Length and Body Mass Index at Birth and Target Height Influences on Patterns of Postnatal Growth in Children Born Small for Gestational Age

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ABSTRACT. Objective. Previous growth studies on children born small for gestational age (SGA) indicate that birth length, weight, and target height are important predictors for postnatal catch-up growth in SGA. Their influences on different phases of catch-up growth are still not described. The aim of this study was to clarify the influences of target height, length, and nutritional status at birth on different phases of postnatal catch-up growth (infancy, childhood, puberty) in SGA and the long-term consequences.

Methods. Data were obtained from a longitudinal population-based growth study on Swedish children (N = 2815). Primary outcome measurements include heights, the changes in height standard deviation scores (SDS) during various phases of growth and relative risk for adult shortness.

Results. The difference in final height in children born SGA was attributable to their difference in target height and the magnitude of catch-up growth during the first 6 months of life, rather than the difference in length or body mass index (BMI) at birth. Length at birth showed negative influence on catch-up growth during infancy (0 to 2 years of age), but no significant influence thereafter. The BMI or weight for length SDS at birth showed no significant influence on catch-up growth during any growth phase. Target height showed positive influence on catch-up growth from the onset of childhood. Neither target height nor length and BMI at birth showed any significant influence on catch-up growth during puberty. The magnitude of catch-up growth during infancy, especially the first 6 months of life, is most critical in decreasing risk at adult shortness. We confirmed that the SGA group had a sevenfold greater risk for adult shortness than the non-SGA group (relative risk = 7.31; 95% confidence interval: 3.96–13.52). However, ~40% of children who were below –2 in height SDS at 2 years of age remained short at final height in both SGA and non-SGA groups. The mean height SDS of children born SGA increased by 1.65 from birth to final height, but the length deficit in centimeters at birth (~5.4 cm) persisted into adulthood (~5.9 cm).

Conclusions. BMI at birth is not related to postnatal catch-up growth in infants born SGA, but birth length and target height are important. The genetic influence on catch-up growth appears to start from the onset of childhood. Being short or becoming short during the first 2 years of life is similar in terms of risk for adult short stature. Pediatrics 1998;102(6). URL: http://www.pediatrics.org/cgi/content/full/102/6/e72; fetal growth retardation, body mass index, birth length, genetics, catch-up growth, short stature.

ABBREVIATIONS: SGA, small for gestational age; SDS, standard deviation score; WLSDS, weight for length standard deviation score; BMI, body mass index; CMS, centimeter score; RR, relative risk.

Children born small for gestational age (SGA) have a sevenfold greater risk of being short in adult stature than do normal children; ~8% of children born SGA are still below ~2 standard deviation score (SDS) in final height, which corresponds to 20% of the short adult population. The most critical period for catch-up growth is during the first 3 to 9 months of life. Birth length and target height are important predictors for catch-up growth in children born SGA. It is not known, however, whether they are equally good predictors during all three growth phases from birth to maturity—in infancy, childhood, and puberty. It is still a matter of debate whether postnatal catch-up growth is influenced by nutritional status at birth, ie, weight for length SDS (WLSDS), ponderal index, or body mass index (BMI). Some studies report that nutritional status at birth is related to postnatal catch-up growth in infants born SGA, but others have not been able to observe such a relationship.

The results of SGA growth studies are quite different. This may be related to a number of methodologic issues, including that 1) the definition of SGA can be based on weight, height, or both; 2) the cut-off points for defining SGA can be ~2 SDS or the 3rd, 5th, or 10th percentile; 3) the study can be hospital- or population-based; 4) premature and postmature infants as well as unhealthy infants could have been included/excluded; and 5) for the expression of outcome measurement, the results can be expressed in SDS being age- and sex-independent or in the measured centimeter unit. Furthermore, most previous studies have included a shorter period of follow-up, for a few years only and not often up to final height.

