

# Small-for-Menstrual-Age Infants: Different Subgroups Detected Using Individualized Fetal Growth Assessment

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**Abstract:** Our purpose was to study the individual fetal growth patterns of infants who were born small-for-menstrual-age. Growth in the second and third trimester was assessed in 98 small-for-menstrual-age infants, using individual fetal growth curves generated by the growth model:  $P = c(t)^{k+s(t)}$ . Growth indices were compared with those previously reported for that method in infants with normal growth. The small-for-menstrual-age infants were distributed into four growth patterns, ie, infants with either normal or decreased second-trimester growth indices, who, by the time of birth, succeed or fail in fulfilling their individual growth potential. These four growth patterns appear to be associated with different pathophysiological mechanisms and incidences of perinatal complications. Individual fetal growth assessment identifies differences in genetically determined growth and differentiates between fetuses who achieve their growth potential and those with growth failure who are at greater risk for fetal compromise. © 1994 John Wiley & Sons, Inc.

**Indexing Words:** Individual fetal growth curve standards · Rossavik growth model · Fetal growth · Intrauterine growth retardation · Small-for-menstrual age

## INTRODUCTION

Fetal growth assessment has traditionally consisted of comparing anatomic measurements of individual fetuses to population standards. As an alternative, one can use the fetus as its own control by comparing fetal anatomic measurements or birth characteristics to expected values generated via the Rossavik growth equation.<sup>1-13</sup> The general form of this growth model is:

$$P = c(t)^{k+s(t)}$$

In this equation,  $P$  is the anatomic parameter;  $k$  is a fixed coefficient determined by the anatomic

characteristics of the parameter being measured<sup>3,7</sup>;  $c$  is related to genetically determined growth<sup>4,5</sup>;  $s$  appears to represent an unknown regulatory system that modifies genetically determined growth<sup>4</sup>; and  $t$  is the duration of growth of the parameter. Coefficients  $c$ ,  $s$ , and  $t$  are determined from the data obtained in serial second-trimester scans.<sup>3</sup> With these coefficients, models can be specified to determine individual growth curves for various fetal anatomic parameters, reflecting the growth potential of individual fetuses.<sup>3</sup>

In the absence of factors interfering with their fetal growth potential, fetuses follow their projected individual growth curves very closely.<sup>12</sup> Hence, fetal growth assessment in the third trimester can be individualized by comparing the actual measurements of various fetal anatomic parameters with the values of their respective individual fetal growth curve standards. Deviation from these standards can be expressed as a percentage of the projected value or as a ratio between actual and projected values, the latter called the Growth Potential Realization Index

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(GPRI) by Deter et al.<sup>12</sup> The GPRI values for various measurements have been combined into a Neonatal Growth Assessment Score (NGAS).<sup>13</sup> Deter et al demonstrated that an NGAS  $\leq 14.7$ , based on GPRI values for weight and for abdominal circumference (AC) and head circumference (HC), discriminated well between infants with normal growth and those with evidence of fetal growth failure, without being affected by differences in genetic growth potential.<sup>13</sup>

Applying the individualized fetal growth assessment method to pregnant women who delivered macrosomic infants, we previously demonstrated several patterns of excessive fetal growth corresponding to different pathophysiological mechanisms.<sup>14</sup> In this study we evaluated the fetal growth patterns of infants who are born small-for-menstrual-age by cross-sectional standards, using coefficients  $c$  to reflect genetically determined growth and the NGAS and GPRI values to indicate the degree of fulfillment of the individual fetal growth potential.

#### MATERIALS AND METHODS

The sample studied consisted of 98 consecutive pregnant women with singleton pregnancies who met the following criteria: (1) ultrasonography dating by crown-rump length before 14 weeks, menstrual age (MA); (2) two ultrasonography scans between 15.0 and 26.0 weeks, MA,<sup>10</sup> separated by an interval of at least 5 weeks<sup>15</sup>; and (3) live birth, with birth weight below the 10th percentile of the age-specific birth-weight distribution curve, previously established for the York County, Pennsylvania population.<sup>16</sup>

