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Nutritional practices and growth velocity in the first month of life in extremely low gestational age newborns

Camilia R. Martin, MD^{a,b}, Yolanda F. Brown, MD^b, Richard A. Ehrenkranz, MD^c, T. Michael O'Shea, MD,MPH^d, Elizabeth N. Allred, MS^{e,f}, Mandy B. Belfort, MD,MPH^b, Marie C. McCormick, MD,ScD^g, Alan Leviton, MD^e, and the ELGAN Study Investigators

^a Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, MA

^b Division of Newborn Medicine, Children's Hospital, Harvard Medical School, Boston, MA

^c Department of Pediatrics, Yale University School of Medicine, New Haven, CT

^d Department of Pediatrics, Wake Forest University, Winston-Salem, NC

^e Neuroepidemiology Unit, Department of Neurology, Children's Hospital, Harvard Medical School, Boston, MA

^f Department of Biostatistics, Harvard School of Public Health, Boston, MA

^g Department of Society, Human Development and Health, Harvard School of Public Health, Boston, MA

Abstract

OBJECTIVES—The goals of this study were to describe nutritional practices in the first month of life for a large cohort of extremely low gestational age newborns and to determine the impact of these nutritional practices on growth velocity over the same period.

METHODS—The sample included 1187 infants born at 23 weeks to 27 weeks of gestation, at 14 institutions, between 2002 and 2004. Inclusion criteria included survival until day 28 and weight information for both day 7 and day 28. Growth velocity, expressed as grams per kilogram per day (g/kg/day), was calculated for the interval between days 7 and 28. Nutritional practices during the first week and on days 14, 21, and 28 were compared to current nutritional guidelines in the literature. Multivariable logistic regression models estimated the contribution of limited nutrition to limited growth velocity.

RESULTS—Protein and fat delivery approximated current nutritional recommendations while carbohydrate and total caloric delivery did not. Despite this, growth velocity of our study infants exceeded the current guideline of 15 g/kg/day. Nevertheless, we found extrauterine growth restriction (i.e., weight for gestational age below the 10th centile) in 75% of infants at 28 days, as compared to only 18% at birth. A growth velocity of 20-30 g/kg/day was associated with infants' maintaining or exceeding their birth weight Z-score, with rates in the upper range for the gestationally youngest infants. Early (day 7) nutritional practices were positively associated with growth velocity measured between days 7 and 28.

CONCLUSION—The early provision of nutrients is an important determinant of postnatal growth. Extrauterine growth restriction remains high in extremely premature infants even when they achieve a growth velocity rate within current guidelines.

Corresponding author: Camilia R. Martin, MD 330 Brookline Avenue, Rose-318, Boston, MA 02215. cmartin1@bidmc.harvard.edu. Tel: 617-667-3276. Fax: 617-667-7040..

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Keywords

Infant, premature; nutrition; growth velocity

INTRODUCTION

Most extremely low gestational age newborns (ELGANs, infants born before 28 weeks of gestation) remain in the neonatal intensive care unit (NICU) during the time that would be equivalent to their third trimester. In that period, one of the goals of the NICU team is to provide nutrition to the infant to achieve a growth velocity (GV) similar to intrauterine GV. However, most infants gain less weight than third trimester fetuses *in utero*. As a result of this growth deficit, a large proportion of infants exhibit extrauterine growth restriction (weight below the 10th centile for postmenstrual age) ¹⁻⁵ and this subnormal growth often persists into early childhood ⁶⁻⁸.

Implementation of early parenteral and enteral nutrition to low birth weight infants during the first 24 hours of life results in a rapid regain of weight lost, improved overall weight gain, and earlier achievement of full enteral feedings ⁹. Early and high protein delivery also has been associated with improved weight gain and head growth ¹⁰. In addition, intersite differences in postnatal growth are partially explained by variations in neonatal nutrition practices ^{11, 12}. Higher calorie and protein intake accounted for significant intersite differences in GV of premature infants at six NICUs even after adjusting for case mix and medical characteristics ¹².

