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Analysis of longitudinal follow-up data of physical growth in singleton full-term small for gestational age infants

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Abstract

Objective: This study aimed to investigate the catch-up growth pattern of singleton full-term small for gestational age (SGA) infants in the first year after birth.

Methods: A single-center retrospective cohort study was performed to assess singleton full-term SGA infants. Weight, length, and head circumference were measured at birth, and at 1, 3, 6, and 12 months of age.

Results: Two hundred ten SGA infants were included in this study. Boys (n = 90) and girls (n = 120) showed a similar gestational age, birth weight, and body length. Weight, length, and head circumference in SGA infants in all age groups increased with age, with the fastest growth stage from birth to 3 months. The speed of weight and head circumference catch-up was higher than that of body length. At 12 months, significant associations of height in boys with height of the fathers, mothers, and both parents combined appeared. The height of girls showed associations with the mothers' and the parents' height.

Conclusions: Full-term SGA infants grow rapidly after birth, with the fastest growth rate in the first 3 months, as examined by weight, body length, and head circumference. However, the catch-up speed of weight and body length were not balanced in this study.

Keywords

Full-term infant, singleton, small for gestational age, catch-up growth, Z score, head circumference, birth weight

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Background

Small for gestational age (SGA) is a term used to characterize newborns whose birth weight is below the 10th percentile of birth weight or <2 standard deviations from the mean birth weight of the same gestational age and sex.[1,2] SGA infants are classified into constitutionally normal infants and those who have growth restriction.[3,4] The first group of SGA infants show a normal birth weight below the 10th percentile due to inherent parameters, including maternal height and/or weight, ethnicity, and parity, with no elevated risk of perinatal mortality or morbidity.[5] The second group includes infants with fetal growth restriction, which is not synonymous with SGA, although these two terms are commonly used interchangeably.[6]

A 2010 survey reported approximately 32.4 million SGA infants born in 138 low- and middle-income nations, representing 27% of all live births, and including 10.6 million full-term infants.[7] China had an incidence of SGA of approximately 6.5%, ranking fifth among the examined countries.[7] Another survey performed in China showed that 9.10% to 10.13% of neonates are SGA, with a mortality rate of 2.45%, which is significantly higher than the overall neonatal mortality rate (1.20%) recorded in the same period.[8]

Special attention should be paid to SGA because of its high incidence. The risk factors for and complications of SGA have been well studied. SGA causes neonatal hypoglycemia and hyperbilirubinemia. Perinatal monitoring and antenatal care should be strengthened to decrease the incidence of SGA and perinatal complications.[9] However, whether and when SGA infants show growth catch-up remains unclear. Therefore, the present study aimed to investigate the catch-up growth pattern of singleton SGA infants within 12 months after birth.

Methods

Study design and participants

This study retrospectively assessed consecutive singleton full-term newborns with SGA on the basis of the 2013 Fenton growth curve[10] in the Department of Child Health Care, Chongqing Health Center for Women and Children from August 2015 to December 2018. During this period, >20,000 full-term singleton fetuses were born at this hospital. Inclusion criteria were as follows: (1) gestational age ≥37 weeks and <42 weeks; and (2) birth weight below the 10th percentile in the same sex. Exclusion criteria were as follows: (1) hereditary endocrine disease; (2) obvious mental retardation; and (3) parents with a family history of mental, genetic, and/or metabolic diseases.

This study was approved by the Ethics Committee of Chongqing Health Center for Women and Children (approval number: 2021KY024) The requirement for informed consent was waived because this was a retrospective study. All data were de-identified before any analysis. The reporting of this study conforms to the STROBE guidelines.[11]

Data collection

The birth weight, body length/height, and gestational age of the infants were obtained from medical birth certificates. The weight, length, and head circumference were measured during regular follow-up visits at the Child Health Care Department of Chongqing Maternal and Child Health Hospital.

All measurements were performed by two trained nurses in our department's measurement room. The weight was measured with a sitting and horizontal lever scale at an accuracy of 10 g. The body length was measured with a standard

measuring bed in the supine position at an accuracy of 0.1 cm. The head circumference was assessed with a soft ruler at an accuracy of 0.1 cm.

