Published by Oxford University Press on behalf of the International Epidemiological Association
International Journal of Epidemiology 2009;38:1401–1410
doi:10.1093/ije/dyp255

Enhanced post-natal growth is associated with elevated blood pressure in young Senegalese adults

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Accepted 25 June 2009

Background Evidence suggests that intrauterine growth restriction followed by rapid post-natal growth is associated with high blood pressure. We assessed the effect of early size and post-natal growth on blood pressure in a population from West Africa, where fetal growth retardation and childhood malnutrition are common.

Methods A total of 1288 Senegalese subjects were followed from infancy to young adulthood (mean age 17.9 years). Adult systolic blood pressure (SBP) was regressed on infant and adult anthropometric characteristics.

Results In unadjusted analyses, infant size was positively associated with adult SBP (1.1 ± 0.3; $P = 0.001$ for weight; 0.7 ± 0.3; $P = 0.04$ for length). With adjustment for current size, the regression coefficients for infant size were reversed (-0.2 ± 0.3; $P = 0.51$ for weight; -0.3 ± 0.3; $P = 0.35$ for length). SBP increased by 4.1 and 2.9 mmHg for 1 standard deviation (SD) increase in current weight or height, respectively. No interaction between infant size and current size was found in the overall models ($P = 0.11$ for weight, $P = 0.95$ for height), but this term interacted with sex for weight effect. A negative interaction was found in males (-0.9 ± 0.4; $P = 0.02$) but not in females (0.3 ± 0.4; $P = 0.46$). The association of current weight with SBP was stronger in lighter weight male infants.

Conclusions These findings support the hypothesis that subjects who were small in early life and experienced enhanced post-natal growth have higher levels of SBP, even in low-income settings.

Keywords Blood pressure, infant body size, growth, developing countries, cohort study

Introduction

The 'fetal origin hypothesis' proposes that intrauterine growth retardation can programme permanent alterations during development of vital organ systems, and that these may have adverse effects later in life, with increased risk of cardiovascular diseases and type 2 diabetes.[1–3] This hypothesis is supported by multiple observations of an association between low birth weight and various cardiovascular risk factors, including high blood pressure.[4]

The relationship between birth weight and systolic blood pressure (SBP) has been extensively studied.[5–7]

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Although many studies reported that low birth weight was associated with elevated blood pressure, in most of them, the association was observed only after adjusting for current body size.[8–13] A valid interpretation of these adjusted results would be that weight change, rather than birth weight alone, is an important aetiologic factor.[14–16] A large number of reports, including experimental studies, have indeed found that rapid growth during childhood or infancy is associated with higher risk of hypertension independently of birth weight.[5,17,18] These observations suggest that subjects at higher risk are those who were small at birth and grew rapidly after birth.[19–21]

Most of the literature on the 'fetal origin hypothesis' is based on cohorts born in developed countries. Studies conducted in sub-Saharan Africa, and particularly in West Africa, are scarce. Contrary to high-income countries, African populations present a high rate of intrauterine growth retardation and a high prevalence of childhood malnutrition.[22–24] Moreover, overweight and obesity in adolescence or young adulthood are rare. Thus, in this context, the influence of early size and post-natal growth on later blood pressure may be different from that of westernized populations. We hypothesized that if fetal nutritional programming is the underlying key mechanism, then the inverse association between early size and later blood pressure would be stronger in developing countries. Alternatively, if both low birth weight and accelerated post-natal growth are involved, then the association is expected to be lower compared with high-income settings. It should also be highlighted that West African populations could be particularly vulnerable to this condition, since they exhibit high rates of hypertension.[25–27]

In this study, we analysed data from a longitudinal prospective cohort from infancy to young adulthood involving subjects born between 1980 and 1982 in a rural area of Senegal. The aim was to determine whether SBP in young adults was related to body size in infancy as well as to current body size and, if so, how. Regression models of SBP on infant and adult body size were run following the approach advocated by Lucas *et al*.[14]