The aim of this study was to describe the influences of target height, length, and nutritional status at birth on different phases (infancy, childhood, puberty) of the longitudinal postnatal catch-up growth in children born SGA and their long-term consequences. The catch-up growth in height is expressed in both SDS and centimeter difference from the corresponding reference mean values.
METHODS

The data came from a large, population-based, longitudinal growth study on 3650 healthy full-term Swedish children that spanned from birth to maturity. To assess the parental height influence on growth patterns, only those children with data available on parental heights were included in the analyses (N = 2815). All height measurements were transformed into height SDS using the reference values for the same study population.1 WLSDS at birth was computed using the current reference values for Swedish children.11,12 The individual height SDS values also were expressed in centimeters by multiplying the SDS with the appropriate height SD for the particular age and sex. This height centimeter score (CMS) simply represents the difference of an individual height value from the reference mean of a particular age and sex. For instance, if the individual height SDS value was −1.5 and the SD of the growth reference height value was 4.0 cm, then the height CMS would be −1.5 × 4.0 = −6.0 cm, ie, 6 cm below the reference mean. The formula for computing height SDS and height CMS also can be expressed as: height SDS = (height observed − mean reference)/SD reference; height CMS = height observed − mean reference. The height CMS value thus is the same as the height SDS value, but without being divided by the SD of the reference values. The advantage of this height CMS expression—the distance of the individual height from the reference mean height—is that adjustment for height differences between ages and sexes have made.

Midparental height was calculated as the average of the mother’s height and father’s height. Target height (Y), ie, the genetic potential of final height, was computed as a linear function of midparental height (X) in centimeters (boys: X = 45.99 + 0.78X; girls: Y = 37.85 + 0.75X). The formula was developed from the simple linear regression analysis of final height and parental heights; it has been reported elsewhere and is different from the commonly applied corrected midparental height method (midparental height, ±6.5 cm), because the corrected midparental height method may underestimate target height for children with short parents, which is not the case with the new model.13,14 The target height values were converted into SDS and CMS based on the reference mean and SD.14 Delta height SDS was computed as the change in height SDS over a certain age interval, delta height CMS as the change in height CMS over a certain age period, and residual height SDS as height SDS minus target height SDS. The BMI was computed in the usual way, ie, weight (kg)/height^2(m). Born SGA was defined as below −2 SDS at birth length adjusted for gender and length of gestation.

There was on average 14.4 height measurements available for each child. An individual growth chart was produced for each child. Children who had gained <0.5 cm during the past year and had reached age at peak height velocity at least 2 years before the last examination were considered to have reached final height.1 The final height value was treated as height at 18 years of age during analyses. Children with a height gain of 0.5 cm or more during the last year were remeasured 1 year later. Height and weight values at 0, 0.5, 2, 8, and 18 years of age were selected for analyses because they can be claimed to describe the individual phases of postnatal growth as depicted by the Infancy—Childhood—Puberty growth model.18 The fetal growth was gauged by the length at birth, the infancy phase by growth from 0 to 2 years of age, the childhood phase by growth from 2 to 8 years of age, and the puberty phase by growth from 8 to 18 years of age. The growth during the first six months of life was analyzed separately, because it was regarded as the most critical period for postnatal catch-up growth in infants born SGA.19 Adult shortness was defined as below −2 SDS in final height.

The Student’s t test and Welch’s approximate t test (for unequal SD) were used to test the difference in means between two groups, or for one group with an expected mean value of zero. Analyses of variance and nonparametric Kruskal–Wallis test were used to compare the difference in the central tendency among several groups. F test and χ² test were used for examining significant trends over ordered groups. Multiple variable regression analyses were used to evaluate the influence of explanatory variables on postnatal catch-up growth during various phases. Only the two-tailed test was used, and a P value <.05 was regarded as statistically significant. All statistics were computed using SAS software.55