Yet, the advancement of nutritional intake is often limited by the preterm infant's ability to metabolize the nutrients offered ¹³⁻¹⁵ and the competing priority of the neonatologist to minimize potential complications with strategies that limit nutrition delivery (e.g. fluid restriction to decrease likelihood of patent ductus arteriosus or chronic lung disease) ¹⁶⁻¹⁸. In addition, the ELGAN Study population, like other low gestational age samples ¹⁹, has a disproportionate number of infants who are growth restricted before birth perhaps limiting the potential for postnatal growth. Further, many ELGANs have increased energy requirements associated with severe illness. ²⁰ In view of these factors, some have suggested that postnatal growth failure in the preterm infant is inevitable ^{21, 22}.

However, there are consequences of postnatal growth failure: persistent growth failure in childhood and potential adverse effects on later neurodevelopment ^{23, 24}. Thus, it remains important to understand the nutritional factors that influence growth in the early neonatal period to identify factors that might maximize growth. In this study, we examine the impact of nutritional practices on growth velocity during the first month of life in a large cohort of ELGANs.

METHODS

Sample

Our sample is comprised of infants enrolled in the ELGAN Study, a prospective cohort study designed to identify characteristics and exposures that increase the risk of structural and functional neurologic disorders in preterm infants. During the years 2002-2004, women delivering between 23 and 27 6/7 weeks of gestation at one of 14 participating institutions in 11 cities in 5 states were asked to enroll in the study. The enrollment and consent processes were approved by the individual institutional review boards. Mothers were approached for consent either upon antenatal admission or shortly after delivery, depending on clinical circumstance and institutional preference. 1249 mothers consented (83%) and approximately

260 women were either missed or did not consent to participate (17%). A total of 1506 infants enrolled in the ELGAN Study. For our analysis of GV through the first 28 days of life, we excluded infants who died before the 28th postnatal day (n=209) and those infants who did not have a weight for both days 7 and 28 (n=110), resulting in a sample of 1187 infants.

Data Collection

Infant Characteristics—Gestational age (GA) estimates were based on a hierarchy of the quality of available information. Most desirable were estimates based on the dates of embryo retrieval or intrauterine insemination or fetal ultrasound before the 14th week of gestation (62%). When these were not available, reliance was placed sequentially on a fetal ultrasound at 14 or more weeks of gestation (29%), last menstrual period without fetal ultrasound (7%), and GA recorded in the log of the NICU (1%). The birth weight Z-score represents the number of standard deviations the infant's birth weight is above or below the median weight of infants at the same GA in a referent sample ²⁵.

Nutritional Practices—Detailed nutritional data were collected daily for the first 7 days of life, then weekly on days 14, 21, and 28. Type and volume of intravenous solutions including composition of parenteral nutrition (PN) and type and volume of enteral feedings including caloric additives were recorded. All nutritional practice variables summarize nutritional intake from both parenteral and enteral routes.

Growth Velocity—Serial weights were measured for each day in the first postnatal week, then on days 14, 21 and 28. GV or the rate in growth expressed as g/kg/day is the primary outcome. Because of the expected weight loss during the first postnatal week ² and the likelihood that the impact of early nutritional management would not be seen until at least day 7, we calculated GV for the interval between days 7 and 28 [GV in g/kg/day: $1000 \times ((wt_{28} - wt_7) / wt_7) / (28 - 7)$].

Statistical Analyses

We evaluated the following hypotheses, expressed in their null form:

1. The daily amount of each nutritional offering (*i.e.*, protein, carbohydrate, fat and total calories) does not differ from current recommended guidelines.
2. The amount of each nutrient offered on selected days does not vary with gestational age or birth weight Z-score.
3. GV does not vary with gestational age or birth weight Z-score.
4. GV does not vary with the amount of each nutritional offering on each of the selected days.

The amount of each nutritional offering on each of the selected days was categorized into quartiles. Thus, the lowest quartile reflects the bottom 25% of intake for each nutrient. Among infants who survived to 28 days and were weighed then, as well as on day 7, the upper bound of the lowest GV quartile was 13.8 g/kg/day, the median was 18.3 g/kg/day, and the lower bound of the highest quartile was 22.6 g/kg/day.

