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ORIGINAL ARTICLE

Relation of maternal hypertension with infant growth in a prospective birth cohort: the ABCD study

M. de Beer[1,2]*, T. G. M. Vrijkotte[3], M. F. van der Wal[2], M. M. van Weissenbruch[1] and R. J. B. J. Gemke[1]

[1]*Department of Pediatrics, EMGO Institute, Institute for Cardiovascular Research VU, VU University Medical Centre, Amsterdam, The Netherlands*
[2]*Department of Epidemiology, Documentation and Health Promotion, Municipal Health Service, Amsterdam, The Netherlands*
[3]*Department of Social Medicine, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands*

The aim of this study was to investigate the assumed positive association of pre-existent and pregnancy-induced hypertension with the offspring's weight and length gain in the first 14 months of life. We studied 3994 pregnant women and their offspring in a prospective community-based cohort study, starting between 2003 and 2004 (Amsterdam Born Children and their Development, ABCD study). Questionnaires obtaining information about hypertension during pregnancy were completed, and this was complemented with additional information from the obstetric caregiver. Anthropometry of the offspring was followed during the first 14 months of life. Main outcome measures were presence or absence of growth acceleration in weight or length (normal: $\Delta SDS \leqslant 0.67$ *v.* growth acceleration: $\Delta SDS > 0.67$). The relation between hypertension during pregnancy and weight and length gain was addressed by logistic regression analyses. We found that pre-existent hypertension was related to growth acceleration in weight and length. After correction for birth weight and pregnancy duration, the effect remained significant for growth acceleration in weight (OR 1.89; 95% CI 1.21–2.97; $P < 0.01$). Pregnancy-induced hypertension showed similar results, although correction for birth weight and pregnancy duration rendered the associations non-significant. In conclusion, infants of women with pre-existent hypertension during pregnancy more frequently have growth acceleration in weight and length, and yet the mechanisms acting on postnatal growth appear to be different.

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Key words: accelerated infant growth, pre-existent hypertension, pregnancy-induced hypertension, prospective birth cohort

Introduction

The 'Developmental Origins of Health and Disease' hypothesis postulates that several chronic diseases in adulthood originate from adaptation to the (compromised) nutritional environment during early (antenatal or postnatal) life.[1] These adaptations, which appear to be mediated by certain epigenetic processes, may result in vascular, metabolic or endocrine changes in the structure and function of the body in adult life.[2]

An array of epidemiological studies in several countries have provided evidence supporting this hypothesis. They have documented that subjects with fetal growth retardation due to intrauterine malnutrition have a higher risk of developing hypertension, obesity, diabetes and coronary heart disease in later life.[3–10] In addition to fetal growth retardation, prematurity has been identified as an independent risk factor for high blood pressure and cardiovascular risk in later life.[11]

Moreover, evolving evidence suggests an independent role of rapid infant growth (also referred to as 'catch-up growth') on cardiovascular disease in later life (the accelerated growth hypothesis). Rapid growth in early postnatal life may be driven particularly by an aim to compensate for intrauterine growth retardation or prematurity, which consequently may increase the adverse effect on cardiovascular disease risk in later life.[3,5,7,12–14] Although rapid postnatal growth also occurs in normal birth weight infants, it may still be the consequence of a fetal response to a compromised intrauterine environment.[2]

One adverse antenatal factor that is potentially associated with fetal adaptation (reprogramming) is maternal hypertension. As maternal hypertension is one of the factors associated with placental dysfunction,[15] resulting in limited maternoplacental delivery of nutrients and oxygen to the fetus, the offspring of mothers with hypertension are expected to have a higher risk of retarded fetal growth and preterm delivery. This may however be restricted to those with severe hypertension.[16–21] It is unknown whether maternal hypertension is related to postnatal growth acceleration, independent from birth weight and pregnancy duration.

The aim of this study was to determine the putative independent role of maternal hypertension (pre-pregnancy and pregnancy-induced hypertension) on the offspring's growth. We hypothesized that maternal pre-existent hypertension and pregnancy-induced hypertension are independent determinants of the offspring's growth acceleration, in addition to birth weight, pregnancy duration and potential confounding variables. When confirmed, these hypotheses provide novel insights

*Address for correspondence: M. de Beer, Department of Pediatrics, VU University Medical Centre, De Boelelaan 1109, Postbus 7057, 1007 MB, Amsterdam, The Netherlands.
(Email m.debeer@vumc.nl)

into the role of the potential determinants of cardiovascular diseases in later life.

