Ambulatory Blood Pressure in 12-Year-Old Children Born Small for Gestational Age

Eero Rahiala, Sirpa Tenhola, Esko Vanninen, Eila Herrgård, Tero Tikanoja, Anneli Martikainen

Abstract—An association between low birth weight and subsequent elevated blood pressure has been demonstrated in a large number of studies, but the number of subjects born small for gestational age in these studies has been negligible. The inverse relationship between birth weight and blood pressure in children has been evaluated previously with an ambulatory blood pressure device, but only in children with normal birth weights. In this prospective case-control study from birth to the age of 12, we evaluated the ambulatory blood pressures in 50 children born at term but small for gestational age and in 50 full-term children born appropriate for gestational age. Children born small for gestational age had similar mean ± SD systolic (117.5 ± 8.5 mm Hg versus 115.3 ± 7.4 mm Hg, P = 0.221), and diastolic (69.2 ± 5.3 mm Hg versus 67.3 ± 4.4 mm Hg, P = 0.075) 24-hour ambulatory blood pressure compared with the values of the children born appropriate for gestational age. However, 24-hour systolic blood pressure in the small-for-gestational-age children was higher (3.90 mm Hg; 95% confidence interval, 0.65 to 7.15) after adjusting for current body mass index. The difference in current body mass index was the only determinant for the difference in systolic blood pressure between the groups. Birth weight had no direct association with the blood pressure values. Impaired fetal growth may have a relationship with higher later blood pressure, but in 12-year-old children, blood pressure differences between small for gestational age and appropriate for gestational age children are much more dependent on current body size. (Hypertension. 2002;39:909-913.)

Key Words: blood pressure monitoring, ambulatory ▪ children ▪ body mass index

In recent years, the effect of intrauterine environment on future blood pressure (BP) has gained increasing interest.1 An inverse relationship between birth weight and BP in adults and in children has been shown in a large number of studies.2–5 In most of the cohort studies in adults, however, the information on perinatal data has been incomplete. The adult subjects were born in the early decades of the 20th century, and as the birth weight information is based on historical records, investigators have not been able to differentiate low birth weight from actual intrauterine growth retardation. If reported, the number of children born at term but small for gestational age (SGA) in most studies has been negligible.6,7

In a recent study, the investigators concluded that it is the variation in fetal growth rate rather than small size at birth that influences the cardiovascular mortality.8 The same investigators reported that men born at term showed a stronger relationship between birth weight and BP than did the study population as a whole.9 The investigators proposed that among full-term babies, birth weight most directly reflects underlying processes of fetal growth impairment. When systolic BP in adolescents born at term, but with birth weights <2.5 kg was compared with BP in adolescents with normal birth weights, however, no difference in the BP values was found.10

Values obtained with ambulatory BP (ABP) monitoring are considered to be more indicative of cardiovascular risk than casual blood pressure (CBP) measurements.11 ABP monitoring has also been shown to be reliable in pediatric populations.12–14 When the association between birth weight and BP in children was evaluated with an ABP device in children age 6 to 16 years, born at term with birth weights >2.5 kg, no significant relationship between birth weight and ABP could be shown.15

We conducted this study to examine the relationship between impaired fetal growth and BP in 12-year-old Finnish children. The aim of this prospective case-control study was to evaluate if children born at term but with SGA have higher ABP values than their gender- and age-matched control children born at term and appropriate for gestational age (AGA).

Methods

All the children were born in Kuopio University Hospital between April 1, 1984 and March 31, 1986.16 Out of 3790 live births, all the 70 nonmalformed singleton children born at term with intrauterine growth retardation were included as cases (SGA).17 With a 30% drop-out and one child being over age, the final number of SGA children studied was 50. Eight of the SGA children were born to mothers with hypertension during pregnancy (16%), corresponding
to that in general population in Eastern Finland (15%). The next AGA child of same gender and born at term was selected as the control subject for every SGA child.

Anthropometric and BP data for all mothers was collected from hospital, and antenatal clinic records and all perinatal characteristics were collected from hospital records. Physical examination was done by one of two of the study investigators (E.R., S.T.). The pubertal status was defined according to Tanner scale. Two study nurses measured height and weight to the nearest 0.1 cm and 0.1 kg, respectively.

The ABP measurements were performed with an oscillometric ABP device (Spacelabs 90207, Spacelabs Inc). The monitor was placed in the nondominant arm of the child. The monitor measured BP in 15-minute intervals during the daytime (7:00 AM to 10:00 PM) and in 30-minute intervals during the nighttime (10:00 PM to 7:00 AM). The daytime/nighttime periods were adjusted according to the diaries kept by the children. The total number of readings at each ABP monitoring session was 85 ± 5 in the SGA group and 84 ± 5 in the AGA group (96% and 95%, respectively).

