Growth of Infants and Young Children Born Small or Large for Gestational Age

Findings From the Third National Health and Nutrition Examination Survey

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Objectives: To compare the growth profiles of infants and young children born small for gestational age (SGA, <10th percentile birth weight for gestation) or large for gestational age (LGA, ≥90th percentile) with those appropriate for gestational age, and to document the expected growth patterns through early childhood based on national health examination survey data.

Sample: Infants and children, 2 to 47 months of age, who were born in the United States and examined using the Third National Health and Nutrition Examination Survey (1988-1994).

Main Outcome Measures: Measurements of growth status based on normalized distributions (z scores or standard deviation units [SDUs] for weight, length, and head circumference.

Results: Prevalence rates were as follows: SGA infants, 8.6%; appropriate for gestational age infants, 80.9%; and LGA infants, 10.5%. Infants who were SGA appeared to catch up in weight in the first 6 months, but thereafter maintained a deficit of about −0.75 SDUs compared with infants who were appropriate for gestational age. The weight status of LGA infants remained at about +0.50 SDUs through 47 months of age. Length and head circumference were also associated with birth weight status, averaging over −0.60 SDUs for SGA infants and +0.43 SDUs for LGA infants.

Conclusions: Birth weight status is related to growth rates in infancy and early childhood, which underscores the importance of considering child growth relative to birth status when using growth charts. Small for gestational age infants remain shorter and lighter and have smaller head circumferences, while LGA infants grow longer and heavier and have larger head circumferences.

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Editor’s Note: With the revision of US growth charts almost completed, this study is timely in that it points out the importance of the first point on the chart.

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Infants who are born growth restricted or small, based on low birth weight for gestational age status, generally show some compensatory growth (catch-up) in the first year, although most catch-up occurs in the first 6 months. The growth of large for gestational age (LGA) infants is thought to slow down in infancy. However, in both of these extreme cases, after an initial period of growth compensation, the growth deficit or surplus is expected to persist. The tendency of birth weight to determine growth status throughout childhood has been demonstrated in several studies of large groups in the United States but the extent to which early growth is associated with fetal growth adjusted for length of gestation has not been shown for an ethnically diverse sample of infants and young children born in the United States. There has been more interest in this relationship in recent years because of new techniques in prenatal diagnosis and neonatal care that allow the survival of infants at the extremes of the spectrum in birth weight. The early growth of infants born at the extremes of birth weight may be best evaluated by considering their birth status.

The Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994), a nationally representative, cross-sectional health examination survey, anthropometrically measured a sample of infants and children from the United States 2 months of age and older. This study produced the largest national data set available on infant and child size for subjects between the ages of 2 and 47 months. The objective of these analyses...
PATIENTS AND METHODS

DESIGN AND SAMPLE

The measurements on infants and children were obtained from NHANES III, conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention (NCHS/CDC), Bethesda, Md, from 1988-1994. The NHANES III included approximately 40,000 people, aged 2 months and older, who were representative of the US civilian, noninstitutionalized population. The analyses reported herein focus on non-Hispanic white, non-Hispanic black, and Mexican American infants and young children ranging in age from 2.0 to 47.99 months. The anthropometric measurements available at ages 2 to 47 months are the largest nationally representative data set available on growth status, including weight, recumbent length, and head circumference. As part of the stratified, multistage probability design of NHANES III, infants and children aged 2 to 71 months were oversampled. Blacks and Mexican Americans were also oversampled to allow adequate sample sizes to support separate estimates; each comprised roughly 30% of the sample.

BIRTH CERTIFICATES

Birth certificates were sought for the US-born infants and young children born in the United States after informed consent was obtained from the parents or guardians. The birth certificate number was then linked to the demographic and medical information from the certificates stored electronically by birth year (national natality files) for the years 1985-1994 at NCHS/CDC.