Methods

Study population

Data from the Amsterdam Born Children and their Development (ABCD) study were used.[22–25] The ABCD study is a prospective cohort study that focuses on the explanatory role of dietary and lifestyle habits during pregnancy on birth outcomes and the future health of the child with specific attention to ethnicity (www.abcd-study.nl).

Between January 2003 and March 2004, all pregnant women living in Amsterdam were invited to participate in this study at their first visit to an obstetric caregiver (Fig. 1). A questionnaire covering sociodemographic data, obstetric history and lifestyle was sent to the pregnant woman's home address. This was around the 12th to 14th week of pregnancy. Questionnaires were returned by 8266 women (response rate: 67%).

From this group, 7809 women gave birth to a viable singleton infant with information on birth weight, gender and pregnancy duration. Mothers with diabetes or with missing information on pre-existent and pregnancy-induced hypertension were excluded from the analysis, leaving us with a group of 7163 mothers.

Three months after delivery, another questionnaire was sent to the mothers who had given permission for follow-up of their health status during pregnancy and of their child after being born ($n = 6693$, 86%). These questions concerned the course of pregnancy and delivery, and maternal lifestyle during and after pregnancy. With 5131 women returning the questionnaire, the response rate was 77%.

Fig. 1. Flowchart.

The length and weight of these children were collected at the Youth Health Care registration of the Municipal Health Service in Amsterdam. The Youth Health Care registration is an organization which is represented all over the Netherlands. It offers regular consults during infancy and childhood at which vaccinations are administered and development is monitored. Length and weight measurements took place during regular follow-up moments and were performed by well-trained nurses. Since these data were not digitized at the time, we had to collect them afterward. Up until now, we have managed to retrieve and digitize the growth data of 3994 of these children. Weight and length at a median age of 4 weeks (range 1–7 weeks) as well as a median of 14 months (range 10 to 18 months) were used. The reason for using anthropometric data at 4 weeks instead of birth data is that length is not always measured unequivocally at birth in the Netherlands.

Measurements

Antenatal risk

Pre-existent hypertension

The pregnancy questionnaire contained questions concerning pre-existent hypertension, pregnancy-induced hypertension and use of anti-hypertensive medication. If a woman reported hypertension or used anti-hypertensive medication before the 20th week of pregnancy, this was classified as pre-existent hypertension. In addition, information from obstetric care, and Dutch perinatal registration, containing information concerning possible complications of the pregnancy (e.g. by pre-existent hypertension) were available for all women to complement this classification.[26] In case of discrepancies between both sources, we chose to use data from the questionnaires because this information was more complete.

Pregnancy-induced hypertension

The infancy questionnaire addressed pregnancy-induced hypertension. If a woman reported hypertension that was not reported in the preceding pregnancy questionnaire, this was regarded as pregnancy-induced hypertension. In addition, data from the perinatal registration were available to complement the presence of pregnancy-induced hypertension. In case of discrepancies between diagnoses of both sources, we chose to use data from the questionnaires because this information was more complete.

Outcome

Infant growth acceleration (weight and length) in the first 14 months

Infant weight and length were expressed as standard deviation scores (SDS), using Dutch reference standards.[27] Infant growth

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acceleration (i.e. change in standardized weight or length gain) was expressed as a change in SDS (ΔSDS) and was calculated by subtracting SDS at 4 weeks from SDS at 14 months. Growth acceleration was defined as ΔSDS > 0.67 between 4 weeks and 14 months. SDS 0.67 represents the width of each percentile band on standard growth charts (that is P2–P9, P9–P25, P25–P50, etc.). Crossing of centiles is the most commonly used indicator of clinically significant accelerated growth.[14,28]

Covariables

Pregnancy duration and birth weight

Pregnancy duration, gender and birth weight were obtained from Youth Health Care centres which perform neonatal screening on congenital inborn errors of metabolism in all Dutch newborns. A standardized birth weight was calculated using the most recent Dutch reference values obtained from the Dutch perinatal registration (www.perinatreg.nl). Measured birth weight was divided by the mean birth weight of a reference group (alike in gender, pregnancy duration and parity) and expressed as a ratio. It was interpreted as an expression of intrauterine growth.

