Original Contribution

The Association of Birth Weight with Developmental Trends in Blood Pressure from Childhood through Mid-Adulthood

The Bogalusa Heart Study

F. Mzayek1, S. Hassig1, R. Sherwin1, J. Hughes2, W. Chen1,3, S. Srinivasan1,3, and G. Berenson1,3

1 Department of Epidemiology, Tulane University Health Sciences Center School of Public Health and Tropical Medicine, New Orleans, LA.
2 Department of Biostatistics, Tulane University Health Sciences Center School of Public Health and Tropical Medicine, New Orleans, LA.
3 Center for Cardiovascular Health, Tulane University Health Sciences Center School of Public Health and Tropical Medicine, New Orleans, LA.

Received for publication August 17, 2006; accepted for publication February 21, 2007.

Low birth weight has been found to be associated with cardiovascular mortality and morbidity and with an adverse profile of several cardiovascular risk factors. The inverse association between birth weight and blood pressure was consistently reported from many populations. Using longitudinal data from the Bogalusa Heart Study (Louisiana), the authors investigated the association between birth weight and progression of blood pressure through early adulthood, comparing that relation between African Americans and Whites. Birth data of 2,275 participants, screened two or more times in the Bogalusa Heart Study between 1973 and 2001, were retrospectively obtained from birth certificates and were linked to their clinical, laboratory, and socioeconomic and lifestyle data in the Bogalusa Heart Study data sets. Birth weight was inversely associated with systolic blood pressure, diastolic blood pressure, and pulse pressure (∼0.01 for all). For every 1-kg increase in birth weight, systolic blood pressure dropped by 1.9 mmHg (95% confidence interval: −2.6, −1.3), diastolic blood pressure by 0.7 mmHg (95% confidence interval: −1.2, −0.2), and pulse pressure by 1.2 mmHg (95% confidence interval: −1.7, −0.7). The interaction of birth weight with ethnicity was not significant for any outcome. Birth weight was inversely associated with later blood pressure. The strength of that association did not differ between African Americans and Whites.

Abbreviation: BMI, body mass index.

Considerable evidence has accumulated indicating a relation between intrauterine growth retardation and the development of many disorders later in life, namely, increased insulin resistance and type 2 diabetes mellitus, hypertension, and abnormalities in lipid metabolism (1–6) as well as their clinical cardiovascular outcomes: coronary heart disease and stroke (7–9). It has become increasingly evident that intrauterine growth retardation plays an important part in the future physiology and function of many organs and body systems. This notion has become to be known as Barker’s hypothesis of fetal origins of adult disease.

Low birth weight at or near term is the most commonly used surrogate measure of intrauterine growth retardation and has been related to increased cardiovascular mortality, presumably because of its adverse effect on many cardiovascular risk factors acting later in life (8, 10–12). Low birth weight has been found to be associated with elevated systolic and diastolic blood pressures (1–3). Several
mechanisms for this effect have been suggested, including altered function of the hypothalamic–pituitary–adrenal axis (13, 14), increased angiotensin-converting enzyme activity (15), and endothelial dysfunction (16, 17). Pulse pressure is an independent predictor of cardiovascular events, including coronary heart disease, myocardial infarction, and heart failure (18–20). However, only a few studies have investigated the association between birth weight and pulse pressure.

Liu et al. (21), from the Coronary Artery Risk Development in Young Adults (CARDIA) study, found that differences in mean blood pressure and prevalence of hypertension between African Americans and Whites can largely be explained by differences in rates of obesity and lifestyle factors such as alcohol consumption and exercise. However, in a recent report from the Bogalusa Heart Study, ethnic differences in birth weight accounted for the differences in adolescent blood pressure between African Americans and Whites, but the strength of that association was similar in the two groups (22).

Few studies that investigated the association of low birth weight with indicators of cardiovascular risk used longitudinal data, and many lacked adjustment for important confounders (23). In this study, we investigated the association of birth weight with change in blood pressure over time in a biethnic population of the United States, using repeated measurements during long follow-up periods and taking into account the effect of important socioeconomic and lifestyle variables.

MATERIALS AND METHODS

Participants

The Bogalusa Heart Study is a longitudinal study of a semi-rural, biethnic community (65 percent White, 35 percent African American). A detailed description of the demographic characteristics of the community, as well as the overall design of the study, has been published elsewhere (24). Between 1973 and 2001, seven cross-sectional surveys of children aged 5–17 years and seven cross-sectional surveys of young adults aged 18–44 years were conducted, resulting in multiple observations during childhood and young adulthood. Names of 2,780 participants, who were examined two or more times in the Bogalusa Heart Study, were identified for this study, and their birth data were obtained from birth records in the Office of Health Statistics in New Orleans, Louisiana.