Catch-up growth evaluation

Catch-up growth was evaluated by measuring the height, weight, and head circumference at the ages of 1, 3, 6, and 12 months during the follow-up period in accordance with the 2006 World Health Organization Children's Growth Standards.[12]

Statistical analysis

SPSS 15.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Normally distributed continuous data are expressed as mean ± standard deviation (SD) and were assessed by the t-test. Categorical variables are expressed as n (%) and were compared by the chi-square test. Z scores were calculated as follows:[13] measured value − mean/SD. Pearson correlation analysis was performed to examine the association of height in full-term SGA infants with that in their parents. $P < 0.05$ was considered statistically significant.

Results

Characteristics of infants and parents

A total of 210 full-term infants with a gestational age of ≥37 weeks and <42 weeks were SGA, including 90 boys and 120 girls, which represented 6.5% of the births during the study period. The mean gestational age was 37.58 ± 0.84 weeks. The mean birth weight was 2306.30 ± 161.11 g and the mean body length at birth was 46.44 ± 1.71 cm. The mean height of the fathers overall was 171.40 ± 5.12 cm, and that in fathers with SGA boys and girls was 171.57 ± 4.58 and 171.22 ± 5.33 cm, respectively. The mean height of the mothers overall was 158.51 ± 4.44 cm, and that in mothers with SGA boys and girls was 158.31 ± 4.98 and 158.66 ± 3.40 cm, respectively. There were no significant differences in any of these variables between SGA boys and girls (Table 1).

Z score

The mean Z score and Z value distribution in the study subjects were examined at 1, 3, 6, and 12 months for body length, weight, and head circumference. All indicators steadily increased with age. Full-term infants of both sexes showed increased Z scores compared with the corresponding birth values (Figure 1).

The mean Z scores of various indicators in children of different ages showed different values. All indicators showed the most growth in the first 3 months after birth. Male and female children showed a faster increase in weight and head circumference compared with that in body length (Table 2).

The Z score distribution of body length, weight, and head circumference in children

Table 1. Birth status of full-term infants of both sexes and parents' height

Subjects	Boys (n = 9)	Girls (n = 12)	Total (=210)	P
Mean birth weight (g)	2297.07 ± 283.70	2306.38 ± 161.11	2306.30 ± 161.11	0.70
Mean birth height (cm)	46.23 ± 1.76	46.52 ± 1.67	46.44 ± 1.71	0.43
Gestational age (weeks)	37.43 ± 0.75	37.69 ± 0.89	37.58 ± 0.84	0.11
Fathers' mean height (cm)	171.57 ± 4.58	171.22 ± 5.33	171.40 ± 5.12	0.69
Mothers' mean height (cm)	158.31 ± 4.98	158.66 ± 3.40	158.51 ± 4.44	0.57

Data are shown as mean ± standard deviation.