Results

The SGA children were, on the average, 0.975 kg lighter and 4.5 cm shorter at birth than were the AGA children. The clinical characteristics of the SGA and the AGA children at birth and the maternal height, weight, and BP during pregnancy in both groups are presented in Table 1. The age of 12, the SGA children were lighter and shorter than the AGA children (Table 2). Birth weight correlated with current height (r = 0.331, P = 0.019) in the AGA children; otherwise no univariate correlations between birth weight and current body size or BP values were found. The girls were more advanced in puberty than were the boys, but no difference in pubertal stages between the SGA and AGA children could be shown, in either boys or girls.

Ambulatory BP

We found no differences in ABP values between the groups, although all mean values were slightly higher in the SGA children. There was a trend for higher diastolic ABP values in the SGA children than in the AGA children (P = 0.075). The means of systolic and diastolic ABP for 24-hour, daytime, and nighttime for the SGA and AGA groups are shown in Table 2. All daytime ABP means were higher than nighttime ABP means, reflecting circadian rhythmicity. The differences between daytime and nighttime values were similar in the

Statistical Analysis

Pearson’s correlation coefficient was used to test the correlation between the BP values and other parameters within each group. McNemar’s test was used to test the pubertal differences. Paired t test was used to test the difference in the BP values between SGA and AGA children. Multiple linear regression analysis was used to test the explanation strength of different variables on BP values. We also subtracted the BPs as well as neonatal, anthropometric, and maternal variables of the SGA children from those of the AGA children. These intrapair values were then tested in multiple linear regression analysis to find predictors for the BP difference between the groups. Statistical analyses were performed with SPSS-PC 9.0 program, (SPSS Inc).

An expanded Methods section can be found in an online data supplement available at http://www.hypertensionaha.org.

TABLE 1. Perinatal Data and Maternal Anthropometric and BP Data During Pregnancy in SGA and AGA Children

<table>
<thead>
<tr>
<th>Variables</th>
<th>SGA (n=50)</th>
<th>AGA (n=50)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks</td>
<td>39.0 (1.4)</td>
<td>39.7 (1.4)</td>
<td>0.006</td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>2.499 (0.251)</td>
<td>3.474 (0.472)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Girls</td>
<td>2.459 (0.215)</td>
<td>3.380 (0.481)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Boys</td>
<td>2.559 (0.292)</td>
<td>3.615 (0.434)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth length, cm</td>
<td>46.4 (2.0)</td>
<td>50.5 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Girls</td>
<td>46.1 (1.6)</td>
<td>49.9 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Boys</td>
<td>46.8 (2.5)</td>
<td>51.3 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ponderal index (kg/m2×100)</td>
<td>2.51 (0.23)</td>
<td>2.69 (0.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Girls</td>
<td>2.51 (0.19)</td>
<td>2.71 (0.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Boys</td>
<td>2.51 (0.28)</td>
<td>2.67 (0.20)</td>
<td>0.056</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>69.1 (12.0)</td>
<td>76.1 (12.4)</td>
<td>0.029</td>
</tr>
<tr>
<td>Maternal weight, kg</td>
<td>62.4 (11.6)</td>
<td>67.2 (11.9)</td>
<td>0.141</td>
</tr>
<tr>
<td>Maternal height, cm</td>
<td>161.9 (5.4)</td>
<td>165.5 (5.9)</td>
<td>0.008</td>
</tr>
<tr>
<td>Maternal systolic BP, mm Hg</td>
<td>131.6 (20.1)</td>
<td>128.0 (11.8)</td>
<td>0.246</td>
</tr>
<tr>
<td>Maternal diastolic BP, mm Hg</td>
<td>85.9 (12.6)</td>
<td>83.5 (7.3)</td>
<td>0.256</td>
</tr>
</tbody>
</table>

All presented values are mean (SD).
*P = t-test for paired samples.
† = McNemar’s test.

