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Early Life Factors and Longitudinal Blood Pressure Trajectories Are Associated With Elevated Blood Pressure in Early Adulthood

BT20 Cohort

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See Editorial Commentary, pp 282–283

Abstract—Multiple perinatal and early life risk factors have been implicated in the development of hypertension. The BT20 (Birth to Twenty Plus) cohort in urban Soweto, South Africa, previously showed a prevalence of elevated blood pressure (EBP) that ranged from 22.4% at 5 years of age to 34.9% at 18 years of age. We sought to determine the prevalence of EBP at 23 years of age within this cohort and whether this could be linked to any maternal and early life factors and childhood and adolescent blood pressure trajectories. Blood pressure and anthropometric measurements were completed on cohort participants aged 23 years (n=1540; 49% men). Early life and maternal factors were obtained from previous data. Thirty-six percent of participants had EBP of whom 63% were men (*P*<0.001). The only association with maternal or early life factors was greater linear growth from birth to 2 years of age, which conferred a 19% increased risk (odds ratio, 1.19; 95% CI, 1.01–1.41). Women had a 77% lower risk of EBP (odds ratio, 0.23; 95% CI, 0.16–0.34) per SD. Participants within the highest systolic and diastolic blood pressure trajectories (where blood pressure was elevated early and remained elevated) were at significantly increased risk of EBP in early adulthood. For those in the highest systolic trajectory, this resulted in a 4-fold increased risk and for those in the highest diastolic trajectory, a 5-fold increased risk. These findings suggest that risk for EBP in adulthood may be set in childhood and adolescence. (***Hypertension*. 2019;73:301-309. DOI: 10.1161/HYPERTENSIONAHA.118.11992.**) • **Online Data Supplement**

Key Words: blood pressure ■ hypertension ■ odds ratio ■ pregnancy ■ risk factors

Cardiovascular disease has been found to be responsible for 17 million deaths per year globally, 9.4 million of which are as a result of complications of hypertension.[1,2] The World Health Organization SAGE (Study on Global Aging and Adult Health; 2007–2010) found the prevalence of hypertension among South African adults to be 50% of whom 27% were <40 years of age.[3] Because hypertension is largely asymptomatic in early stages, it is known as the silent killer, exerting effects on vasculature and major organs, such as the kidney, the heart, and the brain, with blood pressure (BP) levels as low as 115/75 mm Hg having been shown to increase risk for poor cardiovascular and renal outcomes.[4,5]

High-income country longitudinal cohorts, such as the Young Finns (Finland) and Bogalusa Heart Study (LA), have shown that BP tracks through childhood.[6,7] In addition, BP trajectories, defined as subgroups of children following similar patterns of BP development over time, are set as early as in childhood.[8] The BT20 (Birth to Twenty Plus) cohort in Soweto, South Africa, recently published a prevalence of elevated BP (EBP) that ranged from 22.4% at 5 years of age to 34.9% at 18 years of age. Of the children who were hypertensive at some time during childhood, over one-third had EBP at 18 years of age. These results substantiate the tracking of BP that has been observed in high-income cohorts.[9]

Multiple perinatal and early life risk factors have been implicated in the development of hypertension in later life.[10–12] Previously published data from the BT20 cohort have shown that BP trajectories in childhood and adolescence are associated with patterns of early life growth.[13] In boys, accelerated gain in weight and height in infancy is associated with increased risk of being in a higher BP trajectory, whereas in girls, accelerated gain in weight and height in both infancy and early childhood is associated with increased risk.[13]

The relationship between childhood and adolescent BP and the potential risk for hypertension in young adults has been less well researched in low- to middle-income countries

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partly because of the lack of longitudinal birth cohorts. This study aims to (1) describe the prevalence of EBP in the BT20 cohort at 23 years of age; (2) assess whether EBP in early adulthood is associated with maternal, perinatal, and early life factors; and (3) assess whether childhood and adolescent BP trajectories are associated with EBP in adulthood.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

The BT20 cohort is a longitudinal birth cohort following singleton infants (n=3272) born in 1990 to mothers who were residents of Soweto, Johannesburg. The details of recruitment and cohort attrition have been described elsewhere.[14] For this study, participants seen in 2008 aged 18 years (n=1587) returned in 2012 aged 23 years, and data were collected. Participants were excluded if they were pregnant, if they had no BP measurement in adulthood, or if they had not been allocated into a BP trajectory group.