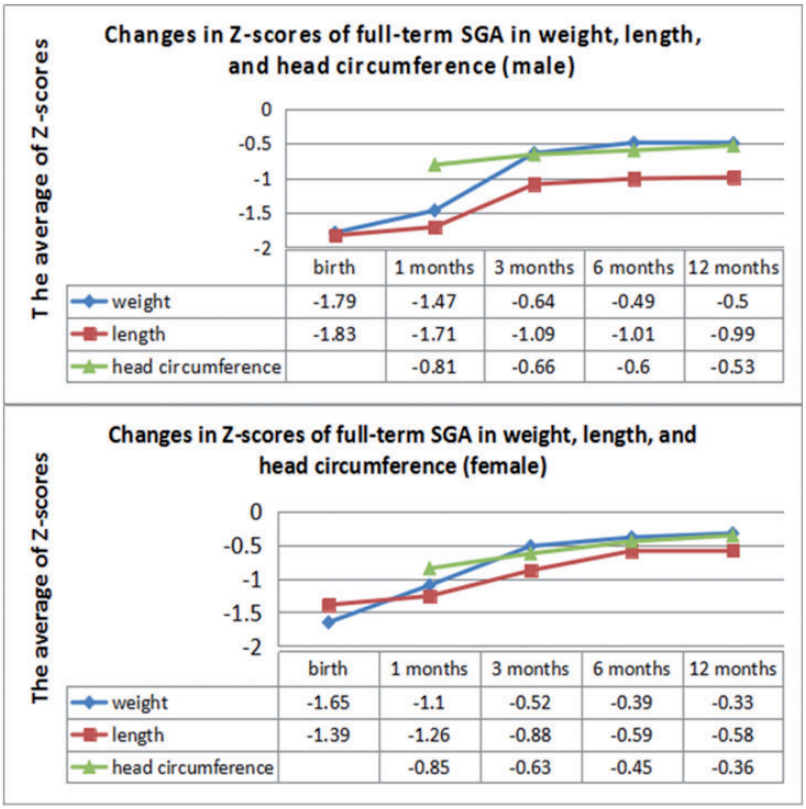

Figure 1. Z scores for weight, length, and head circumference.
SGA, small for gestational age.

Table 2. Z values of body length, weight, and head circumference of small for gestational age infants of different sexes until 12 months.

Sex	n	Birth	1 month old	3 months old	6 months old	12 months old
Boys	90					
Weight		−1.79 ± 0.63	−1.47 ± 0.65	−0.64 ± 0.93	−0.49 ± 0.93	−0.50 ± 0.79
Length		−1.83 ± 0.93	−1.71 ± 0.98	−1.09 ± 1.13	−1.01 ± 0.94	−0.99 ± 1.05
Head circumference		——	−0.81 ± 0.90	−0.66 ± 1.06	−0.60 ± 1.03	−0.53 ± 0.99
Girls	120					
Weight		−1.65 ± 0.71	−1.10 ± 0.74	−0.52 ± 0.73	−0.39 ± 0.81	−0.33 ± 0.74
Length		−1.39 ± 0.90	−1.26 ± 0.81	−0.88 ± 0.94	−0.59 ± 0.85	−0.55 ± 0.58
Head circumference		——	−0.85 ± 2.45	−0.63 ± 0.86	−0.45 ± 0.85	−0.36 ± 0.85
All	210					
Weight		−1.74 ± 0.69	−1.26 ± 0.73	−0.50 ± 0.82	−0.43 ± 0.86	−0.40 ± 0.77
Length		−1.59 ± 0.93	−1.55 ± 0.91	−0.97 ± 1.02	−0.77 ± 0.92	−0.76 ± 0.98
Head circumference		——	−0.80 ± 1.94	−0.60 ± 0.95	−0.50 ± 0.93	−0.40 ± 0.91

at 1, 3, 6, and 12 months old was analyzed. The percentages of full-term male SGA infants whose Z score was <-2 at 0, 1, 3, 6 and 12 months were 58.59%, 17.78%, 6.67%, 5.56%, and 3.33% for weight, 52.22%, 40.00%, 22.22%, 16.67%, and 18.89% for body length, and no data available, 7.78%, 7.78%, 4.44%, and 5.55% for head circumference, respectively. The percentages of full-term female SGA infants whose Z score was <-2 at 0, 1, 3, 6, and 12 months were 65.83%, 9.17%, 2.50%, 0%, and 0.83% for weight, 25.83%, 23.33%, 10.83%, 4.17%, and 5.83% for body length, and no data available, 5.83%, 4.17%, 3.33%, and 0.83% for head circumference, respectively (Table 2).

Associations of height in full-term SGA infants aged $\leq$12 months with parents' height

The birth length/height in boys and girls was not correlated with the parents' height. At 12 months of age, Pearson correlation coefficients between the height of SGA boys and the height of fathers, mothers, and both parents combined were 0.397, 0.484, and 0.565, respectively, all of which were significant (all $P < 0.001$), with a moderately strong correlation (Figure 2 and Table 3). These data indicated that the height in boys at 12 months of age was higher with a greater sum of the parents' height. In girls, Pearson correlation coefficients between the height at 12 months and the height of mothers and both parents combined were 0.188 and 0.199, respectively, with low significant correlations ($P = 0.042$ and $P = 0.03$, respectively). These data indicated that the height in girls was higher at 12 months old with a greater combined parents' height. There was no significant correlation between the fathers' height and girls' height at the age of 12 months (Table 3).