Methods

Study area and population

The present work is based on a cohort study conducted in the region of Niakhar, a rural area of Senegal. The population of this area (approximately 30 000 inhabitants) has been the object of demographic surveillance since 1963, with systematic registration of date of birth, migration and death.[28,29] In this area, mortality for children <5 years of age was 253 per 1000 live births between 1984 and 1991, and the prevalence of malnutrition in preschool children reached 30%.[30]

Cohort study

A baseline survey took place in 1983–84 and included infants and children from birth to 5 years of age. Four rounds were conducted at 6-month intervals from May 1983 to November 1984. All children born between 1 January 1978 and 30 November 1984 and who were still living in the area at the onset of each round of surveys were eligible.[31]

A follow-up survey took place during 2001–02. All subjects eligible for the baseline survey were also eligible for this study. The survey consisted of two rounds. The first was conducted from March to June and included all subjects living in the area at that time; the second round took place during the rainy season (August) so as to include migrants absent at the first round who had returned to their villages during the period of field work, usually from July to October.[32] Whenever possible, information about subjects who were absent during these rounds was collected from family members remaining in the area. To increase the rate of coverage for migrants, three additional rounds were conducted in Dakar (October to December 2001), Mbour and Fatick (February to March 2002) and Koumpentoum in eastern Senegal (May 2002) based on information collected during the main round.[30]

Ethical approval for this study was given by the Ethics Committee of the Ministry of Health in Senegal. Oral informed consent was provided by the parent or guardian of the child, or by the subject himself or herself for young adults.

Anthropometric and blood pressure measurements

In both surveys, anthropometric measurements including weight, height, arm circumference, tricipital and subscapular skinfolds were taken using standard methods as described previously.[30]

In the follow-up survey (young adult survey), blood pressure was assessed from the left arm three times at 1-min intervals after a 5-min rest in the seated position with a mercury column sphygmomanometer with an appropriate cuff size. Phases I and V of Korotkoff sounds were used for SBP and diastolic blood pressure, respectively.

Anthropometric and blood pressure measurements were obtained by five trained interviewers who were supervised and regularly controlled by a physician throughout the survey. Standardization of anthropometric and blood pressure measurements was performed at the beginning of the survey.

Study sample selection

Inclusion criteria in the present analysis were: (i) age <12 months during the first survey; (ii) complete measurements of key variables (weight and height in the infant and young adult surveys, blood pressure in the follow-up survey); and (iii) no physical