There were 5566 infants and children at these ages who were examined and measured, either in the mobile examination centers or (for a few infants) in their homes. Of this number, 137 infants were foreign-born, and for these no birth certificates were sought or obtained. Birth certificates were obtained and positively matched for 5129 (94.5%) of the US-born infants and young children. Information common to the birth certificates and NHANES III (child's sex, race/ethnicity, and mother's age) was compared, and discrepancies were resolved whenever possible. Excluded from further analysis at this point were 4 cases with missing birth weights, 1 case of sex discrepancy between the certificate and NHANES III, and 118 children who were twins or triplets. On the national natality files, the standard measure of length of gestation is that calculated in completed weeks from the mother's last menstrual period (LMP). On the birth certificates, length of gestation from the LMP was examined for completeness and validity, and cases with missing or invalid gestation from the LMP were excluded from further analysis (n = 280). Length of gestation from the LMP was missing for 113 cases (2.3%). Length of gestation was considered valid if it was between 20 and 44 weeks and birth weight was consistent with gestation. Exclusions due to invalid gestations were made for 89 cases (1.8%) where gestation was greater than 44 weeks and for 78 cases (1.5%) where, at a length of 35 weeks or less, birth weight was inconsistent with gestation from the LMP. No live births at less than 20 weeks were present. Clinical estimates of gestation based on ultrasonography or neonatal examination were not used to replace invalid or missing gestations from the LMP, since clinical estimates were not routinely reported on birth certificates before 1989. Very preterm delivery was defined as delivery before 33 weeks' gestation, preterm delivery as delivery between 33 and 36 weeks, and term as delivery from 37 to 44 weeks after the LMP.

Finally, the sample was restricted to non-Hispanic white, non-Hispanic black, and Mexican American infants and young children. Those of all other races/ethnicities (n = 295) were excluded because sample sizes were too small for analyses by age group, leaving a final analytic sample of 4431.

Infants and children were categorized by birth weight for gestational age status using reference percentiles derived for singleton infants from 1989 US Vital Statistics by Zhang and Bowes. Using these reference data, infants are categorized separately by race/ethnicity (white vs black) and within race by infant sex (male vs female) and maternal parity (infants of primiparas vs multiparas). Infants designated by NHANES III as non-Hispanic white and Mexican American were categorized as white, and non-Hispanic black as black, for comparison with the reference data. Mexican American infants were categorized using the percentiles for whites, consistent with the reference data, because their birth weight distributions, at least at the low end, were comparable with whites. Small for gestational age, indicating intrauterine growth retardation, was defined as a birth weight for gestational age below the 10th percentile; appropriate for gestational age (AGA), from the 10th to 89th percentile; and LGA, or macrosomia, at or above the 90th percentile.

was to compare the growth profiles of infants and young children born small for gestational age (SGA, birth weight <10th percentile for gestational age) and LGA (≥90th percentile) with those of normal birth weight children (appropriate for gestational age, AGA) to document the expected growth patterns through early childhood based on NHANES III data.

RESULTS

The overall prevalence of SGA in this sample was approximately 9% (n = 423); 81% (n = 3570) were born AGA, and 10% (n = 438) were born LGA. There was a relatively consistent distribution of birth weight status both by CA group and race/ethnicity. However, Mexican American infants were somewhat underrepresented in the LGA category compared with non-Hispanic white and non-Hispanic black infants (Table 1). There were more female than male infants born either SGA or LGA. Very preterm (15.1%) and preterm (12.0%) infants were disproportionately SGA. At the same time, 9.2% of preterm infants were actually LGA (Table 1). However, the overall prevalence of very preterm delivery was only 1.1% ± 0.2% (n = 49), and 5.8% ± 0.5% (n = 318) were preterm. Within the weighted sample of SGA infants, 1.9% ± 1.0% were born very preterm and 8.1% ± 2.4%, preterm. There were no LGA infants born very preterm, and only 5.1% ± 1.1% of the LGA infants were preterm.