Adult BP Measurements and Child-Adolescent BP Trajectories

BP was measured using an Omron 6 automated machine (Kyoto, Japan). Participants were asked to sit comfortably with legs uncrossed for 5 minutes before 3 individual measurements were taken using an appropriate sized cuff on the left arm at 2-minute intervals. The first reading was discarded, and an average of the second and third readings was recorded for analysis. Participants were grouped into 1 of 3 categories as defined by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC7 report—normotensive: SBP <120 mm Hg and DBP <80 mm Hg; prehypertensive: SBP ≥120 mm Hg and <140 mm Hg or DBP ≥80 mm Hg and <90 mm Hg; or hypertensive: if SBP ≥140 mm Hg or DBP ≥90 mm Hg.[15] For analysis, participants in prehypertensive or hypertensive categories were classified as having EBP. The JNC7 report justifies this classification to better identify those at risk for developing hypertension by combining categories of normal and borderline into one, namely prehypertension.[15]

BP trajectory groups were derived from average BP measurements between mean ages 5 and 18 years using group-based trajectory modeling. These were defined as subgroups of children following similar patterns of BP level (intercept) and change (slope) during the childhood period. Three distinct trajectories for each sex were derived for SBP and DBP. These were labeled as lower, middle, or upper with BP trajectories representing mean BP based on the posterior probabilities of being assigned to a particular class. Height was added as a time-varying covariate. Details of BP trajectory group analyses and model fit criteria for this cohort are described elsewhere.[13]

Adult Anthropometric Measurements

Trained research assistants performed anthropometric measurements. Weight was measured to the nearest 0.1 kg on a digital scale with participants in light clothes with shoes removed. Standing height was measured to the nearest 0.1 cm with a wall-mounted stadiometer (Holtain, United Kingdom). Waist circumference was measured at the midpoint between the lowest palpable rib and the iliac crest in the midaxillary plane to the nearest 0.1 cm with a tape measure. Hip circumference was measured at the most protruding part of the buttocks with the participant standing. The average of 3 measurements was recorded providing there were no significant discordant values between them. Waist:hip ratios and body mass indices (weight [kg] divided by height squared [m^2]) were derived from these data.

Maternal and Early Life Factors

Maternal factors were recorded at the time of birth of the participant. Level of education was divided into 3 categories: primary if the mother had received no formal education or attended school until grade 2, secondary if the mother had attended school from grade 3 to grade 7, and tertiary if the mother had attended high school or had any postmatric qualification. Birth weight and gestational age were obtained from birth notification records entered at birth. Participants were grouped into low birth weight if birth weight was <2.5 kg or normal/high birth weight if birth weight was ≥2.5 kg and defined as preterm if their gestational age was <37 weeks at delivery. Weight was measured using a digital scale to the nearest 0.1 kg at ages 2 and 5, and height was measured using a calibrated stadiometer at 2 years of age. Conditional weight independent of height (relative weight gain) and relative gain in height independent of weight gain (relative linear growth) were computed as standardized residuals derived from sex-specific linear regressions of a current growth measure on a prior measure in infancy (0–2 years) and mid-childhood (2–5 years).[16,17] Duration of breastfeeding was determined through a survey in the first 12 months after delivery.

Assessment of SES

We used an asset-based household SES measured tool, which utilized a validated standardized questionnaire based on the Demographic and Health Survey for Developing Countries (available at http://www.dhsprogram.com/).

Statistical Analysis

All statistical analyses were done using STATA 15.0. *t* tests, χ^2 tests, and ANOVAs were done to compare study characteristics by sex and hypertension risk for categorical and continuous variables, respectively. Multiple linear regressions were used to assess the association between age, sex, early life and maternal risk factors, socioeconomic status, childhood and adolescent BP trajectories, and adult BMI and systolic and diastolic BP at 23 years of age. Odds ratios and 95% CIs were calculated using logistic regression for the above variables and EBP at 23 years of age. The level of significance was set at P <0.05. Not all participants had measures on all occasions; therefore, total numbers differ per variable in tables.

Results

There were no significant differences between the excluded and included samples with regard to education, sex, and socioeconomic status. There were a greater number of less-educated mothers in the analysis sample, and this was adjusted for in the multivariate analysis.

Table 1 shows the study population characteristics by sex at 23 years of age (n=1540; 49% men). Overall, there were significant differences in height, waist, hip circumferences, and BMI when comparing men and women. Average SBP was significantly higher in men by 8 mm Hg.

At birth, men weighed more than women, and more women were born preterm. In early life, men weighed more at 2 and 5 years of age and were also taller at 2 years of age. There were no significant differences between men and women with regard to maternal factors. At 23 years of age, 41% of men were prehypertensive as compared with 22% of women. Six percent of men compared with 4% of women were hypertensive.