Exclusion criteria included congenital heart disease, severe renal disease, type 1 diabetes mellitus, and failing to fast at the time of examination. Participants with type 1 diabetes or with cardiac or renal disease were excluded because of the known effect of these disorders on the outcomes of this study.

Informed consent was obtained from parents during childhood screenings and from participants during adulthood screenings. The study was approved by the institutional review board at Tulane University in New Orleans.

Procedures

Height was measured manually to the nearest 1 mm and weight to the nearest 0.1 kg with a balance-beam scale, both as the mean of two measurements. Blood pressure was recorded by using a cuff size suitable to the arm circumference. The mean of six measurements (two stations with three measurements each), taken in the sitting position after a 5-minute rest, was recorded. Systolic blood pressure was recorded as the first Korotkoff phase. Fifth-phase measurement was used for diastolic blood pressure. Birth weights were obtained from birth certificates to the nearest 0.25 of an ounce and were then converted into kilograms (1 ounce = 28.3 g). The World Health Organization definition for low birth weight, ≤2,500 g, was adopted for this study purpose (25).

Statistical analyses

Data collection and organization. A list of names, birth dates, and unique identification numbers of the 2,780 participants was assembled. Birth certificates of 2,301 of those 2,780 (82.8 percent) participants could be identified thereafter from the Office of Health Statistics, and birth data were entered into the database. Data regarding outcome and independent variables from the 14 files pertaining to the 14 Bogalusa Heart Study screenings between 1973 and 2001 were then linked to the file containing the names, identification numbers, and birth data, keeping the chronological order of the data.

Income was defined as the last self-reported annual income and was classified into four categories: ≤$15,000, $15,001–30,000, $30,001–45,000, and >$45,000. Parent’s education was defined as the highest educational level attained by the father and was categorized into six levels: 1 = grades 1–7, 2 = grades 8–9, 3 = grades 10–12, 4 = technical, 5 = college, and 6 = postgraduate. In case the information for father’s education was missing or the father did not live with the child, the mother’s highest educational level was recorded. Smoking status was defined as the last information available about smoking and was coded into four categories: never/experienced with smoking, former smoker, light current smoker (≤15 cigarettes/day), and heavy current smoker (>15 cigarettes/day). Alcohol consumption was defined as the last information available about drinking and was coded into three categories: none/less than one drink per week, 2–4 drinks per week, and >4 drinks per week. Family history of cardiovascular disease was defined as having a parent who had a heart attack, a stroke, bypass surgery, or an angioplasty or who died of a heart attack or stroke. This variable was coded as 2 if both parents had a history of cardiovascular disease, as 1 if one parent had a history of cardiovascular disease, and as 0 if neither had a history of cardiovascular disease. Available information on the familial and lifestyle variables ranged from 70 percent for income to 99 percent for smoking status. Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m²). Pulse pressure was calculated as the difference between systolic blood pressure and diastolic blood pressure. Prematurity was defined as gestational age less than 37 weeks (25).

Data analysis. In this paper, data are presented as mean (standard deviation). Differences between groups’ means were assessed by using the t test or analysis of variance,
as indicated. Associations between categorical variables were assessed by Pearson’s chi-square test. The multivariate associations between birth weight and study outcomes were assessed by using generalized linear model mixed-models analysis.

Mixed models test fixed and random effects and allow good flexibility in modeling the variance-covariance structure, thereby accounting for the variation in the outcome due to individual differences among the volunteers and for the heterogeneity of variance among the repeated measurements (26). A separate model was constructed for each outcome. Birth weight, gender, ethnicity, age, BMI, parent’s education, income, smoking, alcohol consumption, and family history of cardiovascular disease were entered in the models as fixed main effects. Identification number was included as a random effect to model variations in the outcome due to individual differences between the study participants. Birth weight was entered as a continuous variable. Age and BMI were entered in models as time-variant variables to adjust for their effect as they changed over time.

To investigate whether ethnicity modifies the association between birth weight and blood pressure, the interaction of birth weight with ethnicity (birth weight × ethnicity) was tested in all models. The interaction of birth weight with BMI (birth weight × BMI) was also included in the models to investigate whether BMI modifies the association of birth weight with later blood pressure. Different variance-covariance structures for residuals were tested. First-order autoregressive variance-covariance structure provided the best fit as indicated by Akaike’s Information Criterion; therefore, it was adopted in all analyses. Linear, quadratic, cubic, and exponential \( \log (y) = \log (a) + bx \) models were fitted to the data to explore the association between birth weight and blood pressure, but they essentially produced the same result \( (R^2) \). Therefore, the simple linear model was used. All analyses were repeated with and without adjusting for current BMI, and with and without including those who were born preterm. Multivariate methods exclude cases missing values on independent variables; because the same set of independent variables was included in all models, all multivariate analyses were based on 1,549 subjects for whom information was complete. Two-tailed tests were used in all analyses, with a significance level of \( p < 0.05 \). All analyses were conducted by using the SPSS version 11.0 statistical package (SPSS, Inc., Chicago, Illinois).

