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An inverse relation between blood pressure and birth weight among 5 year old children from Soweto, South Africa

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Abstract

***Study objective*—To examine the relation between birth weight and blood pressure at 5 years in a cohort of South African children.**

***Design*—Prospective cohort study.**

***Participants*—849 five year old children.**

***Setting*—Soweto, a sprawling urban area close to Johannesburg, South Africa, which was a designated residential area for people classified as "black" under apartheid legislation.**

***Main results*—Systolic blood pressure at 5 years was inversely related to birthweight ($r=-0.05$, $p=0.0007$), independent of current weight, height, gestational age, maternal age or socioeconomic status at 5 years. There was no relation between birth weight and diastolic blood pressure. After adjusting for current weight and height, there was a mean decline in systolic blood pressure of 3.4 mm Hg (95% confidence intervals 1.4, 5.3 mm Hg) for every 1000 g increase in birth weight.**

***Conclusions*—These data from a disadvantaged urbanised community in Southern Africa extend the reported observations of an inverse relation between birth weight and systolic blood pressure. The study adds to the evidence that influences in fetal life and early childhood influence systolic blood pressure. Further research is required to assess whether efforts to reduce the incidence of low birthweight babies will attenuate the prevalence of hypertension in future generations.**

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Most of the South African population, formally disenfranchised and classified as "black" has been undergoing rapid urbanisation, to the extent that it is predicted that more than 70% will live in urban areas by the year 2010.[1] This process has been accompanied by a change in the pattern of diseases from predominantly infectious to chronic, as South Africa enters the epidemiological transition.[2] Currently, in this urbanised community, there is a high prevalence of hypertension, a seeming rise in the prevalence of diabetes and the emergence of dyslipidaemia.[3–6] Given the context of shrinking health resource allocation and the growing morbidity and mortality attributable to these diseases, the identification of the potential causes and hence opportunities for their prevention, is increasingly important.

Known risk factors, for example, genetic predisposition, environment and lifestyle do not fully explain the susceptibility of people to these adult chronic diseases. An emerging theory to explain the patterns of these diseases in people and populations, is that an adverse intrauterine environment programmes susceptibility to the diseases and their metabolic risk factors.[7–9] This theory is based on epidemiological evidence of an association between measures of early life experience (predominantly birth weight) and the development of these diseases in later life.[7 8 10]

A number of studies have investigated, and most found an inverse relation between birth weight and blood pressure in childhood, adolescence, and adulthood.[11–24] Interestingly, in the only study reported in full from Africa, no relation between birth weight and blood pressure was found in 675 children aged 1 to 9 years in rural Gambia. However, a significant inverse relation between maternal weight gain in the third trimester of pregnancy and blood pressure of 8 and 9 year old offspring was interpreted as supporting the relation between poor maternal nutrition and higher blood pressures in children.[17]

This paper reports an investigation of the association between birth weight and blood pressure at 5 years of age in a cohort of historically disadvantaged urban children from Soweto in South Africa. Soweto, an acronym for South Western Townships, is a sprawling city of about 2 million people, situated 15 miles from central Johannesburg. It was originally established as a dormitory for Johannesburg's "black" workers. Under the 1960 Group Areas Act, which forced different groups of people to live in demarcated areas, Soweto was reserved for people classified as "black" under apartheid legislation. Today, Soweto is a cosmopolitan city where diverse groups of "black" South Africans have culturally blended together over time.

Most Sowetans are poor, although there is a range of income groups, and large numbers are unable to find formal employment. Most people live in formal housing (mostly small two, three or four room brick or cement block houses), but almost every house has a backyard structure (corrugated iron or wood shack). This is typical of poorer areas where there is an acute housing shortage. Backyard structures are a valuable source of income. Soweto households typically consist of six or fewer people, but are in a constant state of flux with new household members entering and/or old ones leaving. Household fluidity is a common feature in all poorer South African urban areas. Most Sowetans have access to electricity, although coal is still commonly burned. Only a third of the houses in Soweto have indoor water; the most common source of water is an outdoor faucet. About two thirds of Sowetans use an outdoor flush toilet, pit or bucket latrine, while a third have an indoor flush toilet.

