นิพนธ์ต้นฉบับ • Original Article

รูปแบบการเจริญเติบโตในเด็กไทยที่มีน้ำหนักต่ำกว่าอายุครรภ์

กิตติพงษ์ คงสมบูรณ์
ภาควิชาเวชศาสตร์ป้องกันและสังคม คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ นครนายก 26120

Pattern of Growth in Thai Small-for-Gestational-Age Infants

Kittipong Kongsomboon
Department of Preventive and Social Medicine, Faculty of Medicine, Srinakharinwirot University, Nakhonnayok 26120

หลักการและวัตถุประสงค์: เด็กที่มีน้ำหนักต่ำกว่าอายุครรภ์มีความเสี่ยงต่อภาวะตัวเตี้ย ผลการเรียนต่ำ และปัญหาด้านพฤติกรรม เด็กที่มีน้ำหนักต่ำกว่าอายุครรภ์ส่วนใหญ่จะเจริญเติบโตเท่ากับเด็กปกติภายในระยะเวลา 2 ปีแต่รูปแบบการเจริญเติบโตจะแตกต่างกันตามเชื้อชาติ วัตถุประสงค์ของการศึกษานี้เพื่อนำเสนอรูปแบบการเจริญเติบโตในเด็กไทยที่มีน้ำหนักต่ำกว่าอายุครรภ์ ณ ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี

วิธีการศึกษา: ทำการศึกษาในเด็กคลอดครบกำหนด ณ ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี ในช่วงปี ค.ศ.2000 ถึง 2009 ที่มีน้ำหนักต่ำกว่าอายุครรภ์ กำหนดให้เด็กแรกคลอดที่มีน้ำหนักต่ำกว่า 10 เปอร์เซนต์ไทล์จากกราฟการเจริญเติบโตตามเพศเป็นเด็กที่มีน้ำหนักต่ำกว่าอายุครรภ์และกำหนดให้มีการเจริญเติบโตตามเกณฑ์ปกติเมื่อน้ำหนักตามอายุอยู่ในตำแหน่งตั้งแต่ 10 เปอร์เซนต์ไทล์ขึ้นไป นำเสนอระยะเวลาที่เด็กน้ำหนักต่ำกว่าอายุครรภ์มีน้ำหนักตามเกณฑ์ปกติด้วยกราฟ Kaplan-Meier survival estimates และประเมินการเปลี่ยนแปลงของน้ำหนักต่อความยาวตามกลุ่มอายุเพื่อทำนายภาวะน้ำหนักตัวเกินปกติและโรคอ้วนเมื่ออายุ 25-36 เดือนด้วยกราฟ receiver operating characteristic (ROC)

ผลการศึกษา: เด็กน้ำหนักต่ำกว่าอายุครรภ์มีจำนวนทั้งสิ้น 45 ราย เด็กกลุ่มนี้จำนวนทั้งหมดเป็นเด็กที่มีน้ำหนักต่ำกว่าอายุครรภ์แบบไม่สมส่วน ค่ามัธยฐานของระยะเวลาที่น้ำหนักเพิ่มขึ้นจนเท่าเกณฑ์ปกติคือ 4 เดือน (Inter-quartile range = 2-21 เดือน) เด็กน้ำหนักต่ำกว่าอายุครรภ์ส่วนใหญ่ (ร้อยละ 70) มีน้ำหนักตามเกณฑ์ภายในปีแรกและร้อยละ 80 ของเด็ก

Background and Objective: Small for gestational age (SGA) infants are at risk of short stature, poor academic performance and behavioral problems. The majority of SGA infants catch-up growth within two years but the pattern of growth differs in different ethnics. The objective of this study was to determine the pattern of growth in Thai SGA infants at Her Royal Highness Princess Maha Chakri Sirindhorn Medical Center (HRH MSMC).

Methods: All subjects were born at HRH MSMC between 2000 and 2009 who were termed SGA infants were included in the study. SGA was defined as birth weight below the 10th percentile of gender-specific standard growth curve and catch-up growth was defined as weight for age achieves the 10th percentile. Time to catch-up growth of SGA infants is presented as Kaplan-Meier survival estimates. The change of weight for length Z score between age group predicted overweight and obesity (Z score > 1SD) at 25-36 months of age with receiver operating characteristic (ROC) curve.