As expected, LBW infants were disproportionately SGA (59.1%), and macrosomic infants were likely to be
Using these definitions, the infants categorized on the basis of their birth weight for gestational age status at the extremes do not entirely coincide with infants classified at the extremes based on birth weight alone. Infants born SGA, especially those at term, are not necessarily low birth weight (LBW) (<2500 g), and LGA infants are not necessarily macrosomic (≥4000 g) by size criteria.

**AGE GROUPS**

For analysis, the infants and children were grouped by chronological age (CA): 2.0 to 5.99 months, 6.0 to 8.99 months, 9.0 to 11.99 months, 12.0 to 23.99 months (1 year), 24.0 to 35.99 months (2 years), and 36.0 to 47.99 months (3 years), based on age at examination.17 Infants younger than 12 months were divided into 3 groups to more clearly identify rapid growth changes characteristic of infancy. The infants and children were also grouped by gestation-corrected age (GCA).11,18,19 Gestation-corrected age was calculated as age in months, adjusted for length of gestation, using the following algorithm: for those born at 21 to 24 weeks' gestation, GCA = CA (in months) − 3; at 25 to 28 weeks, GCA = CA (in months) − 4; at 29 to 32 weeks, GCA = CA (in months) − 2; at 33 to 36 weeks, GCA = CA (in months) − 1. Using this algorithm, 9 infants were excluded from analyses using the GCA groups because their GCA was 1 month or younger and fell below the age limit for the youngest group, and 1.4% of the sample (64 of 4431) was reclassified into a contiguous younger age group. The GCA groups were used in separate analyses to determine if there was an effect of growth restriction or acceleration independent of degree of prematurity.

**ANTHROPOMETRY AND GROWTH STATUS**

The anthropometric measurements considered were body weight (kilogram), recumbent length (centimeter), and head circumference (centimeter). Because the distribution of anthropometric measurements, particularly weight, can be skewed and because the timing of growth velocity varies in infancy and childhood, the anthropometric variables were transformed to allow for comparison across CA cohorts. Body weight was first transformed to an approximate normal distribution using a power transformation of \(-1/x^{0.2021}\). To control for group differences and to scale the values for comparison across age groups, the anthropometric variables were then converted into \(z\) scores (SD units [SDUs]) within the sample chronological age, sex, and race/ethnicity groups.17 Because the distributions of the anthropometric variables were approximately normal, percentiles corresponding to the \(z\) scores can be determined using the area under the normal curve. A \(z\) score or SDU of 0 represents the median (50th percentile). A \(z\) score of -0.30 would fall at the 10th percentile for the sample and +0.50 at the 69th percentile; the 10th and 90th percentiles are -1.28 SDUs and +1.28 SDUs, respectively. However, the magnitude of the absolute effect in actual measurement units for a positive SDU is larger than that for comparable negative SDU for skewed distributions such as body weight.

**OTHER VARIABLES**

Other variables used in analysis were obtained both from the birth certificates and NHANES III. Maternal parity and infant birth order were determined from the number of previous births reported on the birth certificate. To exclude twins or triplets, plurality of birth was recorded from the birth certificates.

Race and ethnicity were based on self-reports from NHANES III, using US Department of Commerce Bureau of the Census categories.13 Information on maternal smoking during pregnancy and whether the infant received special care at birth were obtained from the questionnaire administered to the infant’s parent or other respondent in the home. Maternal smoking during pregnancy was considered because smoking during pregnancy has an effect on fetal growth and infant size at birth and has possible effects on postnatal growth.22,23

**STATISTICAL METHODS**

Sample weights were used to account for the oversampling and unit nonresponse. SUDAAN software,24 which uses a Taylor series expansion to adjust variance estimates to account for the sample design, was used to estimate SE of the descriptive and prevalent characteristics. Analyses across age groups were accomplished using SUDAAN regression procedures. To estimate the effect for each CA or GCA group, separate indicator variables were created for SGA and LGA for each age group and entered into a regression with AGA infants and children as the reference group and the anthropometry \(z\) scores as the dependent variables. Summary effects for birth weight status were estimated accounting for group effects in the models predicting the anthropometry \(z\) scores. Results from the models are regression coefficients (±SE) in SDUs, tested for statistical significance (\(\alpha = 0.05\)) from 0.
coefficients for each age group were highly significant across all ages significant for weight (P <.001), but the coefficients for each age group were highly significant (P <.001) as well (Table 2).