We created multivariable logistic regression models to estimate the contribution of limited nutrition on days 7, 14, and 21 to limited GV. In early sets of analyses, we adjusted for GA in two ways, by both week of gestation (23, 24, 25, 26, 27), and by groups of weeks (23-24, 25-26, 27). Each provided almost identical results. Here we present data adjusted for GA in groups of weeks. In addition, the models were adjusted for all other nutrient variables for

that day, total fluid intake, birth weight Z-scores, and severity of illness as measured by the Score for Neonatal Acute Physiology-II (SNAP-II) ²⁶. We present the contributions of nutritional practices to GV in the lowest quartile as odds ratios with 95% confidence intervals.

RESULTS

Nutritional practices

Our findings should be viewed in light of the amounts of nutrients currently recommended for premature infants ²⁷⁻²⁹. One recommendation is that protein delivery be initiated within 24 hours of birth at 1.5 – 3.0 g/kg/day with daily advancement in 0.5 – 1.0 g/kg/day increments to a goal of 3.5 to 4.0 g/kg/day. In our cohort of infants, the median protein intake provided by both parenteral and enteral routes was 1.0 g/kg/day on day 1 (Table 1) and 3.5 g/kg/day by day 4 (data not shown). Median protein intake remained 3.5 g/kg/day between days 3 and 28.

Fat and lipid administration is recommended at 0.5 to 1.0 g/kg/day in the first or second day after birth, with incremental advancement to a goal of 3.0 to 3.5 g/kg/day. The majority of our infants did not receive any fat on day 1 (median intake 0 g/kg/day) but by day 3 the median intake provided by both parenteral and enteral routes was 1.4 g/kg/day. By the end of the first postnatal week the median fat intake was 3.1 g/kg/day. For all quartiles of fat intake, the total increased with advancing postnatal age.

The median carbohydrate intakes include both intravenous glucose infusions and complex carbohydrate sources in formulas and breast milk. However, the majority of infants received only minimal amounts of enteral nutrition during the first week of life, so these values mostly reflect intravenous glucose infusions. Glucose infusions are recommended at an initial rate 6 mg/kg/min (8.6 g/kg/day) increasing to 10 mg/kg/min (14.4 g/kg/day) by day 7. In our cohort, the median carbohydrate initially offered was 4.4 g/kg/day and intake increased progressively to 9.3 g/kg/day on day 7 and to almost 11 g/kg/day on day 28.

The generally recommended range for caloric intake considering both parenteral and enteral routes is 115-130 kilocalories per kilogram per day (kcal/kg/day), with the understanding that some severely ill preterm infants (e.g. with sepsis, necrotizing enterocolitis) may require an even higher number of calories. This goal was rarely achieved in our sample. The median energy intake on day 3 was 59 kcal/kg/day, which advanced progressively to 105 kcal/kg/day on day 28. Throughout the first month, the 75th centile did not exceed 104 kcal/kg/day.

The association of nutrient delivery during the first 28 days with birth weight and gestational age is shown in Table 2. The range for protein was narrow and did not vary with GA. On the other hand, gestationally older newborns tended to receive more fat, carbohydrates, and total calories than infants born at earlier GAs. The median carbohydrate, fat, protein, calories, and fluids varied minimally with birth weight Z-score.

Growth Velocity

The recommended GV of 15 g/kg/day is intended to approximate intrauterine growth rates (though this remains controversial)³⁰. For almost all GA groups and birth weight Z-score categories, GV was greater than 15 g/kg/day with the highest growth velocities (33 and 34 g/kg/day) among the gestationally youngest whose birth weight was more than one standard deviation below the expected median (Table 3).

Median GV remained in the 15-20 g/kg/day range for infants who received between the 25th and 75th centile of every nutritional factor on all 5 of the days assessed (Table 4). The GV

approximated 17g/kg/day for infants at the 25th centile of most nutrients, 18 for infants at the 50th centile and 19 for infants at the 75th centile.

Despite a GV above the current recommended rate of 15 g/kg/day, the weight Z-score for the vast majority of ELGANs on day 28 was lower than at birth (Figure 1). The rising straight line in the figure lies where an infant's dot would be expected to fall if the day 28 weight Z-score was identical to the birth weight Z-score. Dots below the line indicate a lower weight Z-score on day 28 than at birth. At birth, 18% of our cohort had a weight Z-score below -1; in contrast, at 28 days of life, 75% of our cohort had a weight Z-score below -1 (data not shown).