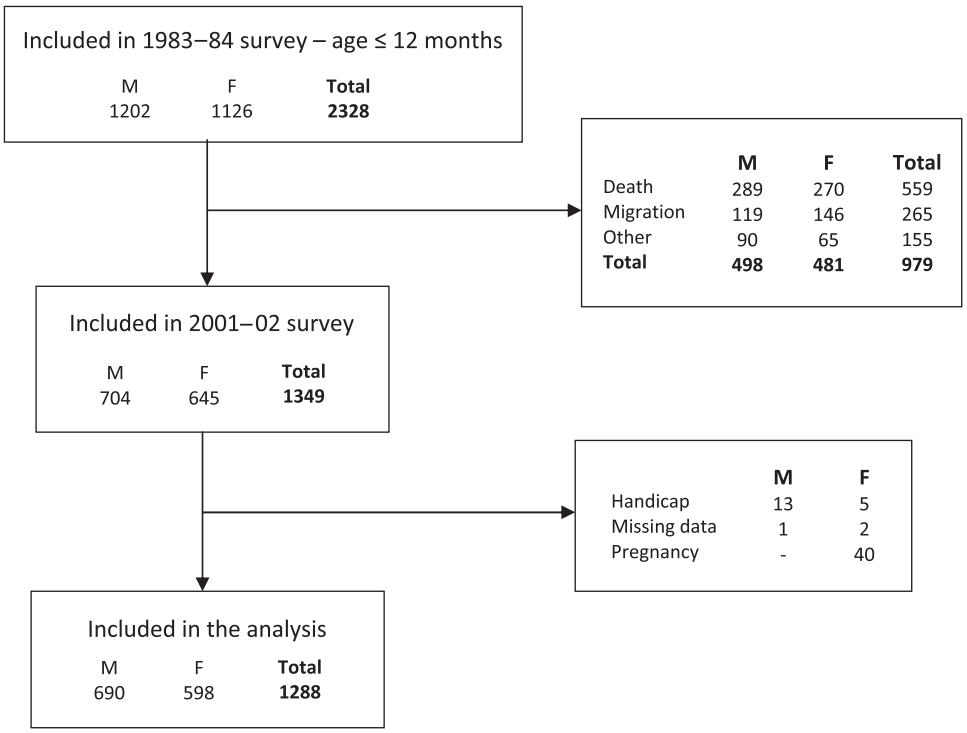

Figure 1 Number of subjects included in the first survey (1983–84), in the follow-up survey in 2001–02 and in analyses, with reasons for non-inclusion

condition likely to alter body dimensions (pregnancy, selected physical handicaps).

Out of 6906 subjects initially eligible for the childhood study, 5887 took part in at least one of the four successive rounds conducted every 6 months, representing a coverage rate of 85.2%. As previously shown, subjects included in the childhood survey did not differ from their non-included counterparts in terms of sex ratio or death rate from 1984 to 2001.[30] A total of 2328 children included in the childhood survey were <12 months of age during at least one of the four rounds (Figure 1).

A total of 559 subjects died between the baseline and follow-up surveys, 265 migrated out of the study area and 155 were absent or refused to participate.

The percentage of loss to follow-up did not differ according to sex (41.4 and 42.7% for males and females, respectively). There was no difference in age, weight, height or mean nutritional indices in the infant survey between those who were included in the follow-up survey and those who were not (Table 1). Among the 1349 subjects included in both surveys, 61 were excluded from the analysis (Figure 1).

Table 1 Infant survey characteristics of subjects who were followed in young adulthood or dropped out

Infant survey characteristics	Followed-up in adulthood ($n=1349$)	Dropped out ($n=979$)	*P*
Age, months[a]	4.5 [4.0]	4.2 [4.4]	0.49
Weight, kg	6.2 ± 1.5	6.1 ± 1.6	0.17
Height, cm	62.4 ± 5.9	62.0 ± 6.2	0.11
WAZ	-0.44 ± 1.20	-0.44 ± 1.24	0.54
HAZ	-0.42 ± 1.10	-0.48 ± 1.14	0.17
WHZ	-0.16 ± 0.96	-0.15 ± 0.98	0.90

[a]Median [interquartile range].

Variables

Weight-for-age *z*-score (WAZ), height-for-age *z*-score (HAZ) and weight-for-height *z*-score (WHZ) were computed according to the National Center for Health Statistics reference.[33] Underweight, stunting and wasting were defined as WAZ <-2, HAZ <-2 and WHZ <-2, respectively. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m). Overweight at young adulthood was defined as BMI $\geqslant 25\,kg/m^2$. Hypertension was defined as SBP >140 mmHg and/or diastolic blood pressure >90 mmHg.

Statistical analyses

Descriptive statistics are given as means ± standard deviation or percentages for qualitative variables.

Comparisons between men and women were performed with standard parametric tests (*t*-tests for continuous variables and chi-squared tests for categorical ones). To take into account the fact that anthropometric measurements were not performed at the same age for all subjects, adjustment on age was performed using regression models. Model building with fractional polynomials was used to express infant and adult weight or length as a polynomial function of age.[34] Residuals were extracted and standard deviation scores (SDSs) for anthropometric measurements were then computed by dividing the residuals by standard deviation. Correlation of anthropometric characteristics between infants and young adults was computed using SDS.

Regression analysis was used to predict SBP, given anthropometric characteristics. SDSs were used to render regression coefficients comparable. In line with recommendations of Lucas *et al*.,[14] four regression models were run with SBP as the outcome variable: (i) the *early model* with infant size (weight or length) as a single covariable; (ii) the *later model* with young adult size (weight or height) as a single covariable; (iii) the *combined model* with both infant and young adult size; and (iv) the *interaction model* with both infant and young adult size and with an additional interaction term between infant and later size. The interaction term was based on continuous data.