After categorizing the height of fathers, mothers, and both parents combined (short, middle, and tall groups), analysis of variance was performed to assess potential differences in the height of SGA infants at the age of 12 months. Among boys, there were significant differences in the height of fathers, mothers, and both parents

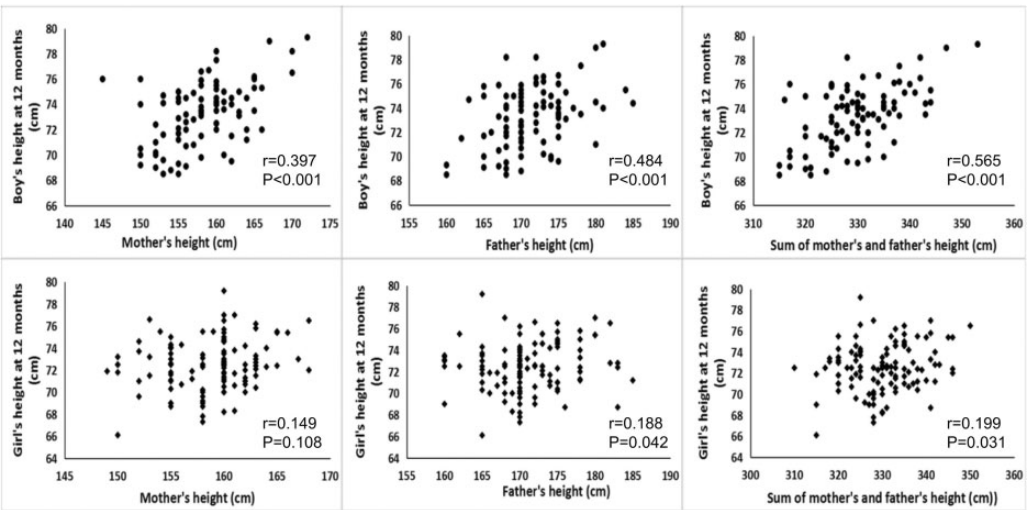

Figure 2. Scatter plots of the correlations between height in SGA children and height in fathers, mothers, and both parents combined.

Table 3. Associations of children's height with parents' height.

		Father's height vs. child's height	Mother's height vs. child's height	Parents' height vs. child's height
Birth				
Height (cm)	Boys	−0.045 (0.678)	0.038 (0.720)	−0.004 (0.973)
	Girls	−0.068 (0.462)	0.070 (0.450)	−0.011 (0.908)
12 months old				
Height (cm)	Boys	0.397 (<0.001)	0.484 (<0.001)	0.565 (<0.001)
	Girls	0.149 (0.108)	0.188 (0.042)	0.199 (0.031)

Values are the correlation coefficient (P value).

combined in all of these subgroups (all $P < 0.01$). However, no significant differences were found among girls (Table 4).

Discussion

The present study showed that full-term SGA infants grew rapidly from birth, especially in the first 3 months of life. Catch-up was better for weight compared with that for body length in the first year of life in SGA infants. Monitoring growth and development is an important part of child healthcare. The growth and development of high-risk infants, especially those with SGA, have attracted widespread attention. SGA is among the top five reasons for pediatric outpatient visits, and 15% to 20% of children with SGA are still not caught up by 3 years of age.[14–17] Therefore, clinicians urgently need evidence-based early prevention and intervention measures.