Results: Forty-five SGA infants were recruited in the present study and all of them were asymmetrical SGA. Median time for catch-up growth was four months (Inter-quartile range = 2-21months). Most of SGA infants (70%) caught-up normal growth in the first year and 80% within two years. After two years, 14% of SGA infants failed to catch-up growth. The area under ROC curve to predict overweight and obesity at 25-36 months of age between 1-6 months and 7-12 months was 0.43 (95%CI: 0.15-0.71), between 7-12 months and 13-18 months was 0.79 (95%CI:

**Corresponding Author: Kittipong Kongsomboon, Department of Preventive and Social Medicine, Faculty of Medicine, Srinakharinwirot University, 62 Moo 7 Rangsit-Nakhonnayok Road, Ongkharak, Nakhonnayok 26120, Thailand. E-mail: kittipoo@swu.ac.th*

กลุ่มนี้มีน้ำหนักตามเกณฑ์ภายในระยะเวลา 2 ปี หลังจาก 2 ปีไปแล้วมีเด็กน้ำหนักต่ำกว่าอายุครรภ์ที่ไม่สามารถมีน้ำหนักตัวตามเกณฑ์ปกติร้อยละ 14 พื้นที่ใต้กราฟ ROC ของการเปลี่ยนแปลงน้ำหนักต่อความยาวในแต่ละช่วงอายุที่ใช้ทำนายภาวะน้ำหนักตัวเกินเกณฑ์ปกติและโรคอ้วนที่อายุ 25-36 เดือน ได้แก่ ช่วงอายุ 1-6 เดือนและ 7-12 เดือน คือ 0.43 (95%CI: 0.15-0.71), ช่วงอายุ 7-12 เดือนและ 13-18 เดือน คือ 0.79 (95%CI: 0.36-1.00), และช่วงอายุ 13-18 เดือนและ 19-24 เดือน คือ 0.74 (95% CI: 0.38-1.00)

สรุป: เด็กคลอดครบกำหนด ณ ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารีที่มีน้ำหนักต่ำกว่าอายุครรภ์ มีการเติบโตตามเกณฑ์ปกติร้อยละ 80 ภายในระยะเวลา 2 ปี และร้อยละ 70 เติบโตตามเกณฑ์ปกติภายในระยะเวลา 1 ปี น้ำหนักต่อความยาวที่เปลี่ยนแปลงในช่วงอายุ 7-12 เดือนถึง 13-18 เดือนและช่วงอายุ 13-18 เดือนถึง 19-24 เดือนสามารถทำนายภาวะน้ำหนักตัวเกินเกณฑ์ปกติและโรคอ้วนในช่วงอายุ 25-36 เดือน อย่างมีนัยสำคัญทางคลินิก

คำสำคัญ: น้ำหนักตัวต่ำกว่าอายุครรภ์, การเติบโตตามเกณฑ์ปกติ, รูปแบบการเติบโต

0.36-1.00), between 13-18 months and 19-24 months was 0.74 (95% CI: 0.38-1.00).

Conclusions: Within two years, 80% of term asymmetrical SGA infants at HRH MSMC caught up normal growth and 70% of them caught-up within one year. Weight for length changed from 7-12 months to 13-18 months and from 13-18 months to 19-24 months were clinically significant to predict overweight and obesity at 25-36 months of age.

Keywords: Small for gestational age (SGA), catch-up growth, pattern of growth

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Introduction

Small for gestational age (SGA) infants are at risk of having short stature, poor academic performance, and behavioral problems[1]. The most common cause is still unknown but fetal nutritional deficiency, exposure to chemical agents, genetic, or chromosomal abnormalities are among the factors likely to play a role[2]. The majority of SGA infants catch-up growth within two years but about 8% of them remain with short stature[3]. In the first three months, catch-up growth for weight dramatically increases as a study of McCowan et al[4] in New Zealand found 84% of term SGA infants. There are several factors affecting catch-up growth such as intrinsic growth defect (placental weight), perinatal factors (sex, gestational age, birth length, hospital stay), and postnatal environment[2,4,5]. Some studies reported that the catch up growth in SGA infants increases adiposity and persists beyond catch-up[6-9]. Previous studies mostly reported results from Europe and America but a few studies have examined cases in Asia or in developing countries. In developing countries, Ugwu[10] reported in 2011 that prevalence of term SGA infants in Nigeria was 6.6% of total live birth, similar to Thailand. However, there are no reports of SGA growth pattern in Thai infants.