TABLE 2. Clinical Characteristics and BP in SGA and AGA Children at the Age of 12

<table>
<thead>
<tr>
<th>Variables</th>
<th>SGA (n=50)</th>
<th>AGA (n=50)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>39.4 (7.9)</td>
<td>48.9 (13.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height, cm</td>
<td>149.7 (6.7)</td>
<td>156.1 (7.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>17.5 (2.9)</td>
<td>19.8 (4.4)</td>
<td>0.005</td>
</tr>
<tr>
<td>Prepubertal or early pubertal stage</td>
<td>26 (52)</td>
<td>24 (48)</td>
<td>NS†</td>
</tr>
<tr>
<td>Late pubertal stage</td>
<td>24 (48)</td>
<td>26 (52)</td>
<td>NS†</td>
</tr>
<tr>
<td>ABP, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-Hour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>117.5 (8.5)</td>
<td>115.3 (7.4)</td>
<td>0.221</td>
</tr>
<tr>
<td>Diastolic</td>
<td>69.2 (5.3)</td>
<td>67.3 (4.4)</td>
<td>0.075</td>
</tr>
<tr>
<td>Daytime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>120.4 (9.0)</td>
<td>118.1 (7.9)</td>
<td>0.219</td>
</tr>
<tr>
<td>Diastolic</td>
<td>72.2 (6.1)</td>
<td>70.1 (4.8)</td>
<td>0.065</td>
</tr>
<tr>
<td>Nighttime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>106.4 (8.3)</td>
<td>105.0 (6.9)</td>
<td>0.383</td>
</tr>
<tr>
<td>Diastolic</td>
<td>58.1 (4.9)</td>
<td>56.6 (5.0)</td>
<td>0.162</td>
</tr>
<tr>
<td>CBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>114.0 (9.9)</td>
<td>112.7 (9.4)</td>
<td>0.487</td>
</tr>
<tr>
<td>Diastolic</td>
<td>73.2 (7.6)</td>
<td>71.9 (6.0)</td>
<td>0.382</td>
</tr>
</tbody>
</table>

All presented value are mean (SD), except the pubertal stage, which represents number of children (%).
*P = t-test for paired samples.
† = McNemar’s test.
groups. After the systolic ABP values were adjusted for current body mass index (BMI), 24-hour and daytime systolic ABPs were higher in the SGA children than in the AGA children (Table 3). Differences between diastolic ABP values were not significant, even after adjustment for current body size.

**Association of Birth Weight, Anthropometric Parameters, and Maternal Data With ABP**

We found no significant univariate correlation between ABP values and birth weight in either the SGA or the AGA children. A weak correlation between current maternal systolic BP and systolic ABP in the AGA children was found ($r=0.301, P=0.047$). Maternal height correlated with systolic ABP ($r=0.298, P=0.044$) and systolic CBP ($r=0.305, P=0.040$) in the AGA children. No correlation between maternal BP during pregnancy, current maternal BP, or maternal anthropometric parameters and the BP values in the SGA children was found.

We applied multiple linear regression analysis to assess the impact of other variables on systolic ABP at the age of 12. The variables included were current weight, height, and BMI, birth length, birth weight, ponderal index, gestational age, maternal systolic and diastolic BP during pregnancy, current maternal systolic BP, and maternal height. No association was found between diastolic ABP and the variables tested. Birth weight had no significant association with systolic ABP values, in the SGA children or in the AGA children. Current BMI was the strongest determinant for systolic ABP values in both the SGA (systolic ABP = 99.8 + 1.122 × BMI, $t=2.85$, $P=0.006$) and the AGA children (systolic ABP = 99.6 + 0.795 × BMI, $t=3.65$, $P=0.001$). This relationship is shown in Figure 1.

We also subtracted the ABPs as well as neonatal, anthropometric, and maternal variables of the SGA children from those of the AGA children. These intrapair values were then tested in multiple linear regression analysis to find out predictors for the ABP difference between the groups. When the 24-hour systolic ABP difference between the groups was analyzed with the differences in other variables, the difference in current BMI was the strongest determinant for systolic ABP difference between the AGA and the SGA children (difference in 24-hour systolic ABP = $-4.001 + 0.799 \times \text{difference in BMI}$, $t=-3.62, P=0.012$). The relationship suggests that only if the current BMI in the AGA child was considerably higher than in the SGA child, the systolic ABP in the AGA child was also higher. The more negative the difference in BMI between an AGA and a SGA child, the greater the difference in systolic ABP within the AGA-SGA pair, SGA child having the higher systolic ABP (Figure 2).

**Casual BP**

At birth, the SGA children had lower systolic CBP than did the AGA children. The systolic and the diastolic CBP at the age of 12 were similar in the SGA and AGA children (Table 2), but after adjustment for current BMI, the mean systolic CBP was higher in the SGA children than in the AGA children (Table 3). Current BMI correlated with both systolic and diastolic CBP in the SGA ($r=0.381, P=0.006$ for systolic BP and $r=0.362, P=0.010$ for diastolic BP) and AGA children ($r=0.673, P<0.001$ for systolic and $r=0.584, P<0.001$ for diastolic). In linear multivariate regression analysis, the only determinant for systolic CBP in both the SGA and the AGA children was current body size. No association between diastolic CBP and the variables tested was found.

