



LETTERS TO THE EDITOR

Maternal hypertension and infant growth[☆]



Hipertensão materna e crescimento infantil

Dear Editor,

The *Jornal de Pediatria* published, in its 91st volume, a very interesting article entitled: "Growth of preterm low birth weight infants until 24 months corrected age: effect of maternal hypertension."¹ The authors tackled a very important issue in the context of infant and maternal health worldwide, mainly considering the impact of the gestational period on the offspring's health and disease pattern during the life course. However, we would like to highlight some points in order to contribute to this subject.

According to the Task Force on Hypertension in Pregnancy, the hypertensive disorders in pregnancy are classified into: preeclampsia/eclampsia; chronic hypertension; preeclampsia superimposed on chronic hypertension; and gestational hypertension.² In our unpublished systematic review, we analyzed 45 papers (from 2008 to 2015) on the association between hypertensive disorders in pregnancy and offspring's medium- and long-term health outcomes. We found that the high heterogeneity of results among the studies was mainly caused by different classifications of maternal hypertension, and by the quality of adjustments performed by the authors. Thus, in this article, some methodological questions were raised.

Firstly, the authors defined two study groups according to the exposure or not to gestational hypertension syndrome; however, in their study description, it is not clear if women with chronic hypertension were also included in the hypertensive group. It is important to highlight that each hypertensive disorder has a different and complex clinical presentation, with diverse consequences in the offspring. Therefore, it is important that studies address the hypertensive disorders independently (*i.e.*, chronic hypertension vs. gestational hypertension vs. preeclampsia) in their analysis.

Secondly, regarding the sample selection used by the authors, all children included in the study were born preterm (gestational age < 37 weeks) and had low birth weight (LBW; 1500 g to 2499 g). It is known that preterm birth and LBW are abnormal events, and the pathways that lead to these conditions are mostly pathological,³ so normotensive mothers must also have been exposed to adverse conditions during pregnancy. Therefore, by restricting the sample to preterm infants with LBW, the authors render normotensive mothers a greater chance of having these other adverse conditions, compared to the average population. The odds ratios (OR) of 0.47 for inadequate weight and 0.20 for inadequate length at 24 months described by the authors reflect this bias. The protective effect of maternal hypertension on growth was probably a result of unmeasured causes of LBW and preterm birth in the normotensive group. These other unmeasured or unknown disorders may possibly influence child growth as much as maternal hypertension.

Thirdly, to decrease the selection bias, the authors should have controlled the outcome for the causes of preterm birth and LBW, such as intrauterine infection, nutritional disorders, smoking, alcohol and drug consumption, violence, lower socioeconomic status, and other chronic diseases. However, the authors limited their logistic regression model to the following variables: gestational age, gender, and adequacy of birth weight for gestational age; a choice of variables that, besides being insufficient, may be a source of collision bias.

In conclusion, cohort studies have great importance in the scientific investigations, and the one conducted by the authors will contribute to this essential field of research. Nonetheless, the analysis of observational studies is extremely challenging and must be carefully performed.

Conflicts of interest

The authors declare no conflicts of interest.

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Author's reply: Maternal hypertension and infant growth[☆]



Resposta do autor: Hipertensão materna e crescimento infantil

We appreciate the comments and questions about our study, which demonstrates the careful and correct assessment that focused on one aspect of concern in cohort studies: the possibility of selection bias.¹

We will use this opportunity of scientific discussion to clarify some methodological aspects of the study and its limitations, ensuring its external validity and helping to increase knowledge on this topic, still scarcely studied in our country: low birth-weight preterm growth – the effect of maternal hypertension.

The first aspect to be discussed refers to maternal hypertension classification, which in our study was performed using the criteria of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy.² As shown in the first paragraph of the results section, preeclampsia was the predominant manifestation in the group of hypertensive women, corresponding to 80% ($n = 63$), which is classically described in the literature.³ The remaining 20% of this group had gestational hypertension. No pregnant woman had chronic hypertension.

The second aspect is the subject of much discussion in the literature: what would be the ideal control group in studies on prognosis of preterm infants?

In development studies, it is important to assess the damage in premature infants in relation to the general population.⁴ In relation to growth, this comparison is obtained by the analysis of the Z-scores of anthropometric measurements.

Our objective was to analyze the growth pattern of low birth weight preterm infants and the effect of maternal hypertension, using a cohort study design. Thus, the groups were formed based on the exposure or not to maternal hypertensive syndrome, excluding cases of multiple pregnancies, infection/congenital malformations, which are classic factors associated with growth alterations. The neonatal characteristics were similar between groups, as well as the post-natal factors that are known to influence growth, such as morbidity and dietary patterns. Logistic regression models were constructed to control for possible confounding factors.

Although the selection of a control group consisting of preterm infants may limit result interpretation, we do not consider that they should be attributed to selection bias. The data obtained allowed us to answer the study question on the effect of maternal hypertension on the growth of preterm low birth-weight infants: there were no risk or protective effects. Also, two important and potentially avoidable risk factors were highlighted: adequacy of birth weight and growth in the first year of life, which are clinically relevant aspects that contribute to guide the obstetric and pediatric conduct in daily practice.

Regarding the third question, the authors consider that there is a low possibility of selection bias, as the study sample size consisted of a population treated at the Brazilian Unified Health System, quite homogeneous in socio-demographic characteristics, which did not differ between the two assessed groups. Smoking was infrequent, observed in 10% of hypertensive and 20% of normotensive women ($p = 0.103$). It is necessary to highlight two aspects of methodological rigor in our study: control of the effect of time on the evolution of anthropometric measurements, and postnatal nutrition assessment, which is an important growth modulating factor in the first years of life.⁵

Finally, we expect that the aspects discussed herein can contribute to improve the interpretation of our study and encourage new studies to investigate other factors that can influence growth in low birth weight preterm infants.

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