Methods

The sample was drawn from the Birth to Ten (BTT) study, a prospective cohort study of determinants of growth, development, and health of children in the metropolitan area of Soweto, Johannesburg. The cohort was drawn from all 5460 singleton births during a seven week period between April and June 1990 to women who gave their permanent address within the defined area. Identification and enrolment of children into BTT took place throughout the first year of the study. The 4029 births enrolled represented about 95% of all births that occurred in the area during the seven weeks to mothers actually resident in the defined area. This is based on earlier pilot studies that found that approximately 20% of mothers who deliver babies in the BTT area were from rural areas, travelling to the metropolitan area to give birth and then returning shortly after delivery.[25 26] The potential sample for this study was restricted to children whose caregivers were living in Soweto at the time of enrolment into the BTT study. This comprised 3170 "black" children. The remaining 859 children were not eligible because they were not resident in Soweto at the time of enrolment (n=632), stillborn (n=106), dying during the first month of life (n=80) or before their first birthday (n=41).

In 1992, 1994, and 1995 when the children were 2, 4, and 5 years old, all the children and caregivers were invited to attend for follow up interviews and examination. Follow up has been logistically difficult because of movement of families within the urban area and between the urban and rural areas, but contact has been maintained with approximately 60% of the enrolled cohort of children and families.

At the age of 5 years, the children and caregivers currently living in Soweto were contacted at home or work by phone, letter or a visit by a BTT research assistant for an interview appointment at health care clinics or the Baragwanath Hospital. People who did not attend the scheduled appointments were reminded by telephone, letter or home visit. This provided a cross sectional sample of 849 "black" children and caregivers who attended for an interview and gave permission to be measured over a four month period. Children's height and weight were measured as previously described.[27] Blood pressure was measured using a Dinamap Vital Signs Monitor (1846SX) and an appropriate cuff size. After 10 minutes at rest, the blood pressure was taken in triplicate, and the lowest diastolic blood pressure observed with its matching systolic were used in the analysis, as described for measurement of blood pressure in the South African guidelines for the management of hypertension at primary care level.[28] Data on current socioeconomic status at 5 years of age were obtained from interviews with the caregivers in which detailed questionnaires were completed. These included questions about living conditions and access to modern amenities such as washing machines within the child's home. Socioeconomic status was assessed using a socioeconomic score based on five variables describing access to four amenities and services. Five categories were constructed using these variables on a hierarchical basis. These were as follows: no electricity in the house (1), electricity in the house (2), electricity in the house and access to a car (3), electricity in the house, access to a car and a washing machine (4), electricity in the house, access to a car and washing machine and private medical insurance (5).[29] Access to higher order variables had no effect on the score unless all lower order variables were also accessible. For example, if a subject had access to a higher order variable like private medical insurance but had no electricity, they were placed in category '1'.

Birth notification records were used to provide data on infants' sex, birth weight, gestational age at birth, maternal age, area of residence, and use of public or private maternity facility. The public maternity facilities available were hospitals, in particular Baragwanath Hospital, and specific facilities attached to primary care clinics. Most women in the sample (95%) delivered at public maternity centres, 5% delivered in private delivery facilities. A negligible number of women in the sample delivered at home, usually because they were unable to get to a delivery centre in time. Gestational ages are routinely measured in public facilities using the date of the last menstrual period and this was the case for the current sample. A small number of gestational ages were measured by ultrasound scan or abdominal palpation.

Ethical permission for the BTT study was obtained from the ethics committee of the University of the Witwatersrand.

STATISTICAL METHODS

The analyses were limited to the 818 children examined at 5 years of age, on whom blood pressure, weight and height data were available. The results are expressed as means and standard deviations. The associations between pairs of categorical variables were examined using the χ^2 test. Analysis of variance was applied when the explanatory variable was categorical and the response variable was numerical. The Pearson correlation coefficient was used to investigate relations among the numerical variables examined.

Multiple regression analysis was used to test for independent effects of the explanatory variables on systolic and diastolic blood pressure. Forward and backward selection procedures were used in separate analyses. Weight, birth

Table 1 Mean (SD) characteristics of the study population, by sex

	Boys	Girls
Number	420	398
Birth weight	3093 (524)	3021 (510)*
Gestational age (weeks)	37.9 (1.8)	37.9 (1.7)
Maternal age (y)	25.2 (6.1)	25.6 (6.4)
Height at 5 y (cm)	108 (4)	108 (5)
Weight at 5 y (kg)	18.4 (2.2)	18.1 (2.3)*
BMI at 5 y (kg/m^2)	15.7 (1.2)	15.5 (1.3)*
Blood pressure (mm Hg)		
systolic	108.2 (13.1)	107.7 (12.3)
diastolic	62.2 (8.3)	63.0 (8.3)

*p<0.05.