Models were run on the total sample, and sex interactions were tested. Regression coefficients were then presented separately for males and females when sex interactions were found.

Regression models with unexplained residuals, as described by Keijzer-Veen *et al*.,[35] were also run to provide an interpretation of early and current weight effects in terms of change in weight from infancy to adulthood. This approach is algebraically similar to standard modelling, but offers a more straightforward interpretation of change in size. In these models, the variable current weight is replaced by the residual of linear regression of current weight on early weight; it thus represents the effect of someone gaining more weight than would be expected from a given early weight.

All models were adjusted on field workers to standardize conditions of measurements. All statistical analyses were performed using SAS statistical package software version 8.1 (SAS Institute, Cary, NC, USA).

Results

Anthropometric characteristics of the study population

General anthropometric characteristics of the study sample are presented in Table 2 for infant and young adult follow-up surveys. At the first survey, the age ranged from 0–12 months by selection. The infant age distribution was skewed towards younger ages, with a median of 4.4 months. As expected, males were slightly taller and heavier than females, but nutritional indices (WAZ, HAZ, WHZ) and prevalence of malnutrition were similar between sexes (Table 2). In the young adult survey, the mean age was 17.9 years (range 16.4–19.8). Males were taller and lighter than females. Only one male subject was overweight. In contrast, the prevalence of overweight was 7.5% in females. The prevalence of hypertension reached 12.2% with no difference between sexes.

Correlation between infant and adult body size

After adjustment for age, correlations between anthropometric characteristics in infant and adult surveys were computed. Adult weight, height and BMI were positively correlated with infant weight, length and BMI, respectively (Table 3). One-third of the variations in young adult body size were explained by infant body size. This indicated strong tracking of body size from infancy to adulthood, which was observed in both sexes (data not shown).

Influence of early and later body size on young adult SBP

When tested in separate models (early and later models), infant and current weight, as well as infant and current height, were positively associated with adult SBP (Table 4). In the combined models, the regression coefficients for infant weight or height were shifted to negative values, but were no different from 0. Adult body size remained positively associated with SBP. A 1 SD increase in adult weight or height led to an increase in SBP of 4.1 and 2.9 mm Hg for weight and height, respectively. Adding an interaction term between infant and adult body size did not improve the model either for weight ($\beta = -0.46 \pm 0.28$, $P = 0.11$) or for height ($\beta = 0.02 \pm 0.33$, $P = 0.95$).

The mean level of SBP did not differ between sexes; however, gender interactions were found for adult body size effect and also for the interaction term effect (between infant and adult body size) (Table 4). These interactions indicate that the effect of adult body size upon SBP and the interaction effect between early and later size differed according to sex.

To take into account gender interactions, regression models were run separately for males and females. In the combined model including both infant and current weight, the estimated coefficients for infant weight effect were negative, but no different from 0 in either sex (Table 5). Adult weight was positively associated with SBP, with a stronger effect in males compared with females. A 1 SD increase in adult weight was associated with an SBP increase of 5.5 mmHg in males and 2.5 mmHg in females. A negative coefficient was found for the interaction term in males, but not in females. This interaction indicated

Table 2 Main characteristics of the study sample in infant and young adult surveys