### RESULTS

Participants in this study had an average of 5.5 screenings per person (a total of 12,440 observations). Of the 2,301 birth certificates that have been identified, 2,275 (98.9 percent) included data on birth weight and 2,173 (94.4 percent) had data on gestational age. Of the 2,275 participants for whom birth weights were available, four were excluded because they had congenital heart disease, six for having type 1 diabetes mellitus, and three for not fasting. The study sample was 63.4 percent White and 36.6 percent African American, which reflects the ethnic composition of the community (27). On average, White males were about 400 g heavier at birth than African-American males, and White females were approximately 300 g heavier than African-American females \( (p < 0.01 \text{ for both}) \). The prevalences of low birth weight \( (<2,500 \text{ g}) \) and premature birth \( (<37 \text{ weeks}) \) in the study population were 8.6 percent and 5.6 percent, respectively. The prevalence of low birth weight was 2.6 times higher among African Americans than among Whites. Premature birth was also more prevalent among African Americans. Table 1 shows the composition of the study population and the distribution of birth characteristics by gender and ethnicity.

Table 2 illustrates the results of the multivariate analyses. Birth weight was inversely associated with systolic blood pressure, diastolic blood pressure, and pulse pressure \( (p \leq 0.01) \). Age, gender, and BMI were independent predictors for all study outcomes. Age was positively associated with systolic and diastolic blood pressures but was inversely associated with pulse pressure \( (p < 0.01 \text{ for all}) \). BMI was

<table>
<thead>
<tr>
<th>Ethnicity and gender</th>
<th>No.</th>
<th>%*</th>
<th>Birth weight (kg)†</th>
<th>Low birth weight‡</th>
<th>Premature§</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>660</td>
<td>29.2</td>
<td>3.44 (0.57)</td>
<td>29</td>
<td>4.4</td>
</tr>
<tr>
<td>Female</td>
<td>775</td>
<td>34.2</td>
<td>3.32 (0.54)</td>
<td>49</td>
<td>6.3</td>
</tr>
<tr>
<td>Total</td>
<td>1,435</td>
<td>63.4</td>
<td>3.38 (0.55)</td>
<td>78</td>
<td>5.4</td>
</tr>
<tr>
<td>African American</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>362</td>
<td>16.0</td>
<td>3.08 (0.61)</td>
<td>51</td>
<td>14.1</td>
</tr>
<tr>
<td>Female</td>
<td>465</td>
<td>20.6</td>
<td>3.02 (0.53)</td>
<td>66</td>
<td>14.2</td>
</tr>
<tr>
<td>Total</td>
<td>827</td>
<td>36.6</td>
<td>3.05 (0.56)</td>
<td>117</td>
<td>14.2</td>
</tr>
</tbody>
</table>

* Percentage of the grand total.
† Values are expressed as mean (standard deviation).
‡ Low birth weight \(<2,500 \text{ g})\.
§ Gestational age \(<37 \text{ weeks})\.

<table>
<thead>
<tr>
<th>Outcome and predictor</th>
<th>Regression coefficient</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg), $n = 1,549$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>−1.9</td>
<td>−2.6, −1.3**</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.2</td>
<td>0.1, 0.2**</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.8</td>
<td>0.7, 0.8**</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>−1.2</td>
<td>−2.1, −0.3*</td>
</tr>
<tr>
<td>African American†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3.8</td>
<td>3.0, 4.5**</td>
</tr>
<tr>
<td>Female†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parents’ history of cardiovascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No history of cardiovascular disease</td>
<td>−1.8</td>
<td>−3.0, −0.5**</td>
</tr>
<tr>
<td>1 parent with a history of cardiovascular disease</td>
<td>−1.1</td>
<td>−2.4, 0.2</td>
</tr>
<tr>
<td>2 parents with a history of cardiovascular disease†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None–&lt;1 drink/week</td>
<td>−3.4</td>
<td>−5.1, −1.7**</td>
</tr>
<tr>
<td>2–4 drinks/week</td>
<td>−2.9</td>
<td>−4.9, −0.9**</td>
</tr>
<tr>
<td>&gt;4 drinks/week†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg), $n = 1,549$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>−0.7</td>
<td>−1.2, −0.2*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.4</td>
<td>0.3, 0.4**</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.5</td>
<td>0.4, 0.5**</td>
</tr>
</tbody>
</table>

