The Optimal Postnatal Growth Trajectory for Term Small for Gestational Age Babies: A Prospective Cohort Study

Xiaoping Lei, MD[1,2,*], Yan Chen, MD[1,*], Jiangfeng Ye, MD, PhD[1], Fengxiu Ouyang, MD, PhD[1], Fan Jiang, MD, PhD[3], and Jun Zhang, PhD, MD[1,4]

Objectives To identify an optimal growth trajectory for term small for gestational age (SGA) babies from birth to 7-years-old.

Study design Data were from the Collaborative Perinatal Project, a US multicenter prospective cohort study from 1959-1976. Five weight growth trajectories of the 1957 term SGA babies were grouped by a latent class model. We selected the optimal growth pattern based on the lowest overall risks of childhood diseases.

Results Compared with appropriate for gestational age children, SGA babies with no catch-up growth (439, 22.4%) had higher risks of infection in infancy (aOR 1.2, 95% CI 1.0-1.6), growth restriction (11.2, 8.6-14.6), and low IQ (2.1, 1.7-2.8) at age 7 years. Those with excessive catch-up growth (176, 8.9%) had higher risks of overweight/obesity (7.5, 5.4-10.5) and elevated blood pressure (1.7, 1.1-2.4) at age 7 years. Babies with slow catch-up growth (328, 16.8%) or regression after 4 months (285, 14.6%) were associated with higher risks of low IQ (1.6, 1.2-2.1) and growth restriction (2.2, 1.5-3.2), respectively. Only babies with appropriate catch-up growth (729, 37.3%) did not have increased risk of adverse outcomes. Further, we also tested linear growth trajectories with similar findings.

Conclusions The optimal growth trajectory for term SGA infants may be fast catch-up growth to about the 30th percentile in the first several months, with modest catch-up growth thereafter, to be around the 50th percentile by 7-years-old. *(J Pediatr 2015;166:54-8)*.

Postnatal growth of small for gestational age (SGA) babies poses a catch-up growth dilemma.[1,2] On one hand, as a compensation for earlier growth restriction, SGA babies are more likely to have rapid postnatal growth.[3] According to the "developmental origins of adult disease" hypothesis, rapid postnatal catch-up growth in early life for low birthweight infants is related to a number of metabolic disorders including obesity,[3-5] hypertension,[6-8] cardiovascular diseases,[9,10] metabolic syndrome, and endothelial dysfunction[5,11] later in life. On the other hand, persistent poor postnatal growth is associated with more frequent infection,[12] short stature,[13,14] and impaired cognitive development.[15,16]

Is there an optimal growth trajectory for SGA infants? Most previous studies[3,9,13,17] only examined weight gain during infancy and not for a longer, continuous period. For this study, term SGA infants were measured 5 times between birth and age 7 years. We identified 5 common growth trajectory patterns from birth to 7 years of age and evaluated the pattern that has the lowest risk of child morbidity as an optimal growth trajectory for term SGA infants.

Methods

The Collaborative Perinatal Project (CPP) was a prospective study with 12 US academic medical centers between 1959 and 1976. The offspring were followed from birth to 7 years of age. Weight and length/height were measured and recorded at birth, 4 months, and 1, 4, and 7 years of age. A detailed description of the study has been provided elsewhere.[18] The CPP data are publicly available through the US National Archives (www.archives.gov). Use of publicly available de-identified data is exempt from the review by our Institutional Review Board.

Of the 56 990 pregnancies enrolled in the CPP, 2195 stillbirths or early terminations and 1148 multiple births were excluded from this analysis (**Figure 1**; available at www.jpeds.com). Because Hispanic, Asian, and other ethnicities (n = 5528) constituted only a small proportion of the population, we restricted this analysis to the White and Black population. We excluded births before 37 weeks

AGA	Appropriate for gestational age
CDC	Centers for Disease Control and Prevention
CPP	Collaborative Perinatal Project
LMP	Last menstrual period
SGA	Small for gestational age

From the [1]MOE-Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2]Department of Neonatology, Affiliated Hospital of Luzhou Medical College, Luzhou, Sichuan, China; [3]Department of Child Development and Behavior, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine; and [4]Shanghai Jiao Tong University School of Public Health, Shanghai, China

*Contributed equally.

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(n = 7226) and after 43 weeks (n = 2315) because growth trajectories of these infants may be different.[19] Births with unknown gestational age (n = 37) also were excluded.

Gestational age was calculated based on the last menstrual period (LMP). We calculated internal race-, sex-, and gestational age-specific birthweight and birthweight to length percentiles in singleton births in the CPP cohort (n = 38 541). Because no appropriate external reference in those years is available and the Centers for Disease Control and Prevention (CDC)/World Health Organization growth charts are only stratified by sex but not race, we defined SGA as birthweight <10th percentile based on these internal race- and sex-specific references.