All women were examined with a dynamic image scanner equipped with a 3.5-MHz sector or linear transducer (models: ATL Mark 8 [Advanced Technology Laboratories, Bellevue, WA], Diasonics DRF-400 [Diasonics, Milpitas, CA], Toshiba 270-A Alpha Sonolayer [Toshiba America Medical Systems, Inc, Yonkers, NY], Acuson 128, [Acuson, Mountain View, CA]). All measurements were obtained between 15.0 and 26.0 weeks, MA, by technician or physician ultrasonographers. Short (HSA) and long (HLA) axes of the head taken from the outer contour of the skull profile were used for the calculation of head circumference (HC) and head cube.<sup>10</sup> For the abdominal circumference (AC) and abdominal cube calculations, the long (ALA) and short (ASA) axes were measured from the outer contour of the abdominal profile at the level of the portoumbilical vein complex. The longest dimension of the femur

diaphysis was taken as the femur diaphysis length (FDL).

Individual fetal growth curve standards for HC, AC, and estimated fetal weight (EFW) were determined for each of the 98 small-for-menstrual-age fetuses, through use of the Rossavik growth model:

$$P = c(t)^{k+s(t)}$$

Values for the coefficient  $c$ , the coefficient  $s$ , and the start point (the latter used for the calculation of  $t$ ) were determined for HC, AC, FDL, and head and abdominal cubes from slope values calculated from the data obtained in the two second-trimester scans.<sup>10</sup>

The equations used to generate the individual growth curves and to calculate EFW from head and abdominal cubes are listed in Table 1.<sup>1,6,10</sup> The coefficients  $a_0$ ,  $a_1$ ,  $b_0$ , and  $b_1$  used in equations 7 and 8 and fixed  $k$  used in equation 9 are listed in Table 2.<sup>7,10,11</sup> For HC and AC, the values of  $a_0$ ,  $a_1$ ,  $b_0$ , and  $b_1$ , were determined from data where the circumferences were calculated from diameter measurements and not directly obtained from the measurements of contours.<sup>11</sup>

All infants were examined within 24 hours of delivery. The weight, fronto-occipital head circumference, and abdominal circumference (at the superior border of the umbilicus) measured at birth in each infant were compared with their predicted values. For these comparisons, the parameter values predicted at 38.0 weeks, MA, were used in all women who delivered from 38.1 weeks through 42.1 weeks, MA. This was based on individual fetal growth assessment data of normal infants showing that little growth occurs after 38.0 weeks, MA.<sup>8,9,12</sup> Anatomic parameter values predicted at the actual birth age were used when delivery occurred at or before 38.0 weeks, MA.

Evaluation of the growth achieved by individual fetuses was made using Growth Potential Realization Index (GPRI) values, determined with the following equation<sup>12</sup>:

$$\text{GPRI} = \frac{\text{actual birth parameter value}}{\text{predicted birth parameter value}} \times 100.$$

[corrected for systematic errors when needed]

The GPRI values for weight, AC, and HC were then combined to calculate the Neonatal Growth Assessment Score (NGAS) for each individual fetus, using the following equation<sup>13</sup>:

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**TABLE 1**  
Equations Used for the Generation of Individual Growth Curve Standards Based on the Rossavik Growth Model<sup>1,6,10</sup>

1. Head or abdominal circumferences	$(LA/2 + SA/2) \times 3.14$
2. Head (A) or abdominal (B) cubes before 26 weeks, MA	$(LA \times SA)^{1.5}$
3. Head cube (A) after 26 weeks, MA	$(BPD \times OFD)^{1.5}$
4. Slope between measurements ( $P_1, P_2$ ) at two points ( $T_1, T_2$ ) before 26 weeks, MA	$\frac{P_2 - P_1}{T_2 - T_1}$
5. Start point (SP)	$-(P_2 - (\text{slope}) \times T_2)$ slope
6. Duration of growth ( $t$ )	Menstrual age - SP
7. Coefficient $c$	$\log_e(c) = a_0 + a_1 + \log_e(\text{slope})$
8. Coefficient $s$	$s = b_0 + b_1 \times (c)$
9. Rossavik growth model	$P = c(t)^{k+s(t)}$
10. Weight-estimating equation	$EFW = 0.46138 \times [1.337(t_A)^{(-0.41 \times 0.00917 \times t_A)}] \times A$ $+ 0.55029 \times [3.517(t_B)^{(-0.074 - 0.00074 \times t_B)}] \times B$

where  
 $t_A$  = duration of growth of head cube  
 $t_B$  = duration of growth of abdominal cube

LA: long axis.  
 SA: short axis.  
 BPD: biparietal diameter.  
 OFD: occipitofrontal diameter.  
 EFW: estimated fetal weight.