The median growth velocity of infants who maintained or exceeded their birth weight Z-score at 28 days ranged between 20 and 30 gm/kg/day with the highest GV rates seen among the gestationally youngest infants (Table 5).

We created multivariable logistic regression models predicting the lowest quartile of GV in light of information about nutrition characteristics on days 7, 14, and 21 while controlling for GA, birth weight Z-score, SNAP-II, total fluid intake, and all other nutritional variables on that day (Table 6). Infants who received protein, fat, and carbohydrate amounts in the lowest quartile on day 7 were more likely than others to have a GV in the lowest quartile. In contrast, these associations were not evident for nutrients on day 14 and only total carbohydrate delivery was important at day 21.

DISCUSSION

Although the nutritional goal is to have ELGANs gain weight in the NICU at the rate they would have if they remained *in utero*, this is often not achieved¹⁻⁴. In our multi-center study of the nutritional practices at 14 NICUs we, too, found that a substantial proportion of infants did not maintain their position in the weight Z-score distribution despite GV rates that exceed the current recommendation.

Nutritional practices

The initiation of protein just fell below recommendations with the median intake on the first day of life at 1.0 versus 1.5 g/kg/day. However, the advancement goal was reached by day 4. Likewise, although fat was unlikely to be initiated as recommended, goal fat intakes were achieved by day 6. In contrast, the remaining nutritional recommendations were not achieved. Our study did not have the ability to determine the reasons for suboptimal carbohydrate and total calories delivery such as limited central line access or the presence of metabolic abnormalities (acidosis, hyperglycemia, hypertriglyceridemia).

Given the different summary measures of nutritional intake in different studies, it is difficult to compare the nutritional attainment of our cohort with previously published studies. However, given these limitations, our cohort does appear to demonstrate a more rapid advancement of protein delivery than has been described in the past in similar cohorts. In a study of six NICUs and for infants < 30 weeks of gestation, the mean protein intake was 0.6 g/kg/day on day 3 and only 2.1 g/kg/day on day 7.¹² Similarly, in another study, infants ≤ 30 weeks of gestation received less than 2 g/kg/day of protein at day 7.²²

Growth velocity

The median GVs in strata of our population almost always surpassed the recommended 15 g/kg/day. Interestingly, this was also true in all quartiles of nutrient delivery despite the fact that current recommendations for all nutritional parameters were not met. However, despite GVs above 15 g/kg/day and protein and fat delivery reaching goal amounts as

recommended, a vast majority of the infants failed to maintain the weight Z-score they had at birth. We consider two explanations for this observation: (1) our definition of GV (chosen interval and calculation) does not reflect growth accurately; and, (2) current recommendations to approximate intrauterine growth rates are too low to achieve the desired effect in extremely low GA newborns.

In our cohort, GV in the first week ranged from -8 to -15 g/kg/day, while the GV from birth to 28 days ranged from 10-11 g/kg/day. We ultimately decided to calculate GV from day 7 to day 28, rather than from birth to day 28, because we felt that weight changes after the first week would more accurately reflect nutritional practices instituted during the first week. However, in the literature, GV has been defined in many different ways. Calculated GVs vary in having different starting points (birth weight, nadir, time regained birth weight; and different time intervals (birth to 28 days, birth to discharge, nadir to discharge, time regained birth weight to discharge, etc.)³¹. That GV has not been defined consistently makes comparisons between studies difficult. In an effort to standardize and accurately measure growth velocity, Patel et al proposed that GV be calculated with an exponential model using weights from two time points. Using Patel's exponential equation the median growth velocity for our cohort was 15.5 g/kg/day, only slightly higher than recommended, versus 18.3 g/kg/day using our calculation.