Table continues

positively associated with all study outcomes ($p < 0.01$ for all). Compared with females, males had higher systolic blood pressure, diastolic blood pressure, and pulse pressure ($p < 0.01$ for all). Nonsmokers had higher diastolic blood pressure and lower pulse pressure compared with heavy smokers ($p < 0.05$). Individuals who did not drink, or drank rarely, had lower systolic and pulse pressures than those of daily drinkers ($p < 0.01$). Family history of cardiovascular disease was associated with systolic blood pressure ($p = 0.02$) and was borderline significant for diastolic blood pressure ($p = 0.08$). Persons for whom both parents had a history of cardiovascular disease had higher systolic and diastolic blood pressures than those with no family history of cardiovascular disease. Ethnicity was associated with systolic blood pressure only, with Whites having a lower blood pressure than African Americans ($p < 0.05$). Parental education and income were not associated with any outcome. The interaction of birth weight with BMI was negative for all three outcomes but was significant for systolic blood pressure only. Figure 1 illustrates this interaction; the relation between birth weight and later systolic blood pressure (at age ≥35 years) was depicted within each tertile of adult BMI.

When data were analyzed without adjustment for later BMI, birth weight was still associated with systolic blood pressure and pulse pressure. The association was weaker for systolic blood pressure ($\beta = −1.2$ mmHg), however.

When data were reanalyzed after excluding persons born prematurely ($n = 120$), the results remained essentially the same (data not shown). In this group, however, the interaction of birth weight with BMI was significantly associated with both systolic blood pressure and pulse pressure. Data for persons of very low birth weight (< 2,200 g, $n = 65$) were also analyzed. In this group, the association of birth weight was stronger for systolic blood pressure ($\beta = −4.3$ mmHg, 95 percent confidence interval: $−8.5, −0.1$) and pulse pressure ($\beta = −3.5$ mmHg, 95 percent confidence interval: $−6.9, −0.2$) but was not significant for diastolic blood pressure ($\beta = −0.7$ mmHg, 95 percent confidence interval: $−4.2, 2.9$). Because some papers reported a U- or J-shaped relation between birth weight and cardiovascular

Am J Epidemiol 2007;166:413–420
The inverse association between intrauterine growth retardation (measured by birth weight) and blood pressure has been reported in children (29–31) and adults (1, 32, 33). It has also been consistently reported in different populations (34–38). Our results are concordant with those of most other studies, both in their direction and magnitude. In general, it has been found that mean systolic blood pressure decreased approximately 2–3 mmHg and diastolic blood pressure decreased 0.6–1.2 mmHg for every 1-kg increase in birth weight (34, 35, 39). This finding is similar to that in this study of −1.9 mmHg (95 percent confidence interval: −2.6, −1.3) and −0.7 mmHg (95 percent confidence interval: −1.2, −0.2) reductions in systolic and diastolic blood pressures, respectively, for every 1-kg increase in birth weight. Particularly, the results of this study agree with the findings of three recent large studies that have features similar to this one: a large sample size and a long follow-up period with repeated measurements of health indicators (34–36).

These findings disagree, however, with those from some other studies that did not find a relation between birth weight and later blood pressure (40, 41). A recent meta-analysis concluded that impaired fetal growth effects on blood pressure are weak at best and unlikely to have an important impact on cardiovascular health (23, 42). Those reports, and others, have questioned the appropriateness of controlling for later body mass and the lack of adjustment for important confounders, such as socioeconomic status and lifestyle variables (23, 42, 43).

The finding in this study that persons of low birth weight had higher pulse pressure sheds more light on possible mechanisms mediating the association between birth weight and increased cardiovascular mortality and morbidity. In particular, brachial pulse pressure has been shown to be a stronger risk factor than systolic blood pressure for coronary heart disease events (44, 45). This effect may be mediated by the positive association between birth weight and endothelial function reported by Leeson et al. (16, 17) in both children and adults, because endothelial dysfunction is also associated with increased arterial stiffness (46) and arterial stiffness is one major determinant of pulse pressure (47).