**Discussion**

In present study, we show that 12-year-old children born full-term but with SGA and their age- and gender-matched control children born with AGA have almost equal ABP values. There was a trend to higher diastolic ABP values in

![Figure 1](https://hyper.ahajournals.org/)

**Figure 1.** The mean systolic ABP values of the SGA and AGA children in relation to their BMI. The lines represent linear regression within the groups.
the SGA children than in the AGA children. In this study population, however, the SGA children were still considerably smaller than the AGA children at the age of 12. Current body size was the strongest predictor of systolic ABP in both the SGA and AGA groups, and after adjusting systolic ABP for current body size, the SGA children had higher systolic ABP than did the AGA children. No suitable regression model for diastolic ABP was found.

The difference in current BMI between the groups was the strongest predictor for the systolic ABP difference between the SGA and the AGA children. We found an intrapair relationship between the difference in current BMI and the difference in systolic ABP. If the AGA control had lower BMI than did the SGA child, the systolic ABP was considerably higher in the SGA child. The closer the BMI in the AGA was to the BMI in the SGA child, the smaller was the difference in systolic ABP. Birth weight had no independent impact on ABP, in either the SGA or the AGA children. Thus, it seems that low birth weight is not the major factor in predicting BP later in childhood, but our results suggest that at least in 12-year-old children, postnatal environment may be a more important determinant of systolic BP than adverse intrauterine environment, though the latter may be an additive risk factor.

As Jern and coworkers have indicated, it seems that impaired fetal growth may lead to substantial increase in adult BP only among those individuals who become obese. The relationship between birth weight and BP has been also shown to be dependent on BMI in children. In a study from the Netherlands, low birth weight in combination with high current BMI seemed to be of particular importance in the development of high BP. In the only previous study, in which the BPs of subjects with or without impaired intrauterine growth have been compared, no difference in systolic BPs between the groups of 15-year-old children was found. Our raw BP data are in agreement with these findings, and only after adjustment for current body size, could systolic BP differences between our study groups be shown.

Both BP and birth weight are influenced by hereditary factors, so there may be a familial association between low birth weight and hypertension that does not depend on intrauterine “programming” of BP. In a study by Walker and coworkers on the relationship between parental hypertension and low birth weight and subsequent raised BP in childhood, it seemed likely that these hereditary factors explain at least a part of the inverse relation between low birth weight and elevated BP. Our regression models explained only a minor part of the systolic BP values in the SGA and AGA children. Thus hereditary factors may have a more important role than birth weight in predicting BP later in life.

In a Swedish study, the investigators proposed that the babies who fail to use their growth potential in utero, but became tall as adults, are at risk for future hypertension. As the SGA children in our study were smaller than the AGA children at the age of 12, one could speculate that if the SGA and the AGA children reach equal body size as adults, the BP values in the SGA children will be considerably higher. After the age of 12, however, significant catch-up growth seldom happens. One may assume the SGA children in our study will also be smaller adults than their AGA controls. The mothers of the AGA children were taller than the mothers of the SGA children, which also gave a possible genetic explanation for the difference in body size at the age of 12.

We wanted to rule out the possible effect of prematurity on later BP by choosing only full-term SGA and AGA babies for this study, but we did not match our SGA and AGA children (all full-term) for gestational age. Because gestational weeks of the SGA children were significantly lower than those of the AGA children, we included gestational age in the multiple linear regression models. The results did not change when gestational age was used as a covariate in the analysis, and this variable was not significant.

The common definitions of SGA are birth weight or height <10th or 3rd percentile for gestational age, birth weight, or height <2 SD below the mean value for gestational age, birth weight <2.5 kg, and gestational age ≥37 weeks. Although we have used the strictest (≤2 SD) definition of SGA, there may be some children in the SGA group who are genetically small at birth and have not really suffered from adverse intrauterine environment.

As there was no difference in neonatal data between the SGA and the SGA drop-out children, we believe the study material represents the average SGA population born at term in eastern Finland. The birth data of the AGA group was very close to the means of Finnish reference curves from 1980s, and as the casual BP values at the age of 12 were comparable with recent Finnish reference values, the group should present the average children born with normal birth weights to normotensive mothers in the area of Kuopio University Hospital.

In conclusion, we found that 12-year-old SGA children had higher systolic BP than did their AGA controls after systolic BP was adjusted to current body size. Current BMI was the main predictor of systolic BP in both SGA and AGA children.
References


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