Table 2 shows the sample characteristics by hypertensive status at 23 years of age. Thirty-six percent had EBP of whom 31% were prehypertensive and 5% were hypertensive. Sixty-four percent of those with prehypertension and 62% of those with hypertension were men. Those participants with EBP were 2 months younger, weighed more, and were taller than those with normal BP. There was no significant difference between BMI in those with EBP and those with normal BP in the overall analysis. However, in the sex-stratified analysis, women with EBP had a significantly higher BMI than

Table 1. Sex-Specific Study Characteristics at 23 y of Age

Variables and Categories	Total*	Men: Mean (SD), Median (IQR), or n (Prop)	Women: Mean (SD), Median (IQR), or n (Prop)	*P* Value
Sample size, n	1540	755 (49%)	785 (51%)	
Age, y	1507	23.1 (0.6)	23.0 (0.6)	0.372
Socioeconomic status	1529	10 (8–11)	10 (8–11)	0.200
Weight, kg	1540	63.8 (11.7)	65.0 (16.2)	0.100
Height, cm	1540	171.8 (6.2)	159.6 (6.1)	<0.001
Waist circumference, cm	1540	75.9 (9.5)	81.6 (13.4)	<0.001
Hip circumference, cm	1540	93.3 (8.5)	104.0 (12.6)	<0.001
Waist:hip	1540	0.81 (0.05)	0.78 (0.75)	<0.001
BMI, kg/m^2	1540	22 (4)	26 (6)	<0.001
Systolic BP, mm Hg	1540	118 (12)	110 (11)	<0.001
Diastolic BP, mm Hg	1540	74 (9)	73 (8)	0.200
Early life factors				
Mode of delivery	888	439 (49%)	449 (51%)	
Vaginal delivery	818 (92%)	406 (92%)	412 (92%)	0.689
Cesarean section	70 (8%)	33 (8%)	37 (8%)	
Birthweight, kg	1537	3.12 (0.5)	3.01 (0.5)	<0.001
Low birth weight	161 (10%)	71 (9%)	90 (11%)	0.186
Normal/high birth weight	1379 (90%)	684 (91%)	695 (89%)	
Gestational age, wk	1514	38.1 (1.7)	37.9 (1.9)	0.196
Preterm	199 (13%)	83 (11%)	116 (15%)	0.024
Term	1315 (87%)	661 (89%)	654 (85%)	
Breastfeeding, mo	1190	13 (4.0 – 24.0)	14 (5 - 21)	0.565
Weight: 2 y, kg	1256	11.5 (1.4)	11.2 (1.3)	0.001
Weight: 5 y, kg	1203	18.2 (2.1)	17.9 (2.4)	0.017
Height: 2 y, cm	1077	83.5 (3.3)	82.6 (3.2)	<0.001
Stunting: 2 y	198 (22%)	111 (26%)	87 (19%)	0.007
Maternal factors				
Age, y	1538	25.9 (6.2)	25.7 (6.1)	0.432
Highest level of education	1432	700 (49%)	732 (51%)	
Primary	847 (59%)	433 (62%)	414 (57%)	0.115
Secondary	484 34%)	219 (31%)	265 (36%)	
Tertiary	101 (7%)	48 (7%)	53 (7%)	
Maternal parity at the time of delivery	1540	755 (49%)	785 (51%)	
1 child only	570 (37%)	267 (35%)	303 (39%)	0.189
>1 child	970 (63%)	488 (65%)	482 (61%)	
BP status (23 y of age)				
Normal BP	980	400 (53%)	580 (74%)	<0.001
Prehypertension	481	306 (41%)	175 (22%)	
Hypertension	79	49 (6%)	30 (4%)	

(*Continued*)

Table 1. Continued

Variables and Categories	Total*	Men: Mean (SD), Median (IQR), or n (Prop)	Women: Mean (SD), Median (IQR), or n (Prop)	*P* Value
Early life BP trajectories†				
Systolic trajectories	1401	691 (49%)	710 (51%)	
Lower	636 (45%)	325 (47%)	311 (44%)	0.478
Middle	679 (48%)	325 (47%)	354 (50%)	
Upper	86 (6%)	41 (6%)	45 (6%)	
Diastolic trajectories	1401	691 (49%)	710 (51%)	
Lower	770 (55%)	416 (60%)	354 (50%)	<0.001
Middle	603 (43%)	258 (37%)	345 (49%)	
Upper	28 (2%)	17 (3%)	11 (1%)	

A *t* test was done to compare continuous variables and a χ^2/Fisher exact to compare categorical variables. A *P* value of <0.05 was considered significant. BMI indicates body mass index; BP, blood pressure; IQR, interquartile range; and Prop, proportion.

*Data were not available for the complete study population for all variables. Numbers in the total column represent the number of participants for whom data were available for each specific variable.

†Represent mean BP from 5 to 18 y based on the posterior probabilities of being assigned to a particular class.

normotensive women and men with prehypertension had a marginally higher BMI than normotensive men (Table S1 in the online-only Data Supplement). Weight at 5 years and height at 2 years were higher in those with EBP compared with those with normal BP. There were no significant differences with regard to maternal factors.

With regard to perinatal factors, no significant differences were found between those with EBP and birthweight or gestational age in the overall analysis; however, a larger proportion of hypertensive women were born preterm (33%) compared with 12% of hypertensive men (Table S1). Gestational age, however, did not contribute significantly to EBP in the multivariate analysis and so was not included in the final model.