Breastfeeding

Information on feeding practices was obtained from the Youth Health Care registration of the Municipal Health Service in Amsterdam. Duration of exclusive breastfeeding was divided into five categories: not started, <1 month, 1–3 months, 4–6 months, >6 months.

Other confounding variables

The pregnancy questionnaire contained questions concerning maternal age in years (continuous), height in m (continuous), pre-pregnancy body mass index (BMI) = maternal weight/height^2 (continuous), parity (0, 1, ⩾2 children), maternal education (<5, 5–10, >10 years after primary school), ethnicity (based on mother's place of birth: Dutch, Surinamese, Turkish, Moroccan, other), paternal height in m (continuous), cohabitant status (living together, single), smoking (yes, no) and use of alcohol during pregnancy (yes, no). We considered all amounts of smoking, and drinking more than once a day to be relevant.[29–31]

Statistics

Differences between participants with and without available growth data (total group: 7163) were analyzed using χ^2 analysis and independent sample *t*-tests. Differences between women without hypertension, pre-existent hypertension and pregnancy-induced hypertension were addressed using χ^2 analysis and ANOVA.

Logistic regression was used to determine the relation between maternal hypertension and infant growth acceleration. After univariate analysis, possible confounding factors that appeared to be different between the three groups, women without hypertension, pre-existent hypertension and pregnancy-induced hypertension were added to the first model, forced entry. Standardized birth weight (as resultant from fetal growth) and pregnancy duration, as a linear term and as a quadratic term, were added to the final model to adjust for their acknowledged independent impact on infant weight gain and to explore their potential intermediating role. Furthermore, to assess whether the use of antihypertensive medication affected the relation between maternal hypertension and the outcome variables studied, sensitivity analyses were conducted excluding mothers who used antihypertensive hypertension.

All analyses were conducted using SPSS statistical software (version 15).

Results

Data sources for hypertension

Data regarding hypertension were available for all women in this subgroup (they were not available for 32 women of the total group of 8266 who initially participated). Pre-existent hypertension was reported by 141 mothers. This was supported eight times by information from the perinatal registration. In addition, in two cases, the perinatal registration classified a mother as having both pre-existent and pregnancy-induced hypertension. These mothers reported pregnancy-induced hypertension. Furthermore, in one case, the mother reported pregnancy-induced hypertension, whereas the perinatal registration reported pre-existent hypertension. All three cases were classified as pregnancy-induced hypertension, which was reported by 294 mothers. This was supported 122 times by information from the perinatal registration. In addition, 59 cases were identified by information from the perinatal registration.

Background variables

In the group with no available growth data ($n = 3169$), the prevalence of maternal pre-existent hypertension was higher compared to the group with growth data ($n = 3994$; 4.9% *v.* 3.5%; $P < 0.01$), whereas the prevalence of pregnancy-induced hypertension was lower (7.1% *v.* 8.8%; $P < 0.01$). Furthermore, in the group without growth data, more infants were born preterm (9.1% *v.* 4.1%; $P < 0.001$), maternal pre-pregnancy BMI was lower (22.9 m/kg^2 *v.* 23.1 m/kg^2; $P < 0.05$), nulliparity was greater (59.0% *v.* 53.7%; $P < 0.001$) and more women of Dutch and Surinamese origin were present (65.9% resp. 5.3% *v.* 64.2% resp. 4.5%; $P < 0.001$). Importantly, the educational level was not significantly different in participants with and without growth data.

Relevant sociodemographic background variables are shown in Table 1. Higher maternal BMI, older age, lower educational level, multiparity and shorter pregnancy duration were positively associated with pre-existent hypertension.

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Table 1. *Background variables in three groups*[a]