Table 2 Mean (SD) characteristics within the study sample of those children examined at 5 years and those not traced

	Children at 5 years	Children not traced
Number	818	2315
Gestational age (weeks)	37.9 (1.8)	37.9 (1.9)
Birth weight (g)	3063 (529)	3065 (517)
Boys/girls (%)	48/52	51/49
Gravidity (no)	2.2 (1.4)	2.5 (1.5)†
Delivery at public health facility (%)	94.6	95.8
Maternal age (y)	25.4 (6.2)	26.1 (6.0)*

*p<0.01. †p<0.0001.

weight, height, gestational and maternal age were all treated as continuous independent variables. Socioeconomic status was treated as a categorical variable. The systolic and diastolic blood pressures were used as continuous dependent variables. The independent variables included in the regression model were those with the highest correlation with the dependent variables.

Results

Table 1 shows the characteristics of the 818 children on whom blood pressure data were available. Comparison of the baseline characteristics of the children available for study at 5 years and those who were not (table 2), demonstrated no significant differences in mean birth weight, gestational ages, sex distribution or proportion of children delivered at public facilities. There were small, but statistically significant differences in the mean gravidity and maternal ages. The distribution of the sample across the categories of socioeconomic status was: Class 1: 2.2%, Class 2: 68.8%, Class 3: 19%, Class 4: 5.2%, Class 5: 4.7%.

Univariate analysis demonstrated significant associations between systolic blood pressure and weight (r = 0.21, p = 0.0001), and height (r = 0.24, p = 0.0001) both at 5 years, but no significant association with birth weight, gestational age, maternal age, or socioeconomic status at 5 years of age. There was a significant inverse relation between systolic pressure and birth weight (one way analysis of variance F = 3.54, p = 0.01) when standardised for current weight (table 3). The highest blood pressure was noted in those with the lowest birth weight and the highest current weight. Univariate analysis demonstrated a significant association between diastolic blood pressure and weight (r=0.18, p=0.0001) and height (r=0.23, p=0.0001) both at 5 years of age and maternal age (r=0.09, p=0.01), but not with birth weight or gestational age. There was also no significant association between birth weight and diastolic blood pressure when standardised for current weight.

While birth weight, current weight, and height were all independently associated with systolic blood pressure in the best fit multiple regression model (see table 4), gestational age (p=0.15), maternal age (p=0.45), and current socioeconomic status (p=0.61) were not. Backward and forward selection yielded similar results. After adjusting for height and weight at 5 years, for every 1000 g increase in birth weight, the mean decline in systolic blood pressure was 3.4 mm Hg (95% CI 1.4, 5.3).

Gestational and maternal age were added to the best fit model because of their association with birth weight. In this model, mean systolic blood pressure fell by 2.2 mm Hg (95% CI 0.6, 5.2) for every 1000 g rise in birth weight after adjusting for the other factors. Additionally the role of socioeconomic status in the association between birth weight, current weight, current height, and systolic blood pressure was examined. In this model the p value for socioeconomic status was not significant (p=0.60) and systolic blood pressure fell by 3.0 mm Hg (95% CI 1.0, 5.0) for every 1000 g increase in birth weight after adjusting for the other factors. The interactions of each of weight, height, and birth weight with socioeconomic status were added to the model. This allowed each of the slope parameters of weight, height, and birth weight with systolic blood pressure to vary over the socioeconomic categories. There was no difference (p=0.40) between the models with and without the interaction terms. The multiple regression analyses failed to detect any association between diastolic blood pressure and birth weight.

Table 3 Mean systolic blood pressure by quartiles of birth weight and current weight

	Birth weight (g)			
Current weight (kg)	<2800	2800–3099	3100–3399	>3400
<16.8	106	104	101	99
(n)	(55)	(56)	(27)	(17)
⩾16.8–18.1	107	109	110	103
(n)	(48)	(45)	(36)	(27)
⩾18.1–19.4	108	111	108	104
(n)	(38)	(37)	(42)	(36)
⩾19.4	118	110	112	110
	(18)	(30)	(40)	(82)

Table 4 Significant independent correlates with systolic blood pressure at 5 years from the best fit multiple regression model

	r*	Estimated coefficient	Standard error	p
Weight at 5 years (mm Hg/kg)	0.22	0.75	0.330	0.0228
Birth weight (mm Hg/kg)	−0.05	−3.36	0.99	0.0007
Height at 5 years (mm Hg/cm)	0.24	0.47	0.16	0.0034

r^2=7.4%, p=<0.0001. *Independent correlation between each variable and systolic blood pressure.