**TABLE 2**  
Coefficients Used in the Calculation of Coefficients  $c$  and  $s$ , as Well as the Fixed Values of  $k$  Required for Specifying Rossavik Growth Models Used in the Generation of Individual Growth Curve Standards<sup>7,10,11</sup>

Fetal Anatomic Parameters	$k$	$a_0$	$a_1$	$b_0$	$b_1$
AC	1.048	-0.1166	1.1802	0.005171	-0.00576
HC	1.300	-0.6580	1.4068	0.001950	-0.01067
FDL	1.156	0.1055	1.2957	0.004660	-0.03845
A	3.856	-0.5197	4.0876	-0.011177	-0.56226
B	3.284	0.1344	3.6820	0.001768	-0.22800

$P = c(t)^{k+s(t)}$   
 AC: abdominal circumference.  
 HC: head circumference.  
 FDL: femur diaphysis length.  
 A: head cube.  
 B: abdominal cube.

$$NGAS = \sqrt{\frac{(GPRI_{WT} - 100)^2 + (GPRI_{AC} - 100)^2}{-100)^2 + (GPRI_{HC} - 100)^2}}$$

The 98 infants were divided into two groups on the basis of Deter's NGAS criterion value of 14.7 discriminating between normal and abnormal growth outcomes: ie, for infants with normal growth outcome:  $NGAS \leq 14.7$ , and for infants with intrauterine growth retardation (IUGR):  $NGAS > 14.7$ . In both groups, the individual coefficient  $c$  values, taken as indicators of growth in the second trimester, were compared with the normal ranges for coefficients  $c$  values observed by Hata et al<sup>17</sup> in infants with normal growth outcome at birth as determined by rigorous neo-

natal evaluation. These ranges were: 0.6107 cm/week to 0.8243 cm/week for HC; 0.0045 cm<sup>3</sup>/week to 0.0201 cm<sup>3</sup>/week for head cube; 0.8770 cm/week to 1.3770 cm/week for AC; 0.0071 cm<sup>3</sup>/week to 0.0575 cm<sup>3</sup>/week for abdominal cube; and 0.1867 cm/week to 0.2915 cm/week for FDL.<sup>13</sup> The coefficients  $c$  for head and abdominal measurements were considered decreased if the coefficients  $c$  for either circumference and/or cube were found below the normal ranges. On the basis of these comparisons, the infants of the two NGAS groups were further separated into groups with normal coefficients  $c$  or those with one or more coefficients  $c$  below Hata et al's normal ranges<sup>17</sup>.

In each of these four subgroups, the individual

GPRI values were compared with the ranges of GPRI values observed in Deter's sample of infants with normal growth outcome (ie, 95% to 105% for HC, and 91% to 108% for AC and weight).<sup>12</sup> The growth pattern achieved at birth, based on these three anatomic parameters, was determined for each infant.

The prevalence of risk factors for growth retardation<sup>18</sup> were determined for each of the four subgroups. These risk factors included prepregnancy weight <100 lbs, average weekly weight gain >0.5 lb in nonobese patients (<155 lbs), heavy smoking (20 or more cigarettes a day), alcohol consumption (three times a week or more), use of any habit-forming drug or chemical, anemia (Hgb <10 g/dL), chronic hypertension with or without renal disease, and pregnancy-induced hypertension. A diastolic blood pressure of  $\geq 90$  mm Hg and standard textbook definitions were used to define these hypertensive disorders.<sup>19</sup>

Similarly, the prevalence of perinatal complications—which included suspected fetal compromise before and during labor, Apgar score <7 at 5 minutes, hypoglycemia (venous serum glucose <40 mg/dL), anemia (venous hematocrit <40), polycythemia (venous hematocrit >65), hyperbilirubinemia (total serum bilirubin >12 mg/dL), and malformations—was determined. There were no neonatal deaths, hypocalcemia (venous serum calcium <7 mg/dL), nor other complications except for those related to prematurity.