Comparable trends were seen for recumbent length (Figure 2 and Table 2) and head circumference (Figure 3 and Table 2), although some cohort effects were apparent due to sample variability. There was continued tracking, but it was impossible to determine the extent of change in the first few months of life because no baseline data on length and head circumference at birth were available on the birth certificates. Again, compared with median reference data,23 at 47 months, SGA infants should be approximately 3 cm below the median and LGA infants 2 cm above the median in length.

Analyses using the GCA groups yielded almost identical results. The regression coefficients for weight and length for the CGA age groups in the first year are presented in Table 3. Only the GCA groups at 2 to 5 months of age for the SGA infants differed from the 2- to 5-month-old CA groups. For the GCA groups at 2 to 5 months of age, the
coefficients for weight and recumbent length were close to −0.75 SDUs compared with −0.85 SDUs for the CA group. However, after the first several months, correction for degree of prematurity does not affect the relative growth of SGA and LGA infants in these analyses.

We have shown persistent associations of birth weight for gestational age status with growth status in infancy and early childhood through age 47 months. Despite catch-up, infants born SGA tend to remain shorter and lighter with smaller head circumferences. After an initial period of compensation, infants born SGA can be expected to remain around the 25th percentile in all dimensions through early childhood. Compared with growth charts currently in use, this means that at 47 months of age, children born SGA may show a deficit of at least 2 kg in weight relative to the median and a deficit of almost 3 cm in length and height. Likewise, despite a decrease in growth, LGA infants tend to remain longer and heavier with larger head circumferences. Large for gestational age infants may remain at least in the upper tertile through early childhood. For LGA infants, this means about 2 kg excess in weight and 2 cm in length/height at age 47 months.

Despite the facts that 64% of the SGA infants were not also LBW and only 10% were born preterm, SGA was consistently associated with later growth status. This is undoubtedly because the factors that restrict or retard fetal growth may vary in intensity and may differ from those that are associated with preterm delivery, although there is considerable overlap in origin and recognition that infants born preterm are more likely to be characterized by suboptimal growth.26

There are a number of risk factors and underlying causes of the growth restriction, including pre-eclampsia, infection, placental insufficiency, maternal smoking, inadequate maternal nutrition, small maternal size, and low maternal weight gain.27,28 However, in most cases, decreased rates of fetal growth as evidenced by an SGA outcome seem to be an adaptation to an inadequate nutrient supply during gestation.

Growth-restricted infants are characterized by fetal hypoglycemia, which acts to maintain the maternal/fetal glucose concentration gradient and transport of glucose across the placenta to the fetus. The hypoglycemia also limits insulin secretion, initially potentiating fetal glucose production, but subsequently resulting in increased protein breakdown, decreased protein accretion, and, thus, slower growth.27

Studies of the body composition of SGA infants at birth have shown that lean body mass (muscle) and bone mineral content are reduced compared with their AGA counterparts.29,30 However, much like young children after an episode of starvation or illness that causes growth to falter,4 SGA infants born small for gestational age at age 9 to 11 months, are statistically different from 0 at P < .05.