	Overall ($n=1288$)	Male ($n=690$)	Female ($n=598$)	P^b
Infant survey				
Age, months[a] (range: 0–12)	4.4 [4.0]	4.4 [3.8]	4.5 [4.2]	NS
Weight, kg	6.2 ± 1.5	6.4 ± 1.5	6.0 ± 1.4	<0.0001
Height, cm	62.4 ± 5.9	62.9 ± 5.9	61.8 ± 5.9	<0.001
WAZ	−0.40 ± 1.19	−0.43 ± 1.14	−0.36 ± 1.25	NS
HAZ	−0.42 ± 1.10	−0.47 ± 1.07	−0.37 ± 1.13	NS
WHZ	−0.14 ± 0.97	−0.15 ± 0.95	−0.13 ± 0.98	NS
Underweight (%)	8.7	8.7	8.7	NS
Stunting (%)	5.9	5.9	5.8	NS
Wasting (%)	3.7	4.1	3.3	NS
Young adult survey				
Age, years (range: 16.4–19.8)	17.9 ± 0.7	17.8 ± 0.7	18.0 ± 0.7	<0.001
Weight, kg	52.3 ± 8.7	50.4 ± 8.8	54.4 ± 8.1	<0.0001
Height, cm	163.2 ± 8.3	165.5 ± 9.2	160.6 ± 5.9	<0.0001
BMI, kg/m^2	19.6 ± 2.6	18.3 ± 1.8	21.1 ± 2.7	<0.0001
Overweight (BMI $\geqslant$25 kg/m^2) (%)	3.6	0.1	7.5	<0.0001
SBP, mmHg	120.5 ± 12.8	120.7 ± 13.6	120.2 ± 11.9	NS
Diastolic blood pressure, mmHg	72.5 ± 12.4	71.4 ± 12.8	73.8 ± 11.8	<0.001
Hypertension[c] (%)	12.2	12.9	11.4	NS

Values are means ± standard deviation or percentages unless specified otherwise.
[a]Median (interquartile range).
[b]*P*-value for comparison between sexes.
[c]Hypertension: SBP >140 mmHg and/or diastolic blood pressure >90 mmHg.
NS = non-significant.

Table 3 Correlation coefficients (r) between infant and young adult body size

	Young adult weight		Young adult height		Young adult BMI	
	r	P	r	P	r	P
Infant weight	0.32	<0.0001	0.23	<0.0001	0.26	<0.0001
Infant height	0.28	<0.0001	0.35	<0.0001	0.11	<0.0001
Infant BMI	0.21	<0.0001	0.03	0.22	0.27	<0.0001

that the effect upon blood pressure of becoming heavier as an adult was increased in male subjects who had had a lower weight in infancy.

Regression models were also run to test the influence of infant length and adult height on SBP (Table 6). Height effects were similar in trend, but weaker than weight effects. Greater adult height was associated with a higher level of SBP in men. A 1 SD increase in adult height was associated with an increase in SBP of 4.7 mmHg in men. No interaction between early and later height was found either in males or females, although a trend towards a negative value for the estimate was observable in males. In females, infant length was not associated with SBP and the effect of current height was weak.

Influence of growth trajectories from infancy to young adulthood on SBP using regression models with unexplained residuals

To better illustrate the effect of change in body size on later blood pressure, regression models with unexplained residuals are presented in Table 7 for weight effects in male. These models are algebraically similar to previous regression analyses, but later body size is assessed by the residual of regression of observed adult body size upon infant body size. The later body size parameter thus represents the influence of more pronounced growth than expected (in weight or height) with respect to infant body size (weight or length). In such models, the 'later growth' parameter is thus independent of early body size. Thus, in the combined model, the effect of early body size and

Table 4 Regression coefficients for main overall effects of infant and current body size on SBP and *P*-values for sex interactions

Models	Weight		Height	
	β (SD)	*P*	β (SD)	*P*
Early model				
Infant body size	1.08 (0.33)	0.001	0.70 (0.33)	0.04
Sex	0.65 (0.69)	0.35	0.63 (0.69)	0.36
Infant body size × sex	–	0.07	–	0.49
Later model				
Current body size	3.99 (0.32)	<0.0001	2.80 (0.33)	<0.0001
Sex	0.62 (0.65)	0.35	0.58 (0.67)	0.39
Current body size × sex	–	<0.0001	–	<0.0001
Combined model				
Infant body size	−0.22 (0.33)	0.51	−0.33 (0.35)	0.35
Current body size	4.06 (0.33)	<0.0001	2.91 (0.65)	<0.0001
Sex	0.61 (0.65)	0.35	0.58 (0.67)	0.39
Infant body size × sex	–	0.71	–	0.23
Current body size × sex	–	<0.0001	–	<0.0001
Interaction model				
Infant body size	−0.18 (0.33)	0.60	−0.33 (0.35)	0.35
Current body size	4.09 (0.33)	<0.0001	2.91 (0.35)	<0.0001
Infant body size × current body size	−0.46 (0.28)	0.11	0.02 (0.33)	0.95
Sex	0.62 (0.65)	0.34	0.58 (0.67)	0.39
Infant body size × sex	–	0.61	–	0.29
Current body size × sex	–	<0.0001	–	<0.0001
Infant body size × current body size × sex	–	0.03	–	0.02