RESULTS

Postnatal Catch-up Growth in Children Born SGA

We report all the results for the two sexes combined because all of the results were similar and not statistically different (P > .05) between boys and girls. Table 1 gives the mean height and mean delta height expressed in both SDS and CMS for the total sample group (N = 2815); the SGA group (n = 108); and the non-SGA group from birth to 0.5, 2.0, 8.0, and 18.0 years of age. The sample size varied slightly at different ages because of a few missing values. The mean target height for the SGA groups was −0.26 SDS, or −1.9 cm below the reference mean value of zero (P < .01), and was also significantly below the mean target height of non-SGA children (P < .01). The catch-up growth in children born SGA was most impressive in the first 6 months of life; the mean delta height was 1.3 SDS, corresponding to an extra gain of 2.6 cm over the reference mean value (P < .001). The mean final height of children born SGA was −0.90 SDS, or −5.9 cm below the reference mean value. The actual mean final heights for boys and girls were 174.5 cm and 161.7 cm in the SGA group and 180.7 cm and 167.9 cm in the non-SGA groups, respectively.

The mean height SDS in the SGA group increased from −2.55 at birth to −0.95 at 2 years of age and remained at this level to final height. However, based on CMS, the picture was different (Table 1, Fig 1). The mean height CMS in the SGA group was −5.4 cm below the reference mean value at birth, which increased to −2.9 cm at 2 years of age and fell back to −5.9 cm in final height—similar to the mean deficit in length at birth (P > .20). The mean delta height from 2 to 8 years of age is close to zero when the calculation is based on SDS (0.12; P = .06), but significantly below zero when expressed in CMS (1.7; P < .001). The mean delta height SDS is close to zero from 8 to 18 years of ages (−0.04; P > .20), but significantly below zero when expressed in CMS (−1.3; P < .001).

SGA, Catch-up Versus Non-Catch-up Groups

The mean final height for children born SGA with height above −2 SDS at 2 years of age was −0.72 SDS, or −4.8 CMS, which is about 1.12 SDS, or 7.3 cm higher (P < .01) than the mean final height of children born SGA with height SDS below −2 at 2 years of age (−1.84 SDS, or −12.1 CMS). However, there is no significant difference in the mean target height between the two groups.

Patterns of postnatal growth were different for children born SGA with length SDS above versus below −2 at 2 years of age. For the SGA group with length SDS above −2 at 2 years of age, they show considerable catch-up growth during the first six months of life (mean delta height, 1.44 SDS or 2.8 CMS; P < .001). The delta height from 6 months to 2 years of age was significant based on SDS (0.29; P = .003), but not significant based on CMS (0.20; P = .53). There was virtually no change in the mean height SDS from 2 years of age to final height. However, the delta height CMS was significantly below...
There was no significant change in delta height SDS (0.2; \( P = .10 \)), but the delta height CMS was significantly below zero (−4.4; \( P < .001 \)). From 8 to 18 years of age, the delta height was above zero based on SDS (0.36; \( P = .04 \)), but close to zero based on CMS (−0.3; \( P = .80 \)).

Figure 2 gives the scatterplot of final height SDS versus midparental height SDS with target height reference lines for the children born SGA. For the children born SGA with height SDS below zero from 2 to 8 (−1.3; \( P = .002 \)) and 8 to 18 years of age (−1.4; \( P = .003 \)). The children born SGA who were below −2 SDS at 2 years of age showed no significant catch-up growth during the first 6 months of life. From 0.5 to 2 years of ages, there was no significant change in delta height SDS (−0.31; \( P = .23 \)), but the delta height CMS was significantly below zero (−2.5; \( P < .001 \)). From 2 to 8 years of ages, there was no significant change in delta height SDS (0.28; \( P = .10 \)), but the delta height CMS was significantly below zero (−4.4; \( P < .001 \)). From 8 to 18 years of age, the delta height was above zero based on SDS (0.36; \( P = .04 \)), but close to zero based on CMS (−0.3; \( P = .80 \)).
years of age \((n = 11)\), 5 of 11 were below \(-2\) SDS at final height and also happened to be below \(-2\) SD of their target height. For the children born SGA with height SDS above \(-2\) at 2 years of age \((n = 77)\), 3 of 77 were below \(-2\) SDS at final height, and 8 of 77 were below \(-2\) SDS of their target height. None of the children born SGA managed to reach a final height that was 1 SD above their target height.