The aim of the present study is to determine the pattern of growth in Thai SGA infants at Her Royal Highness Princess Maha Chakri Sirindhorn Medical Center (HRH MSMC). The pattern of growth would help health care personnel during surveillance time to catch-up growth to improve growth rate of SGA infants.

Materials and Methods

Term SGA who were born at HRH MSMC between 2000 and 2009, were eligible in the present study. The Faculty of Medicine, Srinakharinwirot University ethics committee approved the research (code: SWUEC/EX 30/2555). The design was retrospective study and data from medical records at HRH MSMC were collected. The data comprised maternal age, gestational age, birth weight, gravid, modes of delivery, sex of newborn, birth length, and head circumference at birth. Weight and length of children were recorded at visiting time of well baby clinic from birth to four years of age and were

measured by trained nurse aids. The means of weight and length were calculated at age groups of 1-6, 7-12, 13-18, 19-24, and 25-36 months. The author altered weight for age and weight for length to Z score based on the Least Mean Square (LMS) method[11] and then changed Z score of weight for age to percentile by Z score table.

Gestational age was calculated from last menstrual period and term newborn was gestational age between 37 to 42 weeks. SGA was birth weight below the 10th percentile of gender-specific standard growth curve according to definition of the World Health Organization (WHO)[12]. Catch up growth was defined as a weight for age achieves the 10th percentile.

Nutritional status according to WHO defined as severe thinness means Z score < -3SD, thinness (means Z score < -2SD), overweight (means Z score > 1SD), and obesity (means Z score > 2SD). The present study devided nutritional status into Z score of weight for length was > 1SD (overweight to obesity) and ≤ 1SD (normal to severe thinness).

Quantitative data is presented as mean ± standard deviation and qualitative data presented as frequency (%). Time to catch-up growth of SGA infants presented as Kaplan-Meier survival estimates. Then we calculated incidence of catch-up growth, median time of SGA (median survival time), and rate of catch-up growth at visiting time of well-baby clinic with survival function.

The delta represented the change of weight for length Z score between age group: delta1 was Z score at 7-12 months of age minus Z score at 1-6 months of age, delta2 was Z score at 13-18 months of age minus Z score at 7-12 months of age, and delta3 was Z score at 19-24 months of age minus Z score at 13-18 months of age. Then delta1, delta2, and delta3 were compared to predict overweight and obesity (Z score > 1SD) at 25-36 months of age with receiver operating characteristic (ROC) curve, p-value of less than 0.05 was considered significant.

Results

Forty-five SGA infants were recruited and all of them were asymmetrical SGA (restriction of growth but not the head circumference) and complete followed up at three months. 43 of them were singleton and the others were twins. Baseline characteristic were shown in table 1.

Table 1 Characteristics of study subjects

Variables		Total number
Maternal age (mean ± SD, years)	27.7 ± 5.4	44
Gestational age (mean ± SD, weeks)	37.8 ± 0.9	45
Birth weight (mean ± SD, kilograms)	2.1 ± 0.2	45
Gravid		45
- 1st (%)	27 (60.0)	
- More than 1st (%)	18 (40.0)	
Maternal disease		45
- No (%)	34 (75.6)	
- Yes* (%)	11 (24.4)	
Mode of delivery		45
- Caesarean section (%)	21 (46.7)	
- Normal labour (%)	19 (42.2)	
- Vacuum extraction (%)	3 (6.7)	
- Forceps extraction (%)	2 (4.4)	
Sex of newborn		45
- Male (%)	19 (42.2)	
- Female (%)	26 (57.8)	
Congenital anomaly		45
- No (%)	39 (86.7)	
- Yes** (%)	6 (13.3)	

*mild pre-eclampsia 5, severe pre-eclampsia 2, eclampsia 1, HIV+ve 1, Grave's disease 2

**hypospadia 2, undescended testis 1, undescended testis with hydronephrosis 1, small ventricular septal defect 1, congenital hypothyroid 1

Median time for catch up growth of SGA infants was four months with Inter-quartile range = 2-21 months (Figure 1).