Table 5 Regression models with young adult SBP as the dependent variable and infant and/or young adult weight, expressed as SDSs, as co-variables

Models	Males			Females		
	β (SD)	*P*	R^2	β (SD)	*P*	R^2
Early model						
Infant weight	**1.60 (0.48)**	**0.001**	0.13	0.39 (0.45)	0.39	0.15
Later model						
Current weight	**5.45 (0.44)**	**<0.0001**	0.27	**2.34 (0.44)**	**<0.0001**	0.19
Combined model						
Infant weight	−0.18 (0.47)	0.69	0.27	−0.39 (0.47)	0.40	0.19
Current weight	**5.51 (0.47)**	**<0.0001**		**2.47 (0.46)**	**<0.0001**	
Interaction model						
Infant weight	−0.12 (0.47)	0.80	0.28	−0.42 (0.47)	0.37	0.19
Current weight	**5.54 (0.47)**	**<0.0001**		**2.43 (0.47)**	**<0.0001**	
Interaction	**−0.94 (0.39)**	**0.02**		0.29 (0.39)	0.46	

Bold values are for coefficients with *P*-value <0.05.

later growth can be interpreted independently of each other. Among males, heavier infants tend to have higher blood pressure in adulthood (partly because they become heavier adults), and subjects who grow more in weight than would be expected from a given infant weight also exhibit a higher level of SBP (Table 7). As expected, the interaction term was negative in male subjects, indicating a stronger effect

Table 6 Regression models with young adult SBP as the dependent variable and infant length and/or young adult height, expressed as SDSs, as co-variables

	Males			Females		
Models	β (SD)	P	R^2	β (SD)	P	R^2
Early model						
Infant length	0.88 (0.49)	0.07	0.12	0.45 (0.45)	0.32	0.15
Later model						
Current height	**4.42 (0.46)**	**<0.0001**	0.22	0.90 (0.45)	0.05	0.16
Combined model						
Infant length	−0.76 (0.49)	0.12	0.22	0.15 (0.48)	0.76	0.16
Current height	**4.69 (0.49)**	**<0.0001**		0.84 (0.48)	0.08	
Interaction model						
Infant length	−0.70 (0.49)	0.15	0.22	0.11 (0.48)	0.82	0.16
Current height	**4.63 (0.49)**	**<0.0001**		0.90 (0.48)	0.06	
Interaction	−0.66 (0.46)	0.15		0.82 (0.46)	0.08	

Bold values are for coefficients with P-value <0.05.

Table 7 Effects of infant weight and later increase in weight on young adult SBP in male subjects using regression models with unexplained residuals

Models	**β (SD)**	**P**	**R^2**
Early model			
Infant weight	**1.60 (0.48)**	**<0.001**	0.13
Later model			
Later growth in weight (residual)[a]	**5.52 (0.47)**	**<0.0001**	0.26
Combined model			
Infant weight	**1.56 (0.44)**	**<0.001**	0.27
Later growth in weight (residual)[a]	**5.52 (0.47)**	**<0.0001**	
Interaction model			
Infant weight	**1.58 (0.44)**	**<0.001**	0.28
Later growth in weight (residual)[a]	**5.54 (0.47)**	**<0.0001**	
Interaction	**−0.99 (0.44)**	**0.03**	

[a]Residual of linear regression of adult weight on infant weight.
Bold values are for coefficients with P-value <0.05.