Twenty-seven percent of hypertensives fell into the upper SBP trajectory and 59% into the middle SBP trajectory as compared with only 6% and 49%, respectively, of those with normal BP. Eleven percent of hypertensives fell into the upper DBP trajectory and 66% into the middle DBP trajectory as compared with 2% and 43% of those with normal BP (Table 2).

Multivariate logistic regression models were run to assess contributing factors toward increased risk of EBP at 23 years of age (Tables 3 and 4). Women had a 62% lower risk which increased to 77% when infant and childhood growth variables and BP trajectories were added. Maternal factors, socioeconomic status, and mode of delivery had no significant effect. Mode of delivery was removed from the final model because data were not available for all participants. Of the early life growth factors, relative gain in length or height from birth to 2 years of age was associated with a 23% increased risk. Systolic BP trajectories contributed the most with being in the middle SBP trajectory resulting in a 3× increased risk of EBP and being in the highest SBP trajectory resulting in a 9× higher risk. Body mass index at 23 years of age contributed to a 4% increased risk.

Discussion

In this cohort of young adults at 23 years of age, the prevalence of EBP was 36%, which is comparable with findings from other studies in Sub-Saharan Africa. In Ethiopia, this has been reported as 14.5% for hypertension in 15- to 48-year olds and in Uganda as 59% for EBP among 18- to 40-year olds.[18,19] Internationally reported prevalence ranges from 35.8% for EBP at 38 years of age in Dunedin, New Zealand to 43% EBP in 18- 20-year olds in Jamaica.[20,21]

Our study showed that men were at higher risk of having EBP—a consistent finding in many other studies.[20,22–24] Postulated reasons include sex-related differences in the developmental programming of BP, responses of the renin-angiotensin system to early life stressors, and oxidative stress responses.[25,26]

Birth weight and gestational age were not associated with higher risk for EBP in our cohort. Several studies in mainly white populations have examined these aspects, and conflicting results have been found.[10,11] A cohort study conducted in rural South Africa found no association with birth weight.[27] Factors that contribute to increased risk in premature or low-birth-weight babies include low nephron number, growth restriction, exposure to postnatal insults, such as acute kidney injury, exposure to nephrotoxic drugs, and accelerated catch-up growth.[10]

Interestingly, relative gain in length or height in early childhood was the only early life factor that was persistently associated with an increased risk for EBP at 23 years of age and has been confirmed in other studies. Recently, a Brazilian birth cohort showed that higher than expected height gain from birth to childhood was associated with hypertension in adulthood; however, a different Brazilian cohort found no association with adolescent BP.[28,29] A systematic review of studies that evaluated the role of size at birth and postnatal catch-up growth and relation to SBP found 3 studies that looked specifically at skeletal catch-up growth. All 3 studies reported a positive association. None of these studies were in low- to middle-income countries.[30] Reasons postulated to explain the association include the hypothesis that inadequate nutrition reduces the size and number of nephrons and thus adult renal functional

Table 2. Study Characteristics by Hypertensive Status at 23 y of Age

Variables and Categories	Total*	Normal BP: Mean (SD) or n (Prop)	Prehypertensive: Mean (SD) or n (Prop)	Hypertensive: Mean (SD) or n (Prop)	*P* Value
	1540	980 (64%)	481 (31%)	79 (5%)	
Sex					
Men	755	400 (41%)	306 (64%)	49 (62%)	<0.001
Women	785	580 (59%)	175 (36%)	30 (38%)	
Age, y	1507	23.1 (0.6)†‡	22.9 (0.6)	22.9 (0.5)	<0.001
Socioeconomic status	1529	10 (2)‡§	10 (2)	9 (3)	0.008
Weight, kg	1540	62.7(13.3)†‡	67.2 (14.7)	67.8 (17.8)	<0.001
Height, cm	1540	164.2 (85.0)†‡	168.1 (87.6)	167.4 (89.2)	<0.001
Waist circumference, cm	1540	78 (12)†	80 (12)	81 (14)	<0.001
Hip circumference, cm	1540	98.3 (11.7)	99.4 (12.6)	100.4 (15.4)	0.140
Waist:hip	1540	0.79 (0.07)†	0.80 (0.06)	0.81 (0.08)	0.008
BMI, kg/m^2	1540	24 (5)	24 (6)	25 (7)	0.170
Systolic BP, mm Hg	1540	107 (8)†‡	124 (7)§	138 (12)	<0.001
Diastolic BP, mm Hg	1540	70 (6)†‡	78 (7)§	93 (8)	<0.001
Early life factors					
Mode of delivery	888	559 (63%)	280 (32%)	49 (5%)	
Vaginal delivery	818 (92%)	520 (93%)	257 (92%)	41 (84%)	0.064
Cesarean section	70 (8%)	39 (7%)	23 (8%)	8 (16%)	
Birthweight, kg	1537	3.1 (0.5)	3.1 (0.5)	3.1 (0.6)	0.442
Low birth weight	161 (10%)	105 (11%)	46 (10%)	10 (13%)	0.641
Normal/high birth weight	1379 (90%)	875 (89%)	435 (90%)	69 (87%)	
Gestational age, wk	1514	38.0 (1.7)	38.1 (1.8)	37.6 (2.7)	0.166
Preterm	199 (13%)	130 (13%)	53 (11%)	16 (20%)	0.081
Term	1315 (87%)	835 (87%)	417 (89%)	63 (80%)	
Breastfeeding, mo	1190	12.8 (8.6)	13.7 (8.8)	14.1 (9.7)	0.163
Weight: 2 y, kg	1256	11.3 (1.4)	11.5 (1.3)	11.4 (1.6)	0.086
Weight: 5 y, kg	1203	17.8 (2.2)†	18.4 (2.4)	18.2 (2.4)	<0.001
Height: 2 y, cm	1077	82.8 (3.3)†	83.5 (3.2)	83.1 (3.5)	0.003
Stunting: 2 y	198 (22%)	132 (23%)	52 (20%)	14 (33%)	0.165
Maternal factors					
Age, y	1538	25.7 (6.3)	25.8 (6.0)	27.3 (5.9)	0.070
Highest level of education	1432	905 (63%)	454 (32%)	73 (5%)	
Primary	847 (59%)	533 (59%)	266 (58%)	48 (66%)	0.813
Secondary	484 (34%)	305 (34%)	158 (35%)	21 (29%)	
Tertiary	101 (7%)	67 (7%)	30 (7%)	4 (5%)	
Maternal parity	1540	980 (64%)	481 (31%)	79 (5%)	
1 child only	570 (37%)	368 (38%)	177 (37%)	25 (32%)	0.575
>1 child	970 (63%)	612 (62%)	304 (63%)	54 (68%)	