Relative Risk (RR), SGA Versus Non-SGA Groups

Figure 3 shows the percentage of adult shortness in relation to height SDS at 2 years of age (Fig 3, a) and target height SDS (Fig 3, b). The children born SGA who were still below \(-2\) SDS at 2 years of age had an RR of 11.7 (95% CI: 3.2–42.21; \(P < .01\)) of adult shortness compared with the children born SGA who had reached a height above \(-2\) SDS at 2 years of age. The percentage of adult shortness increased over groups with shorter target heights in both the SGA and the non-SGA groups (χ² test for trend; \(P < .05\)). Table 2 shows that the RR of adult shortness for the SGA versus non-SGA group is 7.31 (95% CI: 3.96–13.52; \(P < .001\)). However, no increased risk could be observed if height SDS were below \(-2\) at 2 years of age, ie, ~40% remain short into adult stature for children who were below \(-2\) SDS at 2 years of age in both SGA and non-SGA groups. The increased risk for adult shortness in the SGA versus the non-SGA group was more evident in groups with higher target heights.

Final Height, Catch-up Growth, Target Height, Length, and BMI at Birth

Table 3 shows the growth patterns in subgroups of children born SGA \((n = 108)\) with various ranges of final height SDS. The target height SDS, residual height SDS, BMI, and WLSDS at birth also are given for each subgroup. For the six groups with different ranges of final height SDS, there was no difference in birth length SDS, BMI, and WLSDS at birth (Kruskal–Wallis test, \(P > .05\)). For the groups with larger final height SDS, the target height SDS, the residual height SDS at birth, and the delta height SDS during the first 6 months of life were larger \((F\) test for trend, \(P < .01\)). There was no significant difference in delta height SDS from 0.5 to 2.0, 2.0 to 8.0, and 8.0 to 18.0 years of age among the six groups. The SGA group with final height SDS below \(-2\) showed virtually no catch-up growth during the entire growth process. Significant catch-up growth in height SDS from 0.5 to 2 years of age was seen only in the SGA group that had a final height SDS above zero. The magnitude of catch-up growth in height SDS during puberty (8 to 18 years of age) was small in any subgroup.

Multiple variable regression was used to evaluate the influences of various factors on the magnitude of catch-up growth (delta height SDS) in different phases of growth in children born SGA. When variable entry level was set at 0.05, no interaction items could be detected between any two factors. BMI at birth showed no significant influence on postnatal catch-up growth during any phase of growth in any model \((P > .05\). If BMI was replaced by WLSDS in regression model, the results were virtually the same. We still retain BMI into the model to obtain the adjusted estimates for birth length and target height influences on catch-up growth (Table 4). Length SDS at birth showed negative influence on catch-up growth during the infancy phase (0 to 2 years of age), but no significant influence thereafter. Target height showed positive influence on catch-up growth from the onset of childhood (0.5 to 2 years of age) and was the only significant factor during childhood phase (2 to 8 years of age). The magnitude of catch-up growth during puberty phase (8 to 18 years of age) is small.
DISCUSSION

In this study, we have described the postnatal longitudinal growth patterns and the influences of birth length, BMI at birth, and target height in children born SGA. The new understanding we gained from the study is that the target height, or genetic influence on postnatal catch-up growth, appears to start from the onset of childhood, and it seems to be the only significant factor during childhood phase of growth. The size at birth negatively influenced the postnatal catch-up growth during infancy phase but had no significant influence thereafter, whereas BMI at birth showed no significant influence during any phase of growth. Another important message is that being born short or becoming short during the first 2 years of life is similar in terms of increased risk for adult shortness. Approximately 40% of children who were below −2 SDS at 2 years of age remained short in adult stature in both the SGA and the non-SGA group. We also have described the different pictures of the postnatal catch-up growth between the height change expressed in SDS and in CMS.