The definition of SAGA is controversial, with different growth curves available (Fenton, World health organization, and INTEGROWTH-21st), but there is an absence of specific curves for China.[15] As a standard, this study used the INTERGROWTH-21st project, which assessed data from eight middle and high-income countries.[18] Although no significant differences were found among the eight nations, using this standard in other countries or regions may show differences. A study in Hong Kong, China[19] showed that when the INTERGROWTH-21st standard was used to determine the birth weight in infants, the proportion of SGA infants was greatly increased compared with local standards. Therefore, a different diagnosis can be obtained for the same newborn just because of differences in the diagnostic criteria. Although China established a birth weight curve for newborns with different gestational ages in 2015,[20] it is not convenient for determining full-term small fetal weight at different gestational ages because these data do not provide a standard for length in newborns based on gestational age. We assessed infant length within 1 year after birth, and the above-mentioned standard was not appropriate for this study. To define SGA more reasonably in China, birth weight and length curves of newborns at different gestational ages should be generated as soon as possible so that clinicians can make a more accurate assessment of birth conditions to facilitate the diagnosis of SGA. This would improve future follow-up and interventions.

The birth weights of twins are generally different from those of singletons. Therefore, in this study, only singleton full-term SGA infants were examined according to the INTERGROWTH-21st standard. Assessing the birth head circumference is challenging. Therefore, we compared the birth length in 210 full-term

Table 4. Associations of children's height of different sexes with height of the parents grouped by weight.

Variables	n	12 months old	P value
Boys			
Father's height (cm)			0.0045
Short ($\leq$166)[a]	11	71.78 ± 2.50	
Middle (167–176)[b]	68	73.29 ± 2.34	
Tall ($\geq$177)[b]	11	75.20 ± 2.48	
Mother's height (cm)			<0.0001
Short ($\leq$154)[a]	17	71.53 ± 2.47	
Middle (155–162)[b]	55	73.38 ± 2.15	
Tall ($\geq$163)[c]	18	75.09 ± 2.39	
Sum of parents' height (cm)			<0.0001
Short ($\leq$322)[a]	15	71.06 ± 2.49	
Middle (323–337)[b]	61	73.28 ± 2.02	
Tall ($\geq$338)[c]	14	76.04 ± 1.89	
Girls			
Father's height (cm)			0.1364
Short ($\leq$166)[a]	23	72.44 ± 2.43	
Middle (167–176)[b]	79	72.30 ± 2.19	
Tall ($\geq$177)[b]	18	73.48 ± 2.22	
Mother's height (cm)			0.1035
Short ($\leq$154)[a]	16	72.36 ± 2.40	
Middle (155–162)[b]	86	72.31 ± 2.29	
Tall ($\geq$163)[c]	18	73.55 ± 1.81	
Sum of parents' height (cm)			0.2108
Short ($\leq$322)[a]	22	72.14 ± 1.93	
Middle (323–337)[b]	78	72.41 ± 2.33	
Tall ($\geq$338)[c]	20	73.29 ± 2.25	

Data are shown as mean ± standard deviation.

If there was significance in an analysis of variance, pairwise comparisons within the group were carried out. Different letters (a, b, and c) reflect a significant difference in pairwise comparison; the same letter means no difference.

infants who were matched for sex and age, and found different Z score distributions. The percentages of boys and girls whose Z scores are <-2 are higher than those of counterparts with Z scores >-2. This finding indicates that defining SGA on the basis of birth weight alone does not fully reflect the level of intrauterine development. Therefore, the 2007 International Pediatric Endocrinology Society and the Growth Hormone Research Society,[21] as well as the 2011 Latin American Consensus,[22] adopted the following definition for SGA infants: newborns whose crown and heel lengths are 2 SDs lower than the average values for newborns of the same gestational age. However, because of the low operability of body length measurement at birth, its accuracy is relatively lower compared with that for weight assessment, which suggests that birth weight is more clinically relevant. However, attention should be paid to the assessment of birth length in the clinical evaluation of children who are below normal for gestational age. We should also pay sufficient attention to those who

did not have a low birth weight, but have a birth length 2 SDs lower than average, by improving the long-term follow-up.