Before labor, fetal compromise was suspected based on the combination of a nonreactive non-stress test with a positive contraction stress test and/or a poor biophysical evaluation.<sup>20</sup> A poor biophysical evaluation was defined as absence of fetal breathing during an observation period of 30 minutes, accompanied or not by a decrease or absence of fetal movement and muscle tone.<sup>20</sup> During labor, fetal compromise was suspected on the basis of a fetal heart rate tracing showing late and/or atypical variable decelerations with decreased or absent beat-to-beat variability and/or a fetal scalp pH <7.25.<sup>20</sup>

Statistical evaluations (independent *t* test, *z* test of proportions) were made when appropriate, with standard statistical methods using the Statistical Package for the Social Sciences (SPSS).<sup>21</sup> In all statistical evaluations, a *p* value of 0.05 or less was taken to indicate a statistically significant difference.

## RESULTS

By the design of this study, the birth weights of the 98 infants were all below the 10th percentile

of our age-specific birth-weight-distribution curve.<sup>15</sup> When evaluated by individualized growth assessment, 32 (32.7%) of these 98 infants had a normal growth outcome at birth as evidenced by a NGAS  $\leq 14.7$  (range: 3 to 14.5). The other 66 (67.3%) infants had a NGAS >14.7 (range: 15.3 to 40.8). The demographic characteristics of the pregnant women of these two groups are listed in Table 3.

Table 4 describes the second-trimester growth profiles of the 98 infants based on the comparisons of the coefficients *c* for five anatomic parameters with the normal ranges.<sup>17</sup> Of the 32 infants with normal NGAS values ( $\leq 14.7$ ), 7 (21.9%) had normal coefficients *c*, and 25 (78.1%) had one or more coefficients *c* below their respective normal ranges. In the latter 25 infants, decreased coefficient *c* values were found in 17 (68%) infants for the head, in 20 (80%) infants for the abdomen, and in 6 (24%) infants for the femur, respectively. Three (12%) infants had decreased coefficients *c* for all anatomic parameters.

In contrast, 30 (45.5%) of the 66 infants with abnormal NGAS ( $\geq 14.7$ ) had all coefficients *c* within their respective normal ranges.<sup>17</sup> In the other 36 (54.5%) infants, decreased coefficients *c* were found for one or more anatomic parameters, ie, for the head in 25 (69.4%) infants, for the abdomen in 17 (47.2%) infants, and for the femur in 12 (33.3%) infants, respectively. Four (11.1%) of these 36 infants had decreased coefficients *c* for all five anatomic parameters. The greater preva-

**TABLE 3**  
Demographic Characteristics of Patients Who Delivered Small-for-Menstrual-Age Infants with Normal and Abnormal Growth by Individual Fetal Growth Assessment

Demographic Characteristic	Neonatal Growth Assessment Score				
	Normal ( $\leq 14.7$ )		Abnormal ( $> 14.7$ )		
Race	<i>n</i>	%	<i>n</i>	%	
White	25	78.1	46	69.7	
Black	6	18.8	14	21.2	
Hispanic	1	3.1	6	9.1	
	<u>Mean</u>	<u>SD</u>	<u>Mean</u>	<u>SD</u>	
Maternal age (year)	22.7	4.7	23.4	5.1	NS*
Parity	2.0	1.4	1.8	1.0	NS
Prepregnancy weight (lbs)	132.3	36.9	122.5	27.3	NS
Weight gain/week (lbs)	0.75	0.3	0.72	0.4	NS
Menstrual age at delivery (week)	39.5	2.3	38.7	1.2	NS
Number of patients	32		66		

\*NS: not significant;  $p \geq 0.05$  (independent *t*-test, two-tailed comparison).