Most of SGA infants (69.7%) caught up-growth within one year, 79.5% caught-up growth within two year. After two years, three children (13.7% of SGA infants) failed to catch-up growth, which persisted through four years of age (Table 2).

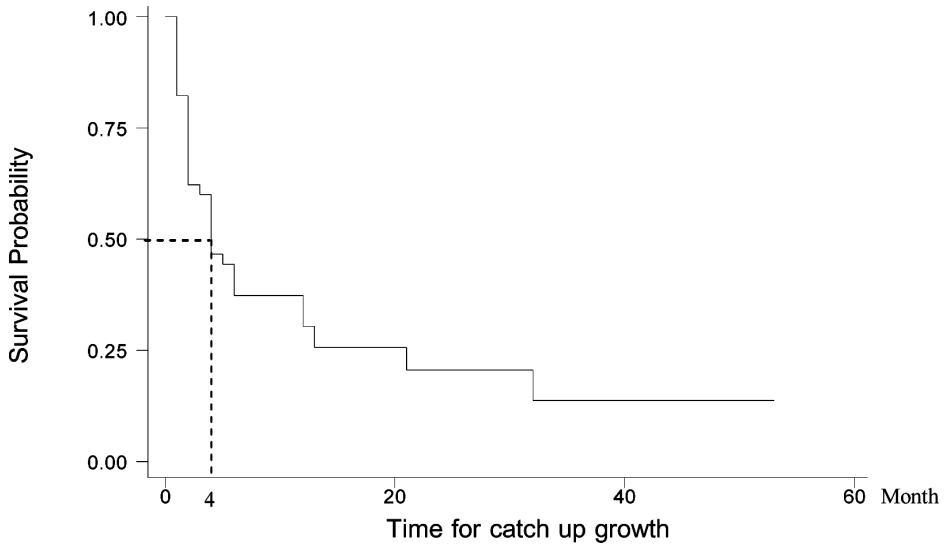

Figure 1 Kaplan-Meier survival estimates of SGA infants demonstrated a median survival time for catch up-growth.

Table 2 Survival function calculated proportion of small for gestational age (SGA) at visiting time of well baby clinic.

Month	Total (N)	Catch up growth (%)	SGA (%)	95% Confidence interval
1	45	8 (17.8)	82.2	67.6-90.7
2	37	9 (37.8)	62.2	46.5-74.6
4	27	7 (53.3)	46.7	31.7-60.3
6	19	4 (62.7)	37.3	23.4-51.2
9	19	0 (62.7)	37.3	23.4-51.2
12	16	3 (69.7)	30.3	17.6-44.1
18	13	2 (74.3)	25.7	13.9-39.1
24	8	2 (79.5)	20.5	10.0-33.7
36	3	1 (86.3)	13.7	3.8-30.0
48	3	0 (86.3)	13.7	3.8-30.0

Note: Overall incidence rate of catch up growth among small for gestational age babies = 8.0 per 100 person-month (95% CI = 5.8-11.1)

Z score of weight for length change of delta 2 had the most area under ROC curve and delta 1 had the least area under ROC curve to predict overweight and obesity at 25-36 months of age (Figure 2).

Delta 2 and delta 3 had area under ROC curve above 0.5 but delta 1 had not. All of them were not statistical significantly different (Table 3).

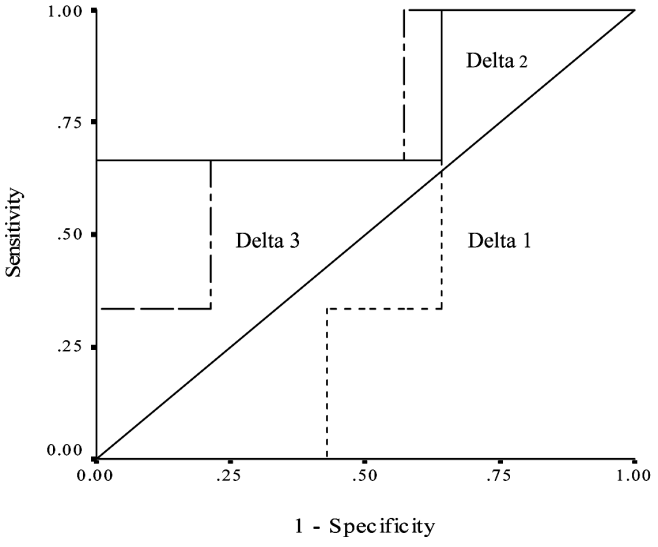

Figure 2 ROC curve presents Z score of weight for length change between 1-6 months and 7-12 months (delta1), between 7-12 months and 13-18 months (delta2), and between 13-18 months and 19-24 months (delta3) to predict overweight and obesity at 25-36 months of age.