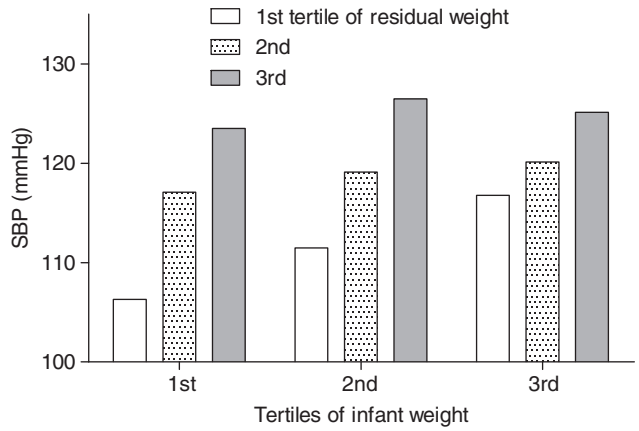

Figure 2 Mean SBP in young adult men by tertiles of infant weight and tertiles of residuals of linear regression of adult weight upon infant weight

of excess in weight gain for small infants. This interaction effect is illustrated in Figure 2, showing the mean SBP in nine groups arising from the combination of tertiles of infant weight with tertiles of excess/deficit in weight gain. The increase in SBP with increasing weight gain excess is sharper for the first tertile of infant weight.

Discussion

We sought to determine, in young Senegalese subjects, whether early body size was associated with blood pressure later in life. We found that, predominantly in male subjects, infant body size was positively associated with both adult body size and adult SBP. Bigger infants tended to become bigger adults with higher SBP. With adjustment for current body

size, the regression coefficient for infant size was reversed, but did not differ from 0. Conversely, adult weight remained strongly positively associated with SBP in both sexes, and an interaction term between early and later size was found for weight in men. Thus, infant weight modifies the effect of later weight upon blood pressure: infants with lower weight exhibit a stronger effect of later weight.

These findings highlight an effect of early body size on later blood pressure, although not independently of later body size. Lower weight infants who became heavy adults exhibited higher levels of blood pressure than higher weight infants. This suggests that in the process of becoming a heavier adult from a light infant, there were adverse consequences of having been a low-weight infant.

There is a growing body of evidence supporting the hypothesis that low-weight newborns have a higher risk of hypertension.[7,36] However, inverse associations between size at birth and blood pressure later in life are commonly statistically significant only after adjustment for current size. The appropriateness of adjusting for current size has long been debated, and this issue was addressed by several studies using empirical[36] and theoretical approaches.[14–16,37] The key point in adjustment lies in interpreting the results. When adjustment for current size applies, then an early size effect should be interpreted as the effect of early size for a group of subjects with similar current size. Lucas *et al*.[14] emphasized that early size adjusted for later size is a measure of change in size between earlier and later measurements, rather than an effect of early size in itself. In such a context, the use of a regression model with unexplained residuals provides a more straightforward interpretation of separate influences of early body size and change in body size later in life. The present study indicated that children who gained more weight than expected (considering their infant weight) had a higher blood pressure level. And the interaction term indicated that the effect of excess weight gain is greater for subjects who had low weights as infants.