After excluding infants with missing weight data at any time point, 21 247 infants remained. Among them, 1957 were SGA infants (birthweight <10th percentile) and, therefore, were included in the final analysis. The appropriate for gestational age (AGA, 10th ≤ birthweight ≤ 90th percentile) infants of at 37-43 weeks of gestation served as the reference.

Growth Trajectory

To group children with similar growth trajectory patterns, we used a latent class analysis, a person-centered approach designed to classify individuals into distinct groups.[20] We used the 2000 CDC growth charts as the reference[21] to calculate sex- and age-specific weight and weight to length distributions for this study population at ages 4 months (16-20 weeks), 1 year (10-14 months), 4 years (46-50 months), and 7 years (82-86 months). These weight and weight to length percentiles were used to define the postnatal growth trajectory. Weight and weight to length percentiles were categorized into 5 groups (<10th percentile, 10th-25th, 25th-75th, 75th-90th, and >90th). The optimal number of growth trajectories (latent groups) was chosen following the Bayesian information criterion. Lower Bayesian information criterion values indicate a more parsimonious model.[20] Moreover, the classification accuracy of the model was assessed with the entropy statistic. Entropy statistic >0.80 suggests sufficient accuracy of the model (range 0-1).[22]

Outcomes

At age 7 years, children with a sex- and age-specific body mass index >85th percentile but <95th percentile were defined as overweight, and sex- and age-specific body mass index ≥95th percentile as obesity using 2000 CDC growth charts as reference.[21,23]

At age 7 years, underweight was defined as sex- and age-specific weight <2.3 percentile; stunting as sex- and age-specific height <2.3 percentile; microcephaly as sex- and age-specific head circumference <2.3 percentile, and wasting as sex- and age-specific weight to length <2.3 percentile by the CDC growth charts (2000).[21] We defined any of underweight, stunting, microcephaly, and wasting at age 7 years as growth restriction.

Children were given a 7 components test (information, comprehension, vocabulary, digit span, picture arrangement, block design, and coding) with the 1949 Wechsler Intelligence Scales for school and preschool children at 7 years. The full-scale score (IQ) was based on the results from all 7 components.[24] The validity and reliability of the 1949 Wechsler Intelligence Scales for school and preschool children have been reported elsewhere.[25] We defined low IQ as IQ <85 at 7 years in the present analysis.

Blood pressure at age 7 years was measured with a manual sphygmomanometer on the right arm of the child in a sitting position. Blood pressure distributions for this study population, stratified by race and sex, were calculated. Using this internal standard, an elevated blood pressure was defined as systolic blood pressure or diastolic blood pressure >90th percentile, as recommended by the 1996 Task Force Report on High Blood Pressure in Children and Adolescents.[26]

Detailed information on child health was collected at each visit.[27] The diagnostic information included all hospital records during the infancy recorded by a senior pediatrician. All clear-cut diagnoses, conditions, or states were coded under the definition. The information of infection in the current analysis was extracted from this summarized data file. A child was classified as infected if he/she had 1 or more definite infections in infancy.

Statistical Analyses

Cochran-Mantel-Haenszel χ^2 was used to assess the differences of baseline characteristics among 5 growth trajectory patterns. We used logistic regression to examine the association between growth pattern and adverse outcome adjusting for potential confounders. The latter included sex, race, socioeconomic status (comprised 5 categories as assessed by the original CPP investigators[15]), highest maternal education (<10th, 10th-12th, and >12th grades), maternal age (<20, 20-35, and >35 years), gestational age (as categorical variable), marital status (married, unmarried, and other), maternal smoking (0, 1-19 and ≥20 cigarettes per day during pregnancy), hypertensive disorders during pregnancy (none, moderate, and severe), delivery hospital, birthweight (<1500 g, 1500-2500 g, and >2500 g), feeding methods (exclusively breast, exclusively bottle, mixed feed, and unknown), and parity (1, 2, and >2). In addition, for low IQ at 7 years, we further adjusted for Apgar score at 5 minutes (<7 and ≥7), and child height at 7 years (<10th, 10th-90th, and ≥90th percentile) in the models for elevated blood pressure. SAS v 9.2 (SAS Institute, Cary, North Carolina) was used for the statistical analysis.

Results

Based on the Bayesian information criterion in the latent class analysis model of weight percentiles by age, 5 trajectories were identified, including no catch-up growth (A) (439, 22.4%), regression after 4 months (B) (285, 14.6%), slow catch-up growth (C) (328, 16.8%), appropriate catch-up growth (D) (729, 37.3%), and excessive catch-up growth (E) (176, 8.9%) (**Figure 2**, **Table I**). By comparing the baseline characteristics of infants in the 5 weight growth trajectories, we found that birthweight, race, gestational