(*Continued*)

Table 2. Continued

Variables and Categories	Total*	Normal BP: Mean (SD) or n (Prop)	Prehypertensive: Mean (SD) or n (Prop)	Hypertensive: Mean (SD) or n (Prop)	P Value
Early life BP trajectories‖					
Systolic trajectories	1401	880 (63%)	447 (32%)	74 (5%)	
Lower	636 (45%)	478 (54%)	148 (33%)	10 (14%)	<0.001
Middle	679 (49%)	370 (42%)	265 (59%)	44 (59%)	
Upper	86 (6%)	32 (4%)	34 (8%)	20 (27%)	
Diastolic trajectories	1401	880 (63%)	447 (32%)	74 (5%)	
Lower	770 (55%)	545 (62%)	208 (47%)	17 (23%)	<0.001
Middle	603 (43%)	329 (37%)	225 (50%)	49 (66%)	
Upper	28 (2%)	6 (1%)	14 (3%)	8 (11%)	

An ANOVA was done to compare continuous variables and a χ^2/Fisher exact to compare categorical variables. A P value of <0.05 was considered significant. BMI indicates body mass index; BP, blood pressure; IQR, interquartile range; and Prop, proportion.

*Data were not available for the complete study population for all variables. Numbers in the total column represent the number of participants for whom data were available for each specific variable.

†Significant difference lies between normal BP and prehypertension.

‡Significant difference lies between normal BP and hypertension.

§Significant difference lies between prehypertension and hypertension.

‖Represent mean BP from 5 to 18 y based on the posterior probabilities of being assigned to a particular class.

capacity.[31,32] This is further compounded by postnatal factors, such as rapid linear growth and weight gain, which stress the preprogrammed kidney further, resulting in an increase in diseases, such as hypertension[33,34]

Of all the factors considered in our study, BP trajectories in childhood and adolescence had the strongest effect on the presence of EBP at 23 years of age. Several studies have confirmed that BP tracks into adulthood.[6,20,35,36] Ours is the first study in

Table 3. Multivariate Analysis of Factors Associated With Young Adult Elevated Blood Pressure (Models 1, 2, and 3)

Exposure Variable	Model 1			Model 2			Model 3		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Age, y	0.47	0.39–0.58	<0.001	0.48	0.39–0.59	<0.001	0.43	0.33–0.57	<0.001
Sex									
Men									
Women	0.38	0.30–0.48	<0.001	0.38	0.30–0.48	<0.001	0.38	0.28–0.51	<0.001
Maternal education									
Primary									
Secondary	1.07	0.83–1.37	0.612	1.12	0.86–1.44	0.403	1.09	0.79–1.50	0.613
Tertiary	0.95	0.60–1.51	0.826	0.98	0.62–1.58	0.958	0.95	0.52–1.72	0.866
Maternal age, y	1.01	0.99–1.03	0.404	1.01	0.99–1.03	0.361	1.01	0.98–1.04	0.556
Maternal parity									
1 child									
>1 child	0.90	0.67–1.21	0.488	0.89	0.66–1.20	0.452	0.93	0.64–1.36	0.714
Socioeconomic status				0.97	0.92–1.02	0.299	0.96	0.90–1.03	0.231
Birth weight (Z score)							1.08	0.93–1.25	0.335
Relative weight gain (0–2: Z score)							1.06	0.91–1.23	0.460
Relative weight gain (2–5: Z score)							1.03	0.90–1.19	0.646
Relative gain length/height (0–2: Z score)							1.19	1.03–1.38	0.022
Relative gain length/height (2–5: Z score)							1.14	0.99–1.31	0.067
Pseudo R^2	0.066*			0.066*			0.080*		

OR indicates odds ratio.