	No hypertension Mean (S.D.) or % $N = 3500$ (88%)	Pre-existent hypertension Mean (S.D.) or % $N = 141$ (3%)	Pregnancy-induced hypertension Mean (S.D.) or % $N = 353$ (9%)		
Maternal factors					
Age (years)	30.9 (5.2)	32.0 (5.8)	31.4 (5.0)	*	b
Height (m)	1.68 (0.07)	1.68 (0.07)	1.69 (0.08)	ns	
Height partner (m)	1.81 (0.11)	1.81 (0.08)	1.82 (0.09)	ns	
Pre-pregnancy BMI (kg/m^2)	22.9 (3.9)	26.3 (6.0)	23.9 (3.9)	***	b,c
Parity (%)				***	b,c
0	52.7	34.8	72.0		
1	33.7	42.6	20.1		
⩾2	13.6	22.7	7.9		
Smoking during pregnancy (%)	10.7	6.4	8.2	ns	
Use of alcohol (%)	22.7	17.7	19.8	ns	
Use of antihypertensive drugs (%)	0	19.1	8.2	**	b,c
Maternal education (%)				***	b,c
<5 years	22.8	34.0	16.7		
5–10 years	37.0	37.6	39.7		
>10 years	40.2	28.4	43.6		
Two parent family (%)	87.3	82.3	90.9	*	c
Ethnicity (%)				***	c
Dutch	63.3	59.6	75.6		
Surinamese	4.3	8.5	4.5		
Turkish	4.8	3.5	2.5		
Moroccan	7.3	9.2	4.2		
Other	20.3	19.1	13.0		
Intrauterine and child factors					
Birth weight (g)	3473 (503)	3482 (615)	3357 (585)	***	c
Standardized birth weight ratio	1.00 (0.12)	1.03 (0.20)	0.98 (0.14)	**	c
IUGR (% < P10 standardized birth weight)	12.0	16.3	17.6	**	c
Pregnancy duration (weeks)	39.9 (1.5)	39.4 (1.7)	39.7 (1.5)	***	b
Preterm (%)	4.0	5.7	4.5	ns	
Male gender (% boy)	50.2	48.2	48.7	ns	
Duration of breastfeeding (%)				***	b,c
Not initiated	28.8	45.0	37.4		
<1 month	9.5	6.4	9.1		
1–3 months	19.4	16.4	16.3		
4–6 months	21.9	10.7	18.6		
>6 months	20.5	21.4	18.6		
Weight SDS 4 weeks	0.18 (1.2)	0.18 (1.3)	−0.14 (1.3)	***	c
Weight SDS 14 months	−0.09 (1.0)	0.11 (1.0)	−0.16 (1.0)	*	b
ΔSDS weight	−0.27 (1.2)	−0.08 (1.3)	0.02 (1.3)	***	c
Accelerated growth weight (%)	18.0	29.8	24.1	***	b,c
Length SDS 4 weeks	0.09 (1.0)	−0.10 (1.1)	−0.05 (1.2)	*	c
Length SDS 14 months	−0.11 (1.0)	−0.05 (1.0)	−0.18 (1.1)	ns	
ΔSDS length	−0.19 (1.0)	0.04 (1.1)	−0.12 (1.2)	*	b
Accelerated growth length (%)	17.7	27.6	22.2	**	b,c

BMI = body mass index; IUGR = intrauterine growth retardation; S.D. = standard deviation; SDS = standard deviation score; ΔSDS = change in standard deviation score.

[a] χ^2 analysis and ANOVA were used.

[b] Difference between pre-existent hypertension and controls.

[c] Difference between pregnancy-induced hypertension and controls.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

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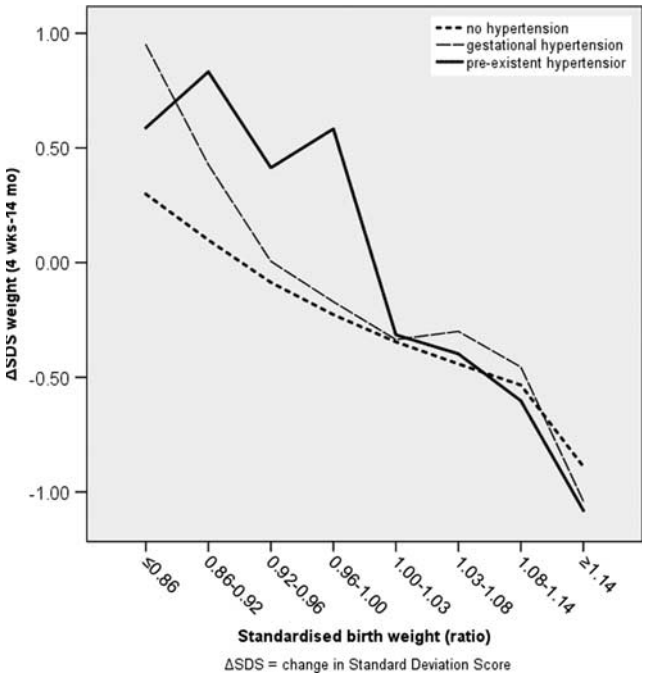

Fig. 2. Accelerated growth in weight. ΔSDS = change in standard deviation score.