It is difficult to compare our results with those from other studies because the definition of SGA might be different by birth weight and/or birth
length. Birth weight is commonly used because it is much more frequently taken as the standard measure of fetal size at birth. We defined SGA as below 

-2 SDS at birth length (adjusted for gender and length of gestation), because this definition may be more accurate for examining postnatal growth in height.4 Other study design differences were that our series was population-based, not hospital-based; it had a long follow-up period, from birth to maturity; and only healthy full-term infants were included. For these reasons, we cannot make direct comparisons with the results of other studies.

What determines the magnitude of catch-up growth in children born SGA is still not clear. It has been reported that both birth length and midparental height are correlated with the magnitude of catch-up growth in children born SGA.1 We used target height, a linear function of midparental height, as a measurement of genetics potential in stature.14 During the first 6 months of life, the dimension of catch-up growth was dominated by birth size: shorter children born SGA showed larger catch-up growth. From 0.5 to 2.0 years of age, the catch-up growth was influenced by both birth size: shorter children born SGA showed larger catch-up growth. From 0.5 to 2.0 years of age, the catch-up growth was influenced by both growth in children born SGA is still not clear. It has been reported that both birth length and midparental height are correlated with the magnitude of catch-up growth in children born SGA.1 We used target height, a linear function of midparental height, as a measurement of genetics potential in stature.14 During the first 6 months of life, the dimension of catch-up growth was dominated by birth size: shorter children born SGA showed larger catch-up growth. From 0.5 to 2.0 years of age, the catch-up growth was influenced by both birth size: shorter children born SGA showed larger catch-up growth. From 0.5 to 2.0 years of age, the catch-up growth was influenced by both
catch-up growth from birth to 18 years of age can be explained by length at birth and target height. Whether WLSDS, ponderal index, or BMI influences postnatal catch-up growth in children born SGA is still a matter of debate. We could not find any significant influence of BMI or WLSDS at birth on postnatal catch-up growth, as has been reported by other investigators. Proportionate and disproportionate (lower weight for length) infants born SGA seem to have an equal magnitude of catch-up growth. The important factor in early life is length at birth, ie, the magnitude of fetal growth retardation. Later, however, the target height (genetic) influence takes over.

In accordance with a previous report, we observed that children born SGA had an approximate seven times greater risk for adult shortness than did non-SGA children. The risk was higher for children with shorter target heights (shorter parents). In children born SGA who showed impressive catch-up growth during the first 2 years of life, the risk for adult shortness decreased dramatically, from ~40% to 4%. To our surprise, ~40% of children with height SDS below ~2 at 2 years of age remain short in adult stature, whether or not born SGA. Being born short or becoming short during the first 2 years of life is similar in terms of increased risk for adult shortness. The understanding here is that we do not really need to know whether a child was born short or not for adult shortness prognosis. This conveys a significant clinical message to pediatricians. However, the response to growth-promoting treatments may be different in the two groups. It is not clear whether SGA and non-SGA short children have similar responses to the same dose of growth hormone treatment. Some studies indicate that children born SGA might need a higher dose of growth hormone to achieve a desirable growth response.

Should we use SDS or CMS to describe catch-up growth? Most growth studies used SDS. This study shows a striking difference in results when CMS rather than SDS is used. For instance, based on SDS, the mean height in children born SGA increased by 1.65 units from birth to final height, which is an impressive catch-up. If we convert SDS into centimeters using the reference mean values, but not in height can be significant when expressed in centimeters (lower weight for length) infants born SGA seem to have an equal magnitude of catch-up growth. The important factor in early life is length at birth, ie, the magnitude of fetal growth retardation. Later, however, the target height (genetic) influence takes over.

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