Table 4. Multivariate Analysis of Factors Associated With Young Adult Elevated Blood Pressure (Models 4, 5, and 6)

	Model 4			Model 5			Model 6		
Exposure Variable	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age, y	0.41	0.31–0.56	<0.001	0.38	0.27–0.52	<0.001	0.36	0.26–0.50	<0.001
Sex									
Men									
Women	0.30	0.22–0.42	<0.001	0.29	0.20–0.40	<0.001	0.23	0.16–0.34	<0.001
Maternal education									
Primary									
Secondary	1.22	0.86–1.73	0.264	1.21	0.85–1.73	0.280	1.25	0.87–1.78	0.226
Tertiary	1.03	0.54–1.95	0.927	1.03	0.54–1.95	0.932	1.01	0.53–1.92	0.986
Maternal age, y	1.01	0.98–1.04	0.558	1.01	0.98–1.04	0.515	1.01	0.98–1.05	0.424
Maternal parity									
1 child									
>1 child	0.93	0.62–1.41	0.736	0.92	0.61–1.39	0.687	0.90	0.59–1.36	0.607
Socioeconomic status	0.98	0.91–1.05	0.539	0.97	0.91–1.05	0.489	0.97	0.90–1.04	0.348
Birth weight (*Z* score)	1.13	0.96–1.33	0.146	1.12	0.95–1.32	0.171	1.09	0.92–1.29	0.305
Relative weight gain (0–2: *Z* score)	1.02	0.86–1.21	0.836	0.99	0.84–1.18	0.952	0.94	0.79–1.12	0.500
Relative weight gain (2–5: *Z* score)	0.98	0.85–1.15	0.888	0.98	0.84–1.14	0.757	0.92	0.79–1.08	0.319
Relative gain length/height (0–2: *Z* score)	1.18	0.98–1.39	0.054	1.20	1.01–1.41	0.034	1.19	1.01–1.41	0.038
Relative gain length/height (2–5: *Z* score)	1.14	0.98–1.32	0.087	1.13	0.97–1.32	0.108	1.12	0.97–1.31	0.128
SBP trajectories									
Lowest									
Middle	3.24	2.31–4.54	<0.001	2.79	1.94–3.99	<0.001	2.76	1.92–3.96	<0.001
Highest	6.50	3.21–13.16	<0.001	4.08	1.89–8.87	<0.001	3.98	1.82–8.71	0.001
DBP trajectories									
Lowest									
Middle				1.51	1.05–2.17	0.028	1.48	1.02–2.14	0.037
Highest				5.63	1.25–25.39	0.025	5.46	1.23–24.23	0.025
BMI							1.04	1.01–1.08	0.005
Adjusted R^2	0.137*			0.145*			0.152*		

BMI indicates body mass index; DBP, diastolic blood pressure; OR, odds ratio; and SBP, systolic blood pressure.

Sub-Saharan Africa to show the same result in a varying genetic and socioeconomic population. In a country where the prevalence of adult hypertension is among the highest in the world, data such as ours are important in establishing whether changes in childhood and adolescence could affect outcomes in adulthood. Whereas much work is being done in improving maternal health and early childhood growth and development, our data suggest that one's life course is set relatively early in childhood and that perhaps identifying individuals at high risk for EBP in early childhood may improve outcomes in adulthood. The Childhood Determinants of Adult Health Study showed that 10% of EBP in adulthood could be attributable to elevated childhood levels.[35] If identification of individuals at risk could occur earlier, this could facilitate targeted interventions that might prevent adverse cardiovascular and renal outcomes associated with hypertension.

The strength of this study is its longitudinal design in a sub-Saharan African setting. However, BP was measured at 1 sitting only at the various survey points, thus we could not classify participants as hypertensive but only as having EBP. To date, we have not conducted 24-hour ambulatory BPs because of logistical challenges on such a large sample; thus we are unable to comment on white coat hypertension or on any masked hypertension, which may have contributed to the high prevalence. However, because this cohort has had engagement with the study team since birth and developed trust with the study personnel, we anticipate a minor white coat effect. More detailed information with regard to maternal nutritional status and maternal comorbidity during pregnancy and early life would have helped to better characterize the early life findings.

Perspectives

In summary, this study highlights the fact that one's life course is influenced early on in childhood and that identification of individuals with EBP in childhood could predict risk for EBP in adulthood. It also suggests that interventions aimed at growth and nutrition in early childhood could help reduce risk for EBP in adulthood. Research now needs to explore whether increased risk translates into actual measures of poor cardiovascular and renal outcomes and whether any interventions in childhood and adolescence could affect movement from one BP trajectory to another.