Furthermore, among these women, breastfeeding was started less frequently.

Infant growth acceleration in weight

For all three groups, the mean ΔSDS for weight (growth acceleration in weight as a continuous variable) are presented for eight different strata of standardized birth weight (Fig. 2). This figure demonstrates the modifying effect of standardized birth weight on the association between maternal hypertension and accelerated growth in weight: only in the below average birth weight group a synergistic effect of maternal hypertension on accelerated weight gain was present.

After adjustment for confounding variables, pre-existent and pregnancy-induced hypertension were independent determinants of growth acceleration in weight. After correction for standardized birth weight and pregnancy duration, the relation between pre-existent hypertension and growth acceleration in weight remained significant (OR 1.89; 95% CI 1.21–2.97; $P < 0.01$); however, the relation of pregnancy-induced hypertension with growth acceleration lost significance (Table 2). Furthermore, we did a sensitivity analysis excluding women who used antihypertensive drugs ($n = 116$), leaving us with a group of 25 subjects. The relation between pre-existent hypertension and growth acceleration in weight was stronger, but it was no longer significant (OR 1.93; 95% CI 0.67–5.61; p: 0.22).

In subsequent analyses including standardized birth weight as a dichotomous variable (below *v.* above average standardized birth weight), a significant interaction was found between pre-existent hypertension and standardized birth weight (OR 3.17; 95% CI; 1.20–8.38; $P < 0.05$). Therefore, we performed a stratified analysis in two birth weight subgroups. In the below average birth weight subgroup, a larger effect size was found for the association between pre-existent hypertension and growth acceleration in weight (OR 2.64; 95% CI 1.48–4.71; $P < 0.01$). This relation was not significant in the above average birth weight group (Table 3). Furthermore, we excluded women who used antihypertensive drugs ($n = 53$), leaving us with a group of 11 subjects. The relation between pre-existent hypertension and growth acceleration in the below average birth weight subgroup was stronger, though of borderline significance (OR 3.53; 95% CI 0.98–12.71; p: 0.05).

Infant growth acceleration in length

In univariate analysis, as well as after adjustments for the confounding variables, both pre-existent and pregnancy-induced hypertension were significantly associated with infant growth acceleration in length. However, after adjustments for standardized birth weight and pregnancy duration, the associations lost significance (Table 4). In subsequent analyses including standardized birth weight as a dichotomous variable (below *v.* above average birth weight), no significant interactions were found between pre-existent or pregnancy-induced hypertension and standardized birth weight.

Discussion

The results of this study show that the offspring of women with pre-existent hypertension are 1.9 times more likely to have growth acceleration in weight during the first 14 months of life. Interestingly, this association appears to be only significant in infants with a below average birth weight, with an even 2.6 times higher odds for growth acceleration in weight. Neither fetal growth retardation nor shorter duration of pregnancy is solely responsible for these findings, but these factors partly act as intermediating variables. It should be mentioned, however, that these secondary analyses were relying on small numbers, and should therefore be interpreted with some caution. Furthermore, we found some indication for a possible attenuating effect of the use of antihypertensive drugs on offspring's accelerated growth in weight. This suggests a better condition of women who are prescribed antihypertensive drugs with a resultant better offspring.

Furthermore, in contrast to growth acceleration in weight, the association of maternal pre-existent hypertension with growth acceleration in length was mainly mediated by birth weight and pregnancy duration.

A significant relation between pregnancy-induced hypertension and offspring's growth acceleration (both weight and length) was found. However, the association of pregnancy-induced hypertension with growth acceleration was mainly mediated by reduced birth weight and shorter pregnancy

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Table 2. *Relation of maternal hypertension with the offspring's growth acceleration in weight*[a]