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**TABLE 4**  
**Second-Trimester Growth Patterns of 98 Small-for-Menstrual-Age Neonates Evaluated by the Individualized Growth Assessment Method**

Second-Trimester Growth Pattern			Neonatal Growth Assessment Score			
Coefficient <i>c</i>			Normal ( $\leq 14.7$ )		Abnormal ( $> 14.7$ )	
Head	Abdomen	Femur	<i>n</i>	%	<i>n</i>	%
N*	N	N	7	21.9	30	45.5
↓†	N	N	3	9.4	11	16.7
N	↓	N	6	18.8	7	10.6
N	N	↓	1	3.1	4	6.1
↓	↓	N	10	31.2	6	9.1
↓	N	↓	1	3.1	4	6.1
N	↓	↓	1	3.1	—	—
↓	↓	↓	3	9.4	4	6.1
Number of neonates			32		66	

Normal ranges ( $\pm 2$  SD) for coefficients *c* expressed in cm or cm<sup>3</sup>/week (Hata)<sup>17</sup>:

Head circumference: 0.6107 to 0.8243.

Head cube: 0.0045 to 0.0201.

Abdominal circumference: 0.8770 to 1.3770.

Abdominal cube: 0.0071 to 0.0575.

Femur diaphysis length: 0.1867 to 0.2915.

\*N: Within normal range.

†↓: Below normal range.

lence of normal second-trimester growth indices in infants with NGAS  $> 14.7$  compared with those with NGAS  $\leq 14.7$  was statistically significant (45.5% versus 21.9%;  $z$ : 2.472;  $p < 0.05$ ).

Table 5 shows the GPRI values for HC, AC, and weight in the 98 infants distributed into four groups as a function of their NGAS value at birth and their second-trimester coefficient *c* values. Seventeen (53.1%) of the 32 infants with normal NGAS ( $\leq 14.7$ ) had one or more GPRI values slightly below the normal ranges for GPRI<sub>HC</sub>, GPRI<sub>AC</sub>, and GPRI<sub>WT</sub>.<sup>12</sup> However, the largest differences between any of these GPRI values and the lower limits of the normal ranges were 3% for HC, 1% for AC, and 4% for weight, ie, differences that were all within the technical variability of the method.<sup>22</sup> In contrast, low GPRI values for AC and weight were found in 40 (60.6%) and 64 (97.0%) of the 66 infants with abnormal NGAS ( $> 14.7$ ), respectively. Twenty-six (40.6%) of these 66 infants had also low GPRI values for HC. These low GPRI values were below the lower limit of their respective normal ranges by as much as 15% for HC, 22% for AC, and 30% for weight. It should also be noted that 70.7% of this group had two or more abnormal GPRI values (compared with 11.1% in the group with normal NGAS values), the relative frequency being 63.3% in the group with normal coefficient *c* values and 78% in the group with decreased coefficient *c* values.

For information, Table 6 shows the prevalence

of risk factors for fetal growth retardation in the patients in each of the four growth groups. Of the seven patients with chronic hypertension in the growth groups with NGAS  $> 14.7$ , three had associated chronic renal disease, ie, renal transplant with immunosuppressive therapy, renal insufficiency, and nephrotic syndrome, respectively.

Similarly, Table 7 shows the perinatal complications observed in each of the four growth groups. Of the eight cases of fetal compromise, five (all in the NGAS  $> 14.7$  groups) were suspected at the time of antepartum fetal assessment. The other three cases occurred during labor and required primary caesarean-section delivery. Congenital abnormalities in three neonates consisted of neonatal diabetes mellitus with a serum glucose at birth of 345 mg/dL, single umbilical artery, and multiple severe anomalies, respectively. The NGAS value of the latter infant was 13.6.

None of the seven infants with both normal coefficients *c* and normal NGAS ( $\leq 14.7$ ) had risk factors for intrauterine growth retardation or abnormal perinatal events. The small number of infants in each cell precluded meaningful statistical evaluation of the differences between subgroups.