Table 3. Regression Coefficients for Weight and Recumbent Length by Birth Weight Categories and Gestation-Corrected Age Groups for Infants and Children, Aged 2 to 11 Months, the Third National Health and Nutrition Examination Survey, 1988-1994*

<table>
<thead>
<tr>
<th>Age Groups, mo</th>
<th>Small for Gestational Age</th>
<th>Large for Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weight (SE)</td>
<td>Length (SE)</td>
</tr>
<tr>
<td>2-5</td>
<td>−0.74 (0.16)†</td>
<td>−0.78 (0.13)†</td>
</tr>
<tr>
<td>6-8</td>
<td>−0.75 (0.19)†</td>
<td>−0.80 (0.15)†</td>
</tr>
<tr>
<td>9-11</td>
<td>−0.77 (0.14)†</td>
<td>−0.52 (0.26)‡</td>
</tr>
</tbody>
</table>

* The regressions coefficients (SD units) are derived from models using normalized anthropometric scores (z scores as the dependent variable and birth weight status by age groups, 2 to 47 months, as the independent variables.
†Coefficient significantly different from 0 at P < .001.
‡Coefficient significantly different from 0 at P < .05.
veloped to evaluate infants born both LBW and preterm.11,19 Unlike SGA infants born at term, preterm LBW infants show limited or no catch-up at least through the first 12 months, although those born AGA and preterm do relatively better.12,31,32 This is unlike most of the findings on SGA infants, especially those born at term, for whom catch-up can be expected.

Fitzhardinge and Steven1 were among the first to look at catch-up for term SGA infants, following a sample of 131 white, singleton infants with birth weights 30% below expected values (generally < 2500 g). The average weight and height of the SGA infants rose from below the third percentile at birth to between the 10th to 25th percentile at 6 months, and remained around the 25th percentile through age 8 years. Low et al33,34 compared the growth through age 5 years of 76 white SGA infants born at term with that of 88 AGA infants (birth weight >25th percentile). The SGA infants demonstrated accelerated growth during the first 3 months, but never completely caught up, remaining smaller at age 60 months by an average of 2.3 kg and 3.6 cm.34

There have also been small, nonrepresentative studies, summarized below, that compared SGA term infants with LGA infants born at term and described the postnatal growth of LGA infants. In our analyses, LGA infants showed consistent differences in growth status through early childhood, despite the fact that 23% of LGA infants weighed 4000 g or less at birth. There are a few rare syndromes associated with accelerated fetal growth,35 but it is believed that the condition of most of the LGA infants is due to abnormalities of maternal glucose metabolism or gestational diabetes mellitus. Large maternal size, obesity, and excessive maternal weight gain are also risk factors. With gestational diabetes, the fetus is exposed to high levels of both glucose and amino acids, and the resulting fetal hyperglycemia is associated with increased insulin secretion (hyperinsulinemia) and accelerated growth of lean body mass and fat.6,36

Davies37,38 followed 51 SGA and 38 LGA infants, defined as below or above the 5th and 95th percentiles,39 respectively, compared with 100 AGA controls. During the first 6 months, there were substantial shifts to the mean in weight, but great diversity in growth pattern. Of the LGA infants, the growth in weight of 26% showed tracking from birth, while 74% showed relative slowdown. On the other side, 32% of the SGA infants remained small (less than fifth percentile), while 68% showed substantial catch-up.

In the largest comparable clinical study, Ounsted et al40,41 conducted a 7-year longitudinal study, enrolling a sample of 238 SGA (18 with gestational ages <37 weeks), 246 AGA (8 preterm), and 241 LGA (1 preterm) white, singleton infants. Abnormal birth weight was ± 2 SDs of mean birth weight for gestational age. In the first 6 months, actual and relative growth was greatest in the SGA group and lowest in the LGA group. Follow-up established that at 4 years1 and 7 years,41 there were still highly significant differences in height and weight among the groups. In findings remarkably similar to those presented here, at age 4 years, the children born SGA were 3 cm shorter than the AGA children, and weighed 2 kg less, while the children born LGA were taller by 3 cm and heavier by 2 kg. The SGA group was still about 3 cm shorter at age 7 years than the AGA group, while the LGA group was 3 to 4 cm taller; the SGA group was 2 kg lighter, and the LGA group 2 to 3 kg heavier than the AGA group.41