	Univariate effects OR (95% CI)	Multivariate effects Model 1 OR (95% CI)	Multivariate effects Final model OR (95% CI)
Maternal factors			
Pre-existent hypertension	1.93 (1.33–2.80)**	1.93 (1.30–2.86)**	1.89 (1.21–2.97)**
Pregnancy-induced hypertension	1.44 (1.11–1.87)**	1.38 (1.05–1.81)*	1.10 (0.81–1.50)
Age	0.96 (0.95–0.98)***	0.99 (0.97–1.01)	0.99 (0.98–1.01)
Pre-pregnancy BMI (kg/m^2)	1.01 (0.99–1.03)	0.99 (0.97–1.01)	1.02 (1.00–1.04)
Parity			
0	Ref.	Ref.	Ref.
1	0.61 (0.51–0.73)***	0.66 (0.54–0.80)***	0.54 (0.43–0.67)***
⩾2	0.73 (0.57–0.94)*	0.67 (0.51–0.90)**	0.54 (0.39–0.74)***
Maternal education			
<5 years	Ref.	Ref.	Ref.
5–10 years	0.71 (0.59–0.87)**	0.85 (0.68–1.07)	0.91 (0.71–1.17)
>10 years	0.56 (0.46–0.69)***	0.83 (0.64–1.07)	0.93 (0.70–1.25)
Cohabitant status (living together)	0.67 (0.54–0.84)***	0.87 (0.68–1.11)	0.88 (0.67–1.15)
Ethnicity			
Dutch	Ref.	Ref.	Ref.
Surinamese	1.85 (1.32–2.61)***	1.53 (1.06–2.22)*	0.98 (0.65–1.48)
Turkish	1.38 (0.96–1.98)	1.46 (0.98–2.18)	1.37 (0.88–2.14)
Moroccan	1.75 (1.32–2.33)***	1.77 (1.28–2.43)**	1.95 (1.37–2.77)***
Other	1.10 (0.90–1.36)	1.13 (0.90–1.41)	0.99 (0.77–1.27)
Intrauterine and child factors			
Standardized birth weight	0.01 (0.00–0.01)***	Not entered	0.00 (0.00–0.01)***
Linear term of pregnancy duration (weeks)	0.19 (0.03–1.32)	Not entered	0.06 (0.01–0.47)**
Quadratic term of pregnancy duration (weeks^2)	1.01 (0.99–1.04)	Not entered	1.03 (1.00–1.06)*
Duration of breast feeding			
Not initiated	3.38 (2.60–4.38)***	3.14 (2.40–4.12)***	2.38 (1.77–3.20)***
<1 month	3.05 (2.20–4.23)***	2.86 (2.05–4.00)***	2.83 (1.96–4.08)***
1–3 months	2.13 (1.59–2.85)***	2.13 (1.58–2.87)***	2.09 (1.52–2.89)***
4–6 months	1.15 (0.84–1.57)	1.19 (0.87–1.64)	1.15 (0.82–1.63)
>6 months	Ref.	Ref.	Ref.

BMI = body mass index.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

[a] Logistic regression analysis was used.

Model 1: adjusted for maternal age, pre-pregnancy BMI, parity, educational level, cohabitant status, ethnicity and duration of breastfeeding.

Final model: adjusted for maternal age, pre-pregnancy BMI, parity, educational level, cohabitant status, ethnicity, duration of breastfeeding, standardized birth weight and pregnancy duration as a linear and as a quadratic term.

duration. There may be numerous differences in the causes and consequences of pre-existent and pregnancy-induced hypertension, respectively, explaining this incongruence. For instance, in contrast with pregnancy-induced hypertension, pre-existent hypertension probably has its effect in early pregnancy. This period of organogenesis seems especially sensitive to permanent alterations in physiological and metabolic homeostatic set points.[32] Furthermore, pre-existent hypertension is one of the risk factors for pre-eclampsia, which in turn is associated with preterm delivery and intrauterine growth retardation (and potentially subsequent accelerated postnatal growth).[19,33] If hypertension was reported before the 20th week of pregnancy, we classified this as pre-existent hypertension, which in a proportion of cases might progress to superimposed pre-eclampsia. It is conceivable that the combination of these two conditions is mainly associated with accelerated postnatal growth.

