home BP in the young individuals studied. A positive influence was detected initially for BMI and for WC (p<0.05), however it was not sustained after adjusted analysis (p= 0.274 and 0.835, respectively). On the other
hand, for each increase of 100 g in birth weight, height increased by 0.33 cm (CI 95% = 0.23-0.43; p<0.01) and, after multivariate analysis, the increase was of 0.28 cm (CI 95% = 0.18-0.37; p<0.01). Independent variables utilized in the model explained 37.6% of height variation (Table 2).

### Table 2. Association of birth weight with blood pressure and nutritional status in adolescents. Goiânia/GO/Brazil, 2010-2011 (n=829).

<table>
<thead>
<tr>
<th>Variables*</th>
<th>β simple (CI 95%)</th>
<th>P value1</th>
<th>β adjusted (CI 95%)</th>
<th>R²</th>
<th>P value2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP (mmHg)³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>-0.01 (-0.16 – 0.14)</td>
<td>0.872</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diastolic</td>
<td>0.03 (-0.06 – 0.13)</td>
<td>0.466</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HBPM (mmHg)⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>0.08 (-0.05 – 0.20)</td>
<td>0.240</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-0.01 (-0.08 – 0.07)</td>
<td>0.881</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.05 (0.01 – 0.09)</td>
<td>0.023</td>
<td>0.03 (-0.02 – 0.07)⁵</td>
<td>0.095</td>
<td>0.274</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>0.13 (0.03 – 0.23)</td>
<td>0.013</td>
<td>-0.01 (-0.09 – 0.11)⁵</td>
<td>0.174</td>
<td>0.835</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.33 (0.23 – 0.43)</td>
<td>&lt;0.001</td>
<td>0.28 (0.18 – 0.37)⁵</td>
<td>0.376</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

1 Simple linear regression analysis; ² Multiple linear regression analysis; ³ n= 776; ⁴ n= 701.
* Expressed by 100 g.
**Model adjusted by prematurity, socioeconomic classification, sex, public or private schools, family history of hypertension, height and age. *** Model adjusted by prematurity, socioeconomic classification, sex, public or private schools, family history of hypertension, BMI, WC, birth-height and age.
CI - confidence interval; β - not standardized regression coefficient; R² - determination coefficient; BP – blood pressure; HBPM - home blood pressure measurement; BMI - body mass index; WC - waist circumference.

### DISCUSSION

The sample’s LBW rate was higher than the Brazilian estimates of 6.1% for children below two years of age (16) and 6.9% for newborns in Goiânia (17). This finding is worrisome due to the negative impact in the newborn’s health and survival. However, higher prevalence of LBW can be observed in more developed regions of Brazil and this phenomenon can be denominated epidemiological transition, caused by the improvement in health assistance for pregnant women and infant mortality reduction, allowing babies with low weight to survive (18).
High birth weight prevalence has also been superior to the 6.5% estimate for newborns in Goiânia (19). Macrosomic fetal repercussion relates to a higher death and prematurity risk, as well as complications such as obstetrical trauma, dystocia and neonatal hypoglycemia (20).

A notable aspect of this study was that children with LBW became shorter in adolescence. This result is in accordance with a 5.9 cm reduction in height, at the end of adolescence, of individuals with low birth rate (1) and with high occurrence of low height (10.3%) in the group of adults who were born small for gestational age (SGA), versus 2.4% in the control group (p < 0.01) (21).

Most SGA children recover their height in the two initial years of life, however it is estimated that between 10% and 15% will maintain a height deficit (-2 z-score) throughout life, requiring therapy with recombinant human growth hormone (rhGH), recently approved in the USA and in Europe (22).

It is not clear, however, whether the relation of birth weight with height has been resulted from genetic mechanisms, from uterine influence, from shared lifestyle, from social condition or a combination of these factors. A probable low height programming mechanism is related to the alteration of thyroid hormone synthesis, through phenylalanine and tyrosine reduction, which would cause an oxygen consumption reduction and a growth retardation (23). Another explanation would be a predisposition to early sexual and bone maturation, which would result in a linear growth deficit (24). Despite no being the focus of this study, the finding of locus (HMGA2 and LCORL) that genetically link intrauterine growth with postnatal height is an aspect worth of discussion (25).

Undoubtedly, uterine life is a critical period of development, due to rapid growth, cellular differentiation and functional maturation of the organs, rather sensitive processes to alterations in the nutrient medium (4). Nevertheless, we have wondered whether childhood or adolescence could be even more determining periods in the development. We also questioned whether postnatal factors could be submitted to the nature of fetal programming.
Therefore, do only adolescents, who presented abnormalities during uterine growth, acquire over weight, low height or high BP or is it the majority of these individuals?

It is known that low height, possibly resulting from past malnutrition, may compromise the female reproductive function, increasing the risk of generating children with LBW (7). Additionally, height deficit has a negative impact on BP and may be a risk factor for obesity. Clemente and collaborators (26) associated height z-score between -2 and -1 to higher body and abdominal fat and to BP increase in Brazilian adolescents.