### DISCUSSION

Four different growth patterns were identified by individualized fetal growth assessment in infants who are considered growth retarded by the tradi-

**TABLE 5**  
**Growth Potential Realization Indices (GPRI) of 98 Small-for-Menstrual-Age Neonates Classified into Four Growth Patterns by the Individualized Fetal Growth Assessment Method**

GPRIc			Neonatal Growth Assessment Score							
			Normal ( $\leq 14.7$ )				Abnormal ( $> 14.7$ )			
			Second-Trimester Coefficients c		Second-Trimester Coefficients c		Second-Trimester Coefficients c		Second-Trimester Coefficients c	
HC	AC	Weight	Normal	Decreased	Normal	Decreased	Normal	Decreased		
			n	%	n	%	n	%	n	%
N*	N	N	1	14.3	14	56.0	—	—	—	—
↓†	N	N	1	14.3	4	16.0	—	—	—	—
N	↓	N	—	—	1	4.0	—	—	—	—
N	N	↓	4	57.1	4	16.0	11	36.7	8	22.2
↓	↓	N	—	—	—	—	—	—	2	5.6
↓	N	↓	1	14.3	2	8.0	2	6.7	5	13.9
N	↓	↓	—	—	—	—	11	36.7	10	27.8
↓	↓	↓	—	—	—	—	6	20.0	11	30.6
Number of neonates			7		25		30		36	

Normal ranges for GPRI values (Deter)<sup>12</sup>:

Head circumference (HC): 95% to 105%.

Abdominal circumference (AC): 91% to 108%.

Weight: 91% to 108%.

Normal ranges ( $\pm 2$  SD) for coefficients c expressed in cm or cm<sup>3</sup>/week (Hata)<sup>17</sup>:

Head circumference: 0.6107 to 0.8243.

Head cube: 0.0045 to 0.0201.

Abdominal circumference: 0.8770 to 1.3770.

Abdominal cube: 0.0071 to 0.0575.

Femur diaphysis length: 0.1867 to 0.2915.

† ↓ : Below normal range.

\*N: Within normal range.

**TABLE 6**  
**Risk Factors for Intrauterine Growth Retardation in 98 Pregnant Women with Small-for-Menstrual-Age Infants Classified into Four Growth Patterns by the Individualized Fetal Growth Assessment Method**

Risk Factors	Neonatal Growth Assessment Score							
	Normal ( $\leq 14.7$ )				Abnormal ( $> 14.7$ )			
	Second-Trimester Coefficients c		Second-Trimester Coefficients c		Second-Trimester Coefficients c		Second-Trimester Coefficients c	
	Normal	Decreased	Normal	Decreased	Normal	Decreased	Normal	Decreased
	n	%	n	%	n	%	n	%
Prepregnancy weight <100 lb	—	—	4	16.0	5	16.7	7	19.4
Weight gain/week <0.5 lb	—	—	3	12.0	5	16.7	9	25.0
Smoking ( $\geq 20$ cigarettes/day)	—	—	4	16.0	9	30.0	9	25.0
Alcohol abuse	—	—	3	12.0	—	—	3	8.3
Drug abuse	—	—	2	8.0	2	6.7	4	11.1
Hypertensive disease	—	—	2	8.0	8	26.7	6	16.7
Chronic $\pm$ renal disease	—	—	—	—	4	13.3	3	8.3
Pregnancy-induced	—	—	2	8.0	4	13.3	3	8.3
Anemia (Hct <30)	—	—	2	8.0	—	—	—	—
Unicornuate uterus	—	—	—	—	2	6.7	—	—
Women with one or more risk factors	—	—	16	64.0	21	70.0	25	69.4
Number of patients	7		25		30		36	

tional cross-sectional fetal growth curve standards.

The first growth pattern consisted of infants (7.1%) with normal second-trimester coefficients c and normal NGAS values at birth. Third-trimester ultrasonographic evaluations would identify these fetuses by showing small anatomic

measurements for menstrual age but normal deviations of their actual measurements from the values predicted by the individual growth curves. They most likely represent normal infants located in the lower end of the birth-weight distribution for the population, who fully achieve their normal growth potential and should not be con-

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TABLE 7

Perinatal Complications in 98 Small-for-Menstrual-Age Infants Classified into Four Growth Patterns by the Individual Fetal Growth Assessment Method