To our knowledge, few studies have specifically addressed the relation between maternal hypertension and accelerated infant growth. Part of the demonstrated associations seem to work through a reduction in birth weight and shorter pregnancy duration. Moreover, there appears to be additional weight gain in the offspring of mothers with pre-existent hypertension. As proposed in the recent literature, a reduction of fetal growth constitutes a surrogate marker of a coordinated fetal response to a restricted intrauterine environment. Growth acceleration is then mainly related to this fetal response.[2] When translating this to our findings, a reduction

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Table 3. *Relation of maternal hypertension with the offspring's growth acceleration in weight after stratifying for standardized birth weight below v. above average*[a]

	Univariate effects OR (95% CI)	Multivariate effects Model 1 OR (95% CI)	Multivariate effects Final model OR (95% CI)
Logistic regression weight			
Birth weight ⩽ average			
Pre-existent hypertension	3.07 (1.86–5.07)***	2.95 (1.72–5.04)***	2.64 (1.48–4.71)**
Pregnancy-induced hypertension	1.71 (1.23–2.37)**	1.60 (1.13–2.26)**	1.13 (0.77–1.67)
Birth weight > average			
Pre-existent hypertension	1.09 (0.55–2.14)	1.04 (0.51–2.13)	1.09 (0.48–2.44)
Pregnancy-induced hypertension	1.03 (0.65–1.65)	0.91 (0.56–1.48)	1.06 (0.63–1.80)

BMI = body mass index.

[a] Logistic regression analysis was used.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Model 1: adjusted for maternal age, pre-pregnancy BMI, parity, educational level, cohabitant status, ethnicity and duration of breastfeeding.

Final model: adjusted for maternal age, pre-pregnancy BMI, parity, educational level, cohabitant status, ethnicity, duration of breastfeeding, standardized birth weight and pregnancy duration as a linear and as a quadratic term.

in birth weight may be a sign for permanent alterations in the constitution of an infant, with further induction of growth acceleration in weight as a result.

This study has a number of strengths. First, we studied a community-based sample with a substantial number of subjects. Second, we collected possible confounding variables known to be related to maternal hypertension and potentially also to infant growth acceleration, for which we could adjust. Third, we assessed growth acceleration not only in weight but also in length. The latter is sparsely used in analysis of growth acceleration, while it is likely to provide an interesting extra dimension of growth. Finally, we used multiple resources to determine the presence of hypertension: two questionnaires assessed at different moments, and in addition information from the obstetric care provider.

A number of limitations to the study should be considered. First, there was a substantial amount of missing data because we were not able to retrieve growth data for all participants. Regarding some background variables, the group that we used for the analysis was different from the rest of the original cohort (for which we did not have growth data). However, the prevalence of both determinants was comparable to the rates reported in a recent review, which are in agreement with the representativeness of our sample.[34] This review reported a prevalence of 3% for pre-existent hypertension and 6% for pregnancy-induced hypertension, compared to 3% and 9%, respectively, in our group.[34] Moreover, in subjects with growth data, some growth acceleration associated factors have a lower prevalence. Therefore, there should be some prudence regarding the external validity of our findings. They may rather be an underestimation of the reality. Second, we used participant self-reporting of pre-existent and pregnancy-induced hypertension, which could affect the accuracy. However, in a recent study comparing self-report questionnaires and medical record data, Okura *et al.* reported reliable agreement for hypertension.[35] Another study, which also addressed the reliability of self-report data on hypertension, suggested that this method may also lead to underestimated prevalence estimates.[36] However, the validity of self-reported information on hypertension in this study is not unequivocal. Third, blood pressure in women was not quantified. This would have enabled us to assess a possible effect of severity of hypertension on the infants' growth. Moreover, it would have shed light on whether well-managed hypertension would have the same effect on offspring growth patterns. Fourth, birth weight was used as a proxy for intrauterine growth. This is a rather crude measure for fetal growth restriction as there may be appropriate for gestational age children who suffered from intrauterine growth restriction. In contrast, there are small for gestational age children who are constitutionally small but not growth retarded. Finally, in the pregnancy-induced hypertension group, no differentiation was made between women with gestational hypertension and the different phenotypes of pre-eclampsia. These conditions are likely to differ in their pathophysiological impact regarding endothelial function, maternal organ development, placentation, placental function and subsequent fetal growth and fetal organ programming.[37] However, as stated earlier, a proportion of the women with pre-existent hypertension may develop pre-eclampsia. Preliminary analyses in a subset of primiparous women showed that pre-eclampsia was related to growth acceleration in weight and length, whereas this was not the case in pregnancy-induced hypertension. The relation seems to be intermediated by birth weight and pregnancy duration (data not shown).