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Disclosures

None.

References

1. World Health Organization. *Causes of Death 2008*. Geneva, Switzerland: WHO; 2008.
2. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. *Lancet*. 2012;380:2224–2260. doi: 10.1016/S0140-6736(12)61766-8
3. Basu S, Millett C. Social epidemiology of hypertension in middle-income countries: determinants of prevalence, diagnosis, treatment, and control in the WHO SAGE study. *Hypertension*. 2013;62:18–26. doi: 10.1161/HYPERTENSIONAHA.113.01374
4. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903–1913. doi: 10.1016/S0140-6736(02)11911-8
5. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. *Lancet*. 2016;387:435–443. doi: 10.1016/S0140-6736(15)00805-3
6. Juhola J, Magnussen CG, Viikari JS, Kähönen M, Hutri-Kähönen N, Jula A, Lehtimäki T, Åkerblom HK, Pietikäinen M, Laitinen T, Jokinen E, Taittonen L, Raitakari OT, Juonala M. Tracking of serum lipid levels, blood pressure, and body mass index from childhood to adulthood: the Cardiovascular Risk in Young Finns Study. *J Pediatr*. 2011;159:584–590. doi: 10.1016/j.jpeds.2011.03.021
7. Webber LS, Cresanta JL, Voors AW, Berenson GS. Tracking of cardiovascular disease risk factor variables in school-age children. *J Chronic Dis*. 1983;36:647–660.
8. Nagin DS, Odgers CL. Group-based trajectory modeling in clinical research. *Annu Rev Clin Psychol*. 2010;6:109–138. doi: 10.1146/annurev.clinpsy.121208.131413
9. Kagura J, Adair LS, Musa MG, Pettifor JM, Norris SA. Blood pressure tracking in urban black South African children: birth to twenty cohort. *BMC Pediatr*. 2015;15:78. doi: 10.1186/s12887-015-0402-z
10. Luyckx VA, Bertram JF, Brenner BM, Fall C, Hoy WE, Ozanne SE, Vikse BE. Effect of fetal and child health on kidney development and long-term risk of hypertension and kidney disease. *Lancet*. 2013;382:273–283. doi: 10.1016/S0140-6736(13)60311-6
11. Järvelin MR, Sovio U, King V, Lauren L, Xu B, McCarthy MI, Hartikainen AL, Laitinen J, Zitting P, Rantakallio P, Elliott P. Early life factors and blood pressure at age 31 years in the 1966 northern Finland birth cohort. *Hypertension*. 2004;44:838–846. doi: 10.1161/01.HYP.0000148304.33869.ee
12. Lackland DT, Bendall HE, Osmond C, Egan BM, Barker DJ. Low birth weights contribute to high rates of early-onset chronic renal failure in the Southeastern United States. *Arch Intern Med*. 2000;160:1472–1476.
13. Kagura J, Adair LS, Munthali RJ, Pettifor JM, Norris SA. Association between early life growth and blood pressure trajectories in black South African children. *Hypertension*. 2016;68:1123–1131. doi: 10.1161/HYPERTENSIONAHA.116.08046
14. Richter L, Norris S, Pettifor J, Yach D, Cameron N. Cohort profile: Mandela's children: the 1990 birth to twenty study in South Africa. *Int J Epidemiol*. 2007;36:504–511. doi: 10.1093/ije/dym016
15. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289:2560–2572. doi: 10.1001/jama.289.19.2560
16. Adair LS, Fall CH, Osmond C, Stein AD, Martorell R, Ramirez-Zea M, Sachdev HS, Dahly DL, Bas I, Norris SA, Micklesfield L, Hallal P, Victora CG; COHORTS Group. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet*. 2013;382:525–534. doi: 10.1016/S0140-6736(13)60103-8
17. Keijzer-Veen MG, Euser AM, van Montfoort N, Dekker FW, Vandenbroucke JP, Van Houwelingen HC. A regression model with unexplained residuals was preferred in the analysis of the fetal origins of adult diseases hypothesis. *J Clin Epidemiol*. 2005;58:1320–1324. doi: 10.1016/j.jclinepi.2005.04.004
18. Abdissa SG, Oli K, Feleke Y, Goshu DY, Begna DM, Tafese A. Spectrum of cardiovascular diseases among Ethiopian patients at Tikur Anbessa Specialized University Teaching Hospital, Addis Ababa. *Ethiop Med J*. 2014;52:9–17.
19. Kayima J, Nankabirwa J, Sinabulya I, Nakibuuka J, Zhu X, Rahman M, Longenecker CT, Katamba A, Mayanja-Kizza H, Kamya MR. Determinants of hypertension in a young adult Ugandan population in epidemiological transition-the MEPI-CVD survey. *BMC Public Health*. 2015;15:830. doi: 10.1186/s12889-015-2146-y
20. Theodore RF, Broadbent J, Nagin D, Ambler A, Hogan S, Ramrakha S, Cutfield W, Williams MJ, Harrington H, Moffitt TE, Caspi A, Milne B, Poulton R. Childhood to early-midlife systolic blood pressure trajectories: early-life predictors, effect modifiers, and adult cardiovascular outcomes. *Hypertension*. 2015;66:1108–1115. doi: 10.1161/HYPERTENSIONAHA.115.05831
21. Ferguson TS, Younger-Coleman NOM, Tulloch-Reid MK, Bennett NR, Rousseau AE, Knight-Madden JM, Samms-Vaughan ME, Ashley DE, Wilks RJ. Factors associated with elevated blood pressure or hypertension in Afro-Caribbean youth: a cross-sectional study. *PeerJ*. 2018;6:e4385. doi: 10.7717/peerj.4385
22. Senthil S, Krishnadasa SN. Prehypertension and its determinants in apparently healthy young adults. *J Clin Diagn Res*. 2016;10:CC05–CC08. doi: 10.7860/JCDR/2016/20626.8447
23. Israeli E, Schochat T, Korzets Z, Tekes-Manova D, Bernheim J, Golan E. Prehypertension and obesity in adolescents: a population study. *Am J Hypertens*. 2006;19:708–712. doi: 10.1016/j.amjhyper.2006.01.012
24. Das P, Basu M, Chowdhury K, Mallik S, Dhar G, Biswas A. Observational assessment and correlates to blood pressure of future physicians of Bengal. *Niger J Clin Pract*. 2013;16:433–438. doi: 10.4103/1119-3077.116884
25. Ojeda NB, Intapad S, Alexander BT. Sex differences in the developmental programming of hypertension. *Acta Physiol (Oxf)*. 2014;210:307–316. doi: 10.1111/apha.12206
26. Reckelhoff JF. Gender differences in hypertension. *Curr Opin Nephrol Hypertens*. 2018;27:176–181. doi: 10.1097/MNH.0000000000000404
27. Monyeki K, Kemper H, Mogale A, Hay L, Sekgala M, Mashiane T, Monyeki S, Sebati B. Association between blood pressure and birth weight among rural South African children: Ellisras longitudinal study. *Int J Environ Res Public Health*. 2017;14:E974. doi: 10.3390/ijerph14090974
28. Menezes AM, Hallal PC, Dumith SC, Matijasevich AM, Araújo CL, Yudkin J, Osmond C, Barros FC, Victora CG. Adolescent blood pressure, body mass index and skin folds: sorting out the effects of early weight