Discussion

This study supports numerous previous observations demonstrating an inverse relation between birth weight and systolic but not diastolic blood pressure in children.[11 12 18 22–24] This relation, independent of current weight, current height, gestational age, maternal age, and a crude measure of socioeconomic status has not previously been reported from Southern Africa. The findings from a poor urban setting in Africa add further evidence that blood pressure in childhood is related to factors operating in fetal life and infancy. The mean birth weights in this study were less than American norms but the percentage of low birth weight children of normal gestational age (7.1%) was similar to that of developed countries.[30] Our data contrast with the only other study reported from the African continent in which no association was found between birth weight and blood pressure in rural Gambian children[17] but support a brief report from Nigeria,[31] from an unspecified setting. Although the reason for this difference is unclear, it is tempting to speculate that factors specific to the urban setting, whose influence start in utero, may contribute to the higher prevalence of hypertension in urban, compared with rural, areas.[32 33]

The extent of changes in blood pressure in relation to birth weight observed in this study, although small, were similar to those previously reported in children.[11 12 18 22] Although the contribution of birth weight to the variance in systolic blood pressure of children in this and other studies is small, studies in adults in other settings have found larger differences in blood pressure between those with low and high birth weight, particularly in those with the highest current body mass index.[12 16 34] This tends to support the theory that higher blood pressure is initiated by processes that begin in utero and become amplified in later life.[12 35] Furthermore, should this apply to communities in Southern Africa, the link between birth weight and blood pressure may have important implications for the future prevalence of hypertension.

In this 10 year longitudinal study, in which it was never planned that all participants were to be seen at each time point, the relatively small proportion of the eligible cohort followed up at 5 years could be a source of systematic bias. Indeed the major source of bias in cohort studies is loss to follow up, which is selectively related to exposure and/or outcome. This can create systematic bias and an underestimate or overestimate of the association between exposure and outcome. For example, in our study if normal/higher birth weight babies with higher blood pressure were more likely to die, migrate away or not attend the 5 year examination, this would exaggerate the size of, or create an inverse relation between low birth weight and blood pressure at 5 years. We believe that it is implausible that the relatively small variations in blood pressure reported within the cohort would have any effect on loss to follow up either non-differentially in the whole cohort, or differentially in relation to exposure status (birth weight). The high rate of loss to follow up also could create selection bias if the relation between low birth weight and blood pressure at 5 years differed between those examined at this stage and those not. This possibility cannot be excluded, although we can think of no plausible reason why this should be the case. Finally, the high rate of non-attendance at 5 years may reduce the generalisability of the findings to the whole cohort. However, the lack of significant differences between the attenders and non-attenders in all the baseline characteristics studied, except maternal age, and gravidity (neither of which had any independent association with blood pressure at 5 years of age) suggest that generalising the findings in the cohort is probably justifiable.

The question of how low birth weight induces an increase in blood pressure in children and adults is unanswered. Two hypotheses, not mutually exclusive, are the subject of intense investigation. The one suggests that birth weight may be a proxy for nutrition in utero and that undernutrition during gestation results in long term programming of the cardiovascular and endocrine systems and their responsiveness.[7 8 36] The other suggests that fetal exposure to high glucocorticoid concentrations could affect the development of fetal vasculature, its responses to pressor agents, hypothalamo-pituitary-adrenal axis responsiveness or expression of glucocorticoid receptors.[37–39]

In South Africa, the apparently inexorable increase in hypertension, diabetes, and cerebrovascular disease among the rapidly urbanising population is profoundly worrying. The association of low birth weight and higher blood pressure in this cohort of children—if maintained into adult life—may suggest one possible method of primordial prevention for adult hypertension. However, this conclusion may be premature because of uncertainties about the causal pathway linking low birth weight with raised blood pressure, and possible unforeseen adverse effects to the mother and infant of such interventions.[40] More research is required, including intervention trials, to assess whether efforts to reduce the incidence of low weight infants and improve antenatal care will reduce the prevalence of hypertension among future generations.

KEY POINTS

- The prevalence of hypertension is high in the rapidly urbanising population of South Africa.
- This study showed an inverse association between birth weight and systolic blood pressure in 5 year old urban children from Soweto, South Africa.
- This relation was independent of current size and socioeconomic status, gestational age, and maternal age.
- These findings add to the evidence that influences in foetal life and early childhood influence systolic blood pressure.

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Conflicts of interest: none.

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