In conclusion, we have shown that maternal hypertension during pregnancy is an important risk factor for accelerated growth in offspring. Yet the mechanisms which act on postnatal growth in weight and length appear to be different. In contrast to pre-existent hypertension, the association between

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Table 4. *Relation of maternal hypertension with the offspring's growth acceleration in length*[a]

	Univariate effects OR (95% CI)	Multivariate effects Model 1 OR (95% CI)	Multivariate effects Final model OR (95% CI)
Maternal factors			
Pre-existent hypertension	1.77 (1.19–2.63)**	1.82 (1.19–2.79)**	1.58 (0.99–2.51)
Pregnancy-induced hypertension	1.32 (1.01–1.74)*	1.39 (1.04–1.85)*	1.17 (0.85–1.60)
Age (years)	0.95 (0.93–0.96)***	0.98 (0.96–0.99)**	0.98 (0.96–1.00)*
Pre-pregnancy BMI (kg/m^2)	1.00 (0.98–1.02)	0.97 (0.95–0.99)*	0.99 (0.97–1.02)
Parity			
0	Ref.	Ref.	Ref.
1	0.70 (0.58–0.85)***	0.76 (0.62–0.93)**	0.68 (0.55–0.85)**
⩾2	0.84 (0.65–1.08)	0.82 (0.61–1.10)	0.74 (0.54–1.02)
Maternal education			
<5 years	Ref.	Ref.	Ref.
5–10 years	0.68 (0.55–0.83)***	0.84 (0.67–1.06)	0.88 (0.68–1.12)
>10 years	0.45 (0.37–0.56)***	0.70 (0.54–0.92)*	0.73 (0.55–0.98)*
Cohabitant status (living together)	0.56 (0.45–0.71)***	0.75 (0.59–0.96)*	0.74 (0.57–0.97)*
Ethnicity			
Dutch	Ref.	Ref.	Ref.
Surinamese	2.05 (1.41–2.99)***	1.57 (1.05–2.35)*	1.05 (0.68–1.63)
Turkish	1.96 (1.37–2.79)***	1.85 (1.24–2.75)**	1.68 (1.10–2.56)*
Moroccan	1.63 (1.20–2.21)**	1.45 (1.03–2.05)*	1.49 (1.04–2.14)*
Other	1.49 (1.21–1.84)***	1.49 (1.20–1.86)***	1.36 (1.07–1.73)*
Intrauterine and child factors			
Standardized birth weight	0.03 (0.01–0.06)***	Not entered	0.02 (0.01–0.04)***
Linear term of pregnancy duration (weeks)	0.10 (0.01–0.88)*	Not entered	0.02 (0.00–0.20)***
Quadratic term of pregnancy duration (weeks^2)	1.02 (1.00–1.05)	Not entered	1.04 (1.01–1.07)**
Duration of breast feeding			
Not initiated	3.22 (2.45–4.22)***	3.06 (2.31–4.06)***	2.35 (1.74–3.16)***
<1 month	2.78 (1.97–3.92)***	2.66 (1.87–3.79)***	2.49 (1.71–3.62)***
1–3 months	1.87 (1.37–2.53)***	1.93 (1.41–2.64)***	1.84 (1.32–2.55)***
4–6 months	1.45 (1.06–1.98)*	1.59 (1.15–2.18)**	1.54 (1.10–2.15)*
>6 months	Ref.	Ref.	Ref.

BMI = body mass index.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

[a] Logistic regression analysis was used.

Model 1: adjusted for maternal age, pre-pregnancy BMI, parity, educational level, cohabitant status, ethnicity and duration of breastfeeding.

Final model: adjusted for maternal age, pre-pregnancy BMI, parity, educational level, cohabitant status, ethnicity, duration of breastfeeding, standardized birth weight and pregnancy duration as a linear and as a quadratic term.

pregnancy-induced hypertension and accelerated growth appears to work entirely through a reduction in birth weight and pregnancy duration. Future studies should further explore the role of maternal hypertension on the offspring's growth. If our findings are confirmed, growth of hypertensive mothers' offspring should be monitored more attentively.

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Statement of Interest

None declared.

Ethical considerations

Approval of the study was obtained from the Central Committee on Research involving Human Subjects in the Netherlands, the Medical Ethical Committees of participating hospitals, and from the Registration Committee of the Municipality of Amsterdam. Date of approval: 29-03-2002, reference number: 02.17.392.

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