Table 3 Comparing areas under ROC curve of delta1, delta 2, and delta 3 to predict overweight and obesity at 25-36 months of age

	Number	ROC area	95% Confidence interval	p-value
Delta 1	17	0.4286	0.1495-0.7077	0.1013*
Delta 2	17	0.7857	0.3568-1.0000	
Delta 3	17	0.7381	0.3827-1.0000	

*Chi-squared test

Delta 1 = Z score of weight for length change between 1-6 months and 7-12 months

Delta 2 = Z score of weight for length change between 7-12 months and 13-18 months

Delta 3 = Z score of weight for length change between 13-18 months and 19-24 months

Discussion

All of SGA infants in the present study were asymmetrical SGA who had late onset of intrauterine growth restrictions. Their birth weights were below 10th percentile but spared their head circumferences. Growth pattern of these infants were affected by genetic factor and hormonal change[13]. In the present study, median time of SGA infants were four months, their weight gains were more accelerate at early postnatal life and most of them (70%) could catch-up growth within one year. Fidanci et al[14] reported that accelerated weight gain in SGA infants associated with higher Ghrelin during neonatal period (affected from intrauterine growth restriction), and Iñiguez et al[15] showed that Ghrelin had an orexigenic drive to sustain postnatal catch-up growth in SGA infants especially during the first year of life. Bozzola et al[16] found that leptin, which is mainly produced by white adipose tissue, was low in SGA infants, but increased during the catch-up growth.

The adiposity in present study is measured by weight for length according to Marjorie reviewed from Centers for Disease Control and Prevention (CDC) in 2005[7] that early childhood should use weight for length (height) for assessing overweight and obesity instead of body mass index because the muscle, bone, and fat mass components in early childhood are difference from older children. The study of Olivier et al[8] reported that catch-up growth in early life of SGA infant is risk to overweight and obesity in later life. The changes are obvious when they grow up to adulthood and may explain by the development of insulin resistance. The same as study of Barbara et al[9] found that rapid infant weight gain relates to risk of overweight at four years of age. The present study finds that weight for length changing from 7-12 months to 13-18 months and 13-18 months to 19-24 months relate to overweight and obesity at 25-36 months of age despite they are not statistical significantly different. The reason is small sample size which leads to imprecision (wide confidence interval) and low power to get statistical significant difference. Nevertheless, they have area under ROC curve of more than 0.5 so they still have clinical significance. Their catch-up growth ended when they achieved their genetic potential, generally within two years but 10-15% of those infants weight and height deficiency remains[13], a value which is close to the 14% of the present study. In these cases (14%), they should be investigated to determine if there are genetic disorders, hormonal dysfunctions, or other common pediatric diseases.

The present study recruited only SGA infants with enough data for survival analysis. These samples are 45 of a total of 120 SGA infants, may not represent the whole population or may have precision problem. In a next study, the author would collect data from well baby clinic and design as a prospective study. Although several factors affect growth pattern, postnatal factors may also affect to weight gain such as infant feeding or chronic diseases[4]. Infant feeding, however, may depend on socio-economic status of their parents in the rural areas around HRH MSMC so the present study concludes growth pattern on this status. And the chronic diseases that they have a few congenital anomalies as show in table 1. All of them were under treatments at the department of pediatric so these diseases have no significant effects on growth pattern. Another factor is that all of them are term and asymmetrical SGA which specify the growth pattern.

In conclusion, 80% of term asymmetrical SGA infants at HRH MSMC could catch-up growth within two years and 70% within one year. Weight for length change from 7-12 to 13-18 months and from 13-18 to 19-24 months were clinical significant to predict overweight and obesity at 25-36 months of age but they were not statistically significant difference.

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