and length gains. *J Epidemiol Community Health*. 2012;66:149–154. doi: 10.1136/jech.2010.124842
29. Ferraro AA, Barbieri MA, da Silva AAM, Grandi C, Cardoso VC, Stein AD, Bettiol H. Contributions of relative linear growth and adiposity accretion from birth to adulthood to adult hypertension. *Sci Rep*. 2017;7:8928. doi: 10.1038/s41598-017-09027-1
30. Huxley RR, Shiell AW, Law CM. The role of size at birth and postnatal catch-up growth in determining systolic blood pressure: a systematic review of the literature. *J Hypertens*. 2000;18:815–831.
31. Brenner BM, Garcia DL, Anderson S. Glomeruli and blood pressure. Less of one, more the other? *Am J Hypertens*. 1988;1(4 pt 1):335–347.
32. Mackenzie HS, Brenner BM. Fewer nephrons at birth: a missing link in the etiology of essential hypertension? *Am J Kidney Dis*. 1995;26:91–98.
33. Tarry-Adkins JL, Ozanne SE. Mechanisms of early life programming: current knowledge and future directions. *Am J Clin Nutr*. 2011;94(suppl 6):1765S–1771S. doi: 10.3945/ajcn.110.000620
34. Dötsch J, Plank C, Amann K. Fetal programming of renal function. *Pediatr Nephrol*. 2012;27:513–520. doi: 10.1007/s00467-011-1781-5
35. Kelly RK, Thomson R, Smith KJ, Dwyer T, Venn A, Magnussen CG. Factors affecting tracking of blood pressure from childhood to adulthood: the Childhood Determinants of Adult Health Study. *J Pediatr*. 2015;167:1422.e2–1428.e2. doi: 10.1016/j.jpeds.2015.07.055
36. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation*. 2008;117:3171–3180. doi: 10.1161/CIRCULATIONAHA.107.730366

Novelty and Significance

What Is New?

- This is the first study in this population group to show that childhood and adolescent blood pressure (BP) trajectories predict risk for elevated BP in early adulthood and confirms findings reported in other cohorts with different genetic and socioeconomic backgrounds.

What Is Relevant?

- Determination of BP trajectories in childhood and adolescence may help identify those at risk for elevated BP in adulthood and aid early intervention.

Summary

Early identification of BP trajectories and interventions to improve early childhood nutrition may help reduce the risk for elevated BP in adulthood.