The height index for adolescents evaluation in Brazilian capitals notified a 2.9% of height deficit (z-score <-2), with higher magnitude in males (27). In the present study, it is noted a considerable low predominance of mild low height in females, a fact that may be a consequence of the beginning of the puberty period. Testosterone, masculine sexual hormone, starts to act in later ages than estrogen in females, increasing bone formation, protein synthesis and height (28).

The most recent recommendation of the WHO (9) has modified the previous classification of mild low height to normal, probably due to the world decline in height deficit prevalence among young individuals in the population. However, the height increase tendency throughout generations demands the need of reassessing the reference curves and revising the very definition of low height, in order not to underestimate nutritional disorders in the population, mainly in newborns with low weight (21).

Birth weight increase was associated to BMI and WC increase in adolescents; however, this relation was not sustained after an adjusted analysis, that is, the oscillation of these anthropometric variables may be totally or partially explained by postnatal period factors, more than by fetal biology (29). This result corroborated studies (1,30,31) that found no significant risk of low weight or obesity, associated with birth weight, during and at the end of adolescence.

Controversies about this relation remain. A Chilean study has concluded that approximately one third of obesity cases in high school individuals might have been averted with an early interventions in macrosomic newborns (3). A cohort study with newborns in the
most economically developed region of Brazil have demonstrated an increase of 1.2 kg/m² (CI 95% = 0.0-2.4) in BMI at age 18 in individuals with birth weight ≥ 4 kg (32).

Fetal hyperglycemia throughout uterine life, frequently followed by high birth weight, may lead to permanent programming of the hypothalamic circuit that regulates food intake, to leptine concentration reduction, to fetal hyper insulinism and mitochondria copy reduction, predisposing to late period adiposity (33,34). Nevertheless, most of these hypotheses are based on experimental studies involving animals.

Overweight was observed in more than one fifth of this population, exceeding by six times the weight deficit frequency. These results confirm the nutritional transition, characterized by malnutrition progressive reduction and continuous increase in obesity prevalence. Weight deficit prevalence among Brazilians aged between 10 and 19 is 3.4%, also with little variation between genders, and 20.5% of overweight, being 4.9% of obesity, both with higher prevalence in males (35).

There was no association between birth weight and BP (office and home) in adolescence, contradicting authors, who propose that LBW, consequence of inadequate uterine development, would be associated with higher risk of developing hypertension in youth (2,29). A meta-analysis with 22 studies has found a 12% reduction in cardiovascular death risk in adult life per increased kg of birth weight (36).

The investigation of the impact of birth weight on BP is, nevertheless, controversial. Nair and collaborators (37) have not found a significant association between LBW and systolic blood pressure (SBP) in 13-year-old adolescents. A Brazilian study revealed sleep SBP and lower sleep dip of SBP in students with LBW, however, it did not find correlation with daytime SBP(38).

The main limitation of this study was the lack of knowledge about the gestational age, thus, not allowing the classification of SGA individuals by intrauterine growth restriction (IUGR). However, the term SGA presents limitations in an epidemiological perspective by disregarding factors such as biological variability, gender, multiplicity, ethnicity and parity, inferring that all small babies result from a pathological growth restriction. In this sense, there
is no golden standard method to determine IUGR with accuracy, which hampers the accomplishment of studies on fetal programming (39).

Moreover, birth weight is the only perinatal health indicator widely collected in Brazil, due to its practicality and strong association with infant mortality (39). Other limitations refer to the socioeconomic condition, which does not correspond to the context in which the child was born, to the collection of birth variables, which was performed exclusively by parents or guardians of the adolescents and to the absence of data on sexual maturation, parents height, smoking during gestation and breastfeeding.

The adjustment of estimates by potential confounding factors, the obtaining of data by a duly trained team, using standardized methods and instruments, the absence of Brazilian studies that investigated the relation between birth weight and BP through HBPM and the scarcity of studies on fetal programming in developing countries, mainly in the adolescent population, justify the relevance of this study. Despite not representing a causal model, since it is a cross-sectional study, the estimates presented may contribute greatly to the debate on the hypothesis of fetal origin of diseases.

In conclusion, LBW was a predictor of growth deficit in adolescence, reinforcing the plausibility of the hypothesis of fetal origin of diseases. On the other hand, the increase in the baby’s weight did not result in a significant increase of BMI and WC in adolescents, which emphasized the relevance of postnatal factors in these outcomes. There was no association between birth weight and BP (office and home) in this age group. The high prevalence of newborns with low or high birth weight in the population studied demonstrates the need for prenatal assistance and nutritional attention to the pregnant woman, in order to promote maternal health, prevent neonatal mortality and guarantee normal growth/development of the child.

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CONFLICT(S) OF INTEREST / DISCLOSURE(S)

None.

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REFERÊNCIAS