A few large US studies have looked at the entire range of birth weights and demonstrated that growth status based on size at birth tends to track during infancy and early childhood; that is, relative rankings are maintained. Among the more than 10 000 white, singleton infants followed prospectively through age 7 years by the National Collaborative Perinatal Project (1956-1974),8 those infants light for term (<5th percentile for birth weight) weighed 4 kg less at age 7 years compared with those heavy for term (>95th percentile). Infants short for term (<5th percentile for birth length) were shorter by 6 cm at age 7 years than those long for term (>95th percentile).7 In a later study, a similar discrepancy was seen for weight at the extremes for black children in the National Collaborative Perinatal Project.8 The sample of 4689 white, term infants measured at ages 6 to 11 years in cycle 2 of the National Health Examination Survey (1963-1965) for whom birth certificates were obtained also showed a small but consistent positive association between birth weight and child size.10 For each additional kilogram of birth weight, attained weight from ages 6 to 11 years was about 2 to 4 kg higher.

Finally, Binken et al9 looked at the growth through age 5 years for children in Tennessee enrolled in the Special Supplemental Food Program for Women, Infants, and Children from 1975-1984, basing the analysis of growth outcomes on 500-g categories of birth weight without regard to gestation. Outcomes included age-adjusted length and weight (z scores), adjusted using CDC references. They found considerable tracking through age 5 years; and the children in the birth weight strata maintained their relative positions through time, after an initial period in the first 6 months of catch-up for infants weighing less than 2500 g and a slowdown for infants weighing 4000 g or more.

Thus, the findings reported here on an ethnically diverse sample of US-born infants and children confirm those from clinical or national cohort studies, both in the direction of the findings and the magnitude of the effects. However defined, SGA infants remain shorter and lighter in early childhood with smaller head circumferences, and LGA infants remain longer and heavier with larger head circumferences. These findings underscore the need to evaluate the growth of infants and young children relative to their birth weight status, whether they are born preterm or their absolute birth weights fall outside currently accepted limits.

Both birth weight and a reliable estimate of gestation are needed to determine birth weight status. A limitation of these analyses is the necessity of relying on estimates of gestation from the LMP to determine birth weight status when more clinically accurate estimates may be available. However, our use of gestation from the LMP is unlikely to have caused a bias in the findings. Although widely recognized as being prone to error,62 gestation estimated from the LMP is still used as the basis for the development of birth weight for gestational age reference percentiles,43 including those used in these analyses.14 Further, most infants in the analyses were born at term (93%), and the probability that a term infant will be correctly classified as such based on the LMP estimate (positive predic-
tive value) is close to 95%. Cases born postterm, where the positive predictive value for the LMP estimate is very poor, were excluded from the analyses.

The NCHS/CDC growth charts for the US are currently being revised to include the infant and child growth data collected in the most recent National Health Examination surveys, including NHANES III. When these charts become available for general clinical use, there will be opportunity to evaluate growth status based on an infant’s weight at birth and, we would suggest, gestation. Although infants born preterm and small (LBW) may be best evaluated using charts specific to such children, moderately LBW (1500- to 2500-g) infants born at term can be evaluated using the NCHS/CDC charts, recognizing that since they are also likely to be SGA, they may show catch-up but track at the lower percentiles through early childhood. However, of equal importance, SGA status is associated with later growth despite the fact that 64% of the infants classified as SGA in this sample were not LBW, and only 10% were born preterm. Infants born SGA, who account for about 9% of all live births, normally have a period of catch-up growth in early infancy (by 3-6 months), but remain deficient in size (hovering around the 25th percentile) through age 47 months. Small for gestational age infants account for about 11% of births, and almost 25% of the infants classified as LGA in this sample weighed less than 4000 g at birth. Nevertheless, these LGA infants slowed down in growth, but remained around the 75th percentile (upper tertile) for size through early childhood. Thus, it seems that for the 20% of US-born infants who are born at the extremes of birth weight, their growth may be best considered in light of their status at birth.

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REFERENCES

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