That adjustment for later body mass strengthens the association between birth weight and cardiovascular risk variables suggests that it is a negative confounder; therefore, the adjustment for later size not only provides more correct estimates of birth weight coefficients but also allows for exploring the existence of other pathways that might explain the association between birth weight and cardiovascular disease risk, as demonstrated by Gillman (48). On the other hand, if later size is considered a mediating variable on the causal pathway between birth weight and adult cardiovascular risk, then adjusting for it would be inappropriate, and it would be expected to weaken—or remove—the effect of birth weight, not to strengthen it. Recently, two large studies found no evidence that the effect of birth weight on blood pressure was mediated (or confounded) by childhood BMI or height (35, 36). However, it cannot be totally ruled out that later size may mediate at least part of the association of birth weight with blood pressure. Therefore, the “true value of the effect of birthweight may lie somewhere between the two models” (49, p. 159).
In this study, we controlled for several important factors. Because of the long follow-up period of this study, parental educational level and participant’s annual income were included in the analysis as indicators of childhood and adulthood socioeconomic status. To our knowledge, only two other studies have adjusted for socioeconomic status in both childhood and adulthood (8, 50). Both variables, however, had little impact on the relation between birth weight and adult blood pressure. The minimal influence of the socioeconomic and lifestyle variables on the association of birth weight with cardiovascular risk factors is in accord with findings from other studies, which found little or no effect of adjusting for socioeconomic factors on the relation between birth weight and coronary heart disease (35, 50). The reason why former smokers had higher diastolic blood pressure than heavy smokers did might be because smokers generally weigh less than nonsmokers, an argument supported by the fact that the BMI of nonsmokers and former smokers in this study was 30.3 vs. 28.1 in smokers (p < 0.01). A similar observation was found in another large study (35).

Few studies have examined the differential association of birth weight with cardiovascular risk factors between African Americans and Whites (51, 52). There was no interaction between birth weight and ethnicity for the study outcomes. This result agrees with previous reports from the Bogalusa Heart Study that found little or no ethnic differences in the association between birth weight and cardiovascular risk factors in younger age groups (51). However, it contrasts with a previous report from the Bogalusa Heart Study, which found a significant interaction between birth weight and ethnicity for systolic blood pressure in a younger age group (52). The reason for the discrepancy is perhaps due to the cross-sectional design of the previous study and the lack of adjustment for important factors, especially family history and smoking. In all, the evidence supporting the effect of ethnicity on the association between birth weight and coronary heart disease (35, 50). The lack of adjustment for important factors, especially family history and smoking. In all, the evidence supporting the effect of ethnicity on the association between birth weight and coronary heart disease (35, 50).

In this study, we controlled for several important factors. Because of the long follow-up period of this study, parental educational level and participant’s annual income were included in the analysis as indicators of childhood and adulthood socioeconomic status. To our knowledge, only two other studies have adjusted for socioeconomic status in both childhood and adulthood (8, 50). Both variables, however, had little impact on the relation between birth weight and adult blood pressure. The minimal influence of the socioeconomic and lifestyle variables on the association of birth weight with cardiovascular risk factors is in accord with findings from other studies, which found little or no effect of adjusting for socioeconomic factors on the relation between birth weight and coronary heart disease (35, 50). The reason why former smokers had higher diastolic blood pressure than heavy smokers did might be because smokers generally weigh less than nonsmokers, an argument supported by the fact that the BMI of nonsmokers and former smokers in this study was 30.3 vs. 28.1 in smokers (p < 0.01). A similar observation was found in another large study (35).

Few studies have examined the differential association of birth weight with cardiovascular risk factors between African Americans and Whites (51, 52). There was no interaction between birth weight and ethnicity for the study outcomes. This result agrees with previous reports from the Bogalusa Heart Study that found little or no ethnic differences in the association between birth weight and cardiovascular risk factors in younger age groups (51). However, it contrasts with a previous report from the Bogalusa Heart Study, which found a significant interaction between birth weight and ethnicity for systolic blood pressure in a younger age group (52). The reason for the discrepancy is perhaps due to the cross-sectional design of the previous study and the lack of adjustment for important factors, especially family history and smoking. In all, the evidence supporting the effect of ethnicity on the association between birth weight and coronary heart disease (35, 50). The lack of adjustment for important factors, especially family history and smoking. In all, the evidence supporting the effect of ethnicity on the association between birth weight and coronary heart disease (35, 50).

In conclusion, this study adds more evidence to the role of intrauterine growth retardation in predicting cardiovascular risk factors in adulthood. Size at birth appears to predict later cardiovascular risk, independent of familial and other lifestyle factors operating later in life. This finding is especially true for systolic blood pressure. However, the evidence also suggests that later health indicators, such as BMI, appear to modify the effect of birth weight on adult blood pressure (figure 1).

ACKNOWLEDGMENTS

This study was supported by AHA predoctoral fellowship 0315042B from the American Heart Association.
Conflict of interest: none declared.

REFERENCES