Although many studies as well as meta-analyses have been conducted to assess the association between birth weight and blood pressure, most of them used data from developed countries, where birth weight is registered in a more systematic manner than in developing countries. Results from studies in low- and middle-income settings are scarce and appear less conclusive. In agreement with the present findings, two studies, one among young Brazilian adolescents and the other in Indian adults, reported positive associations between early size and blood pressure in crude analyses; these became negative but did not differ from 0 after adjustment for current size.[38,39] In five cohorts followed from birth to adulthood in Brazil, Guatemala, India, The Philippines and South Africa, Victora and colleagues[13] indicated an inverse association between birth weight and SBP after adjustment for current body size. An analysis of the association between size at birth and blood pressure in 3- to 6-year-old children in China, Guatemala, Chile, Nigeria and Sweden was conducted by Law *et al*.[40] In agreement with Victora and colleagues, they reported a weak inverse association after adjustment for current size. Similar results were found in studies from Zimbabwe and the Philippines.[19,41] Most studies in developing countries rely on prospective birth cohorts with a relatively short follow-up. The outcome variable, blood pressure, is measured in childhood or in adolescence, but seldom in adulthood. In the present study, participants were followed until early adulthood. Unfortunately, birth weights were not measured, since most births took place at home. We therefore had to rely on a measurement during the first year of life. Some catch-up may have already occurred between birth and the first available measurement, and this would weaken the inverse association. Subanalyses were performed on smaller samples, for which the first measurement was taken before 6 months or before 3 months of age. In the combined model, the regression coefficient for infant weight became more negative. The interaction term was also enhanced for weight effect. These additional results suggested a probable inverse association between adult blood pressure and birth weight (after adjusting for current weight).

In the present work, tests for sex interactions indicated that the association between early or current body size and SBP differed according to sex. Some studies have reported sex differences, but a meta-analysis suggested that reports of sex differences in the association between birth weight and blood pressure are most often chance findings.[42] The reasons for the sex differences in our study are not clear. An unexpected result of our study was that young women had similar SBP and a higher diastolic blood pressure compared with men, whereas in most studies on similar age groups, women tend to have lower blood pressure. In this setting, young women also happened to be markedly more corpulent than men and this may be an explanation for their higher blood pressure. This particular situation may contribute to explaining the sex differences observed in our study, although we would have expected a stronger association in women in relation to their corpulence.

It has been suggested that puberty and sexual maturation may modify the association between birth weight and SBP during adolescence.[43] The association appeared to be weakened in early to late pubertal stages compared with the pre-pubertal stage. A recent study suggested that early sexual maturation was associated with higher blood pressure independently of height or BMI, but this was found in girls only.[44] In our study, many of the subjects are still in late adolescence. Sexual maturation may have a confounding effect and potentially contribute

to the observed sex differences, assuming that the effects of puberty on blood pressure are sex related.

Although a role of early size was found in the present study, current size was a much stronger predictor of blood pressure. Although rarely emphasized, the effect of current size is consistently found and points to the importance of post-natal growth.[11,12,45] The present study highlights the fact that the post-natal growth effect is not specific to high-income countries with a low prevalence of malnutrition and a high or increasing prevalence of overweight and obesity. Indeed, the prevalence of childhood malnutrition in the present population was high, with 27.6% of stunting for preschool children <5 years of age.[30] In the present study sample, this figure was much lower (5.8%), as it concerned children <1 year of age who had not yet experienced the full period of linear growth retardation. Being overweight was virtually non-existent in young men (0.1%) and quite mild in women (7.5%). This suggests that mechanisms involved in the association between blood pressure and post-natal growth are independent of the onset of being overweight.

One of the key findings of this study was the observation of a negative interaction between early and current weight as a 'predictor' of SBP. This finding is consistent with the hypothesis that subjects at higher risk are those who were small in early life and experienced increased growth after birth. It provides direct support for the statement that the growth trajectory as a whole is of importance, as recently recalled.[36]

Funding

The Nestlé Foundation and the IRD; a 3-year scholarship from the IRD to A.C.N.

Acknowledgements

The authors acknowledge Amady Ndiaye, Tofène Ndiaye, Adama Marra, Denis Boulanger and François Simondon for contributions to data collection and logistic help. They are also grateful to Annick Fontbonne for comments on the manuscript.

Conflict of interest: None declared.

KEY MESSAGES

- Evidence suggests that intrauterine growth restriction followed by rapid post-natal growth is associated with high blood pressure.
- Few studies have been carried out in low-income settings where obesity is rare and malnutrition common, in contrast to the situation in developed countries.
- In this study, lower weight male infants who became heavy adults exhibited higher levels of blood pressure than higher weight infants.
- These findings support the hypothesis that subjects who were small in early life and experienced enhanced post-natal growth have elevated blood pressure, even in low-income settings.

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