Perinatal Complications	Neonatal Growth Assessment Score							
	Normal ( $\leq 14.7$ )				Abnormal ( $> 14.7$ )			
	Second-Trimester Coefficients <i>c</i>				Second-Trimester Coefficients <i>c</i>			
	Normal		Decreased		Normal		Decreased	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Suspected fetal compromise	—	—	1	4.0	2	6.7	5	13.9
5-Min. Apgar score $< 7$	—	—	—	—	1	3.3	—	—
Hypoglycemia ( $< 40$ mg/dL)	—	—	—	—	2	6.7	3	8.3
Anemia (H.c.t. $< 40$ )	—	—	—	—	3	10.0	1	2.8
Polycythemia (H.c.t. $> 65$ )	—	—	3	12.0	5	16.7	6	16.7
Hyperbilirubinemia ( $> 12$ mg/dL)	—	—	2	8.0	4	13.3	1	2.8
Congenital abnormalities	—	—	1	4.0	—	—	2	5.6
Number of neonates with one or more perinatal complications	—	—	7	28.0	11	36.7	14	38.9
Number of neonates	7		25		30		36	

sidered growth retarded. These infants are at low risk for adverse perinatal outcome. In fact, no risk factors for intrauterine growth retardation or perinatal complications were observed in infants with such a growth pattern in our study.

The second pattern included infants (25.5%) with small coefficients *c* but normal NGAS values, indicating complete fulfillment of their reduced growth potential. Ultrasonographic evaluation in the third trimester would also show small-for-menstrual-age anatomic measurements and normal deviations of actual measurements from predicted ones. The only difference from the fetuses of the previous group would be the small coefficients *c* observed in the second trimester. Reduced growth potential in these fetuses may result from malformation, chromosomal anomaly, or simply from a still-unknown genetic growth controller set at a lower level (genetically small infants). Pathologic events altering normal genetically determined growth in the first or second trimester could also be responsible for this pattern. Because complications occurred in only 7 (28.0%) of the 25 infants in this study, this growth pattern may be associated with a much more benign course than that observed when the growth indices at birth were abnormal, ie, NGAS  $> 14.7$  and decreased GPRI value(s).

In the third growth pattern (30.6% of the infants), normal coefficient *c* values were observed, although these infants had abnormal growth indices at birth. Third-trimester ultrasonographic evaluation of these fetuses would be expected to reveal small-for-menstrual-age anatomic measurements and abnormal negative deviations of actual measurements from their predicted values.

These fetuses with a normal genetic growth potential experience growth failure late in gestation, presumably from malnutrition and/or hypoxia resulting from complications or conditions altering genetically determined growth.<sup>23,24</sup>

The fourth growth pattern included infants (36.7%) who exhibited both small coefficients *c* and abnormal growth indices at birth. This group includes fetuses with reduced growth potential, who suffer from growth failure later in gestation, or normal fetuses exposed to factors adversely affecting genetically determined growth throughout gestation. Third-trimester ultrasonographic evaluation would also show small-for-menstrual-age fetuses and ultrasonographic measurements falling significantly below their individual fetal growth curves.

More low maternal weight gain, hypertensive disease, heavy smoking, perinatal complications, and suspected fetal compromise before and during labor were observed in the pregnancies associated with the latter two growth patterns. Fetuses experiencing growth failure in the third trimester, irrespective of growth potential, appear to be at the greatest risk for adverse perinatal outcome and, for that reason, require intensive surveillance for fetal well-being.

This study shows that individualized growth assessment may add considerably to the information provided by cross-sectional growth assessment. In these small-for-menstrual-age infants, traditionally considered growth retarded, individual growth assessment identified differences in genetically determined growth and differentiated between fetuses who achieve or fail to achieve their individual growth potential. These growth

patterns seem to result from different pathophysiological mechanisms and represent different categories of risk for adverse perinatal outcome. The complexity of fetal growth retardation is further evidenced by the observation that the process involved one or several anatomic measurements in various combinations, early and/or late in gestation.

If, among small fetuses, those at greatest risk for fetal compromise can be identified, individualized fetal growth assessment would offer considerable help to the clinician in managing pregnancies with suspected growth retardation. Prospective studies are, of course, needed to establish more firmly the relationship between growth patterns and perinatal outcome and to validate the clinical usefulness of this method.

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