Bocca-Tjeertes et al.[23] followed up full-term SGA infants and found that catch-up growth was mainly completed during infancy. A prospective study with a birth weight $\leq$ the 10th percentile of the same gestational age defined as SGA[16] showed that 60% of full-term SGA infants completed catch-up at 1 year old. A previous study showed that the best growth trajectory for full-term SGA infants is to catch up to the 30th percentile in the first few months and then have a milder catch-up speed, reaching the 50th percentile at the age of 7 years and maintaining that level.[24] This study performed a 1-year follow-up of the growth and development of 210 singleton full-term infants who were smaller than matched gestational age newborns in the first year after birth. We measured their body length, weight, and head circumference at 1, 3, 6, and 12 months old. Mean Z scores for various indicators in full-term infants of both sexes after birth continuously increased at various months of age. Most SGA infants showed rapid growth. Although growth rates were different in both sexes, the growth rate was highest in the first 3 months in all infants. Additionally, boys and girls showed a faster increase in weight and head circumference compared with that for body length. The rates of body weight, length, and head circumference 2 SDs below the mean at 12 months old were 1.90%, 10.48%, and 2.86%, respectively. These rates are consistent with those found by Karlberg and Albertsson-Wikland,[25] as well as by a meta-analysis that showed a catch-up growth rate of 87.4% among 11 studies.[15] However, a study from Korea reported a catch-up rate of <80% at 12 months. This difference between studies might be due to different definitions.[26] Studies have used weight, body length, and head circumference for evaluation, with catch-up growth defined as an increase in the corresponding physical index Z scores by >0.67.[14] Full-term SGA infants tend to have rapid catch-up growth after birth. Although the definition of a full-term SGA infant uses birth weight, the core of their catch-up growth lies in height. A recent study by Shi et al.[27] showed that, in full-term SGA infants, catch-up growth was maintained at >2 cm in the first few months, from <the 10th percentile to the interval between the 25th and 50th percentiles, with a median catch-up maintained until 2 years old. Catching up with such a growth trajectory and minimizing the risk of adverse health consequences for children may be optimal. Therefore, more attention should be paid to the body length in full-term SGA infants. A 2006 World Health Organization study in developing and developed countries showed that the nutritional needs of SGA infants are similar to those of their counterparts who are appropriate for gestational age[28] (e.g., the nutritional requirements of a 2.4-kg SGA newborn are the same as those of a 3.2-kg newborn, leading to catch-up). Therefore, feeding strategies for SGA children should mainly be based on gestational age rather than birth weight. This strategy should not only promote moderate growth, especially linear growth, to ensure a good nervous system outcome, but also avoid overfeeding to reduce the risk of long-term metabolic syndrome.[28] This possibility needs to be examined in China, where nutritional requirements might not be met in some areas and where the prevalence of metabolic syndrome is high.[29]

When assessing the growth rate of children, the potential effects of genetic factors should be considered. In this study, the body length at birth and at 12 months of age in full-term SGA infants of both sexes were analyzed in relation to the height of fathers, mothers, and both parents

combined. There were no associations of birth length in boys and girls with the height of the fathers, mothers, and both parents combined. However, at 12 months old, Pearson correlation coefficients between boys' height and height of the fathers, mothers, and both parents combined were significant, which indicated that the parents' height affected the child's height. The height in boys at 12 months of age was higher with a greater sum of the parents' height. In girls, Pearson correlation coefficients between girls' height and the mothers' and combined parents' heights were significant. Therefore, height in girls was higher at 12 months old with a greater combined parents' height. These findings are consistent with the positive correlation between the height of the offspring and that of parents in the normal population.[30–32]

This study has some limitations. First, its retrospective design resulted in inherent shortcomings. Additionally, the sample size was relatively small, which may explain why the correlations between children and parents' height had different coefficients. Finally, the study was performed in a single institution, and the findings have limited generalizability.

Conclusions

The physical growth of SGA full-term infants within 1 year may show a catch-up pattern, with the first 3 months showing the fastest growth rate. However, the catch-up speeds of weight and body length did not appear to be not balanced in this study. These findings indicate that child height is important. Therefore, in actual clinical work, the growth and development of full-term infants might have to be assessed on the basis of developmental and genetic characteristics. Assessment of these factors could also be the basis for developing improved individualized guidance and intervention.

Availability of data and materials

The data set supporting the results of this article are included within the article. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Author contributions

XF contributed to the conception of the study. YZ performed the data analysis and wrote the manuscript. JW and WLG carried out data collection. GYX helped with statistical analysis. All authors reviewed the results and approved the final version of the manuscript.

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