The failure of our cohort to achieve the desired growth despite a GV of greater than 15 g/kg/day may reflect the current inadequacy of this recommendation. As previously discussed, the GV recommendation comes from intrauterine growth curves. Although intrauterine growth charts are useful in determining an infant's status at birth, they do not reflect expected growth patterns in the extrauterine environment after premature delivery. The healthy fetus *in utero* does not encounter an interrupted nutritional supply, a depletion of nutritional stores, a deprivation of growth factors provided by the mother and placenta, or increased energy consumption as seen in the preterm infant *ex utero*.³² Collectively, these factors result in weight loss during the first week of life (as much as 15% in our cohort) which is not appreciated in intrauterine growth curves and this deficit may be too much to overcome in the early postnatal period. As a result, it may not be possible to emulate the intrauterine growth curves and postnatal growth failure may be inevitable^{21, 22}. Growth velocity alone is not a sufficient indicator of nutritional attainment. Other measures need to be considered, including other anthropometric measures or measures of body composition. However, the desirable curves or ranges for these outcomes have yet to be established.

For our infants to stay above their birth weight centile, GVs of 20 – 30 gm/kg/day were necessary, with GVs in the higher end of this range for the gestationally youngest infants. Infants who demonstrated a growth velocity greater than 20 g/kg/day were more likely to be growth restricted and more likely to receive greater amounts of protein and carbohydrates by day 21. The physician's decision to offer more nutrition to the newborn with severe intrauterine growth restriction conveys information about the infant, the physician (and institutional practices), and the perceived level of illness of the infant. These issues are so closely intertwined that we cannot determine with confidence the relative contribution of each to growth velocity.

Although the nutritional practices we observed in our study are an improvement over what has been reported previously in the literature, we still fell short of meeting all recommendations. However, we still do not know to what extent extrauterine growth failure can be minimized with earlier provision and advancement of nutrition. Perhaps more important, the assumed benefits of catch-up growth on developmental outcomes should be weighed against the possibility that it might be detrimental to long-term health.^{33, 34}

Our study supports the importance of providing early nutrition to promote postnatal growth. Even though recommended nutritional intakes were not achieved, early delivery of nutrients remained important to overall GV during the first month of life. We found that GV in the lowest quartile is predicted by the lowest quartile of protein, carbohydrate, and fat intake on day 7 of life. No nutritional characteristics on day 14 had a significant impact on GV; and only total carbohydrate at day 21 was associated with GV. The influence of early nutrition on GV remained important even after we adjusted for birth weight Z-score, SNAP-II, GA, and total fluid intake. This observation supports the findings of other authors who have demonstrated that early nutritional practices influence postnatal growth and reinforces the call for early provision and advancement of nutrients during the NICU stay in order to promote optimal postnatal growth. The optimal composition of nutrients, however, remains undetermined^{35, 36} and barriers (practice or clinical) to achieving recommended intakes need to be studied further.

CONCLUSION

In this large, multicenter, prospective study of extremely preterm infants we demonstrate improved protein and fat delivery compared to previous reports and a GV, as defined, that exceeds current recommendations. Despite these improvements, the majority of our infants failed to maintain the weight Z-score they had at birth. It is likely that intrauterine growth rates might not be achievable ex utero for most ELGANs and new standards need to be developed with the goal of establishing growth patterns that promote optimal long-term growth and neurodevelopmental outcomes. The *early* provision of nutrients remains an important determinant of postnatal growth and will be a critical component to these standards.

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Abbreviations

ELGAN	extremely low gestational age newborn
g/kg/day	grams per kilogram per day
GA	gestational age
GV	growth velocity
kcal/kg/day	kilocalories per kilogram per day
NICU	neonatal intensive care unit
PN	parenteral nutrition
SNAP	Score for Neonatal Acute Physiology

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Figure 1. Scatterplot of weight Z-scores at birth (X-axis) and at 28 days (Y-axis). The vast majority of infants have a lower weight Z-score on day 28 compared to their weight Z-score at birth.

Table 1

Median values of nutrient intakes (from both parenteral and enteral routes) in quartiles of GV and by postnatal day.

Nutritional characteristic		Centiles		
		25 th	50 th	75 th
Protein (g/kg/day)				
	Day 1	1.0	1.0	0
	Day 3	2.7	3.0	3.0
	Day 7	3.3	3.5	3.9
	Day 14	3.5	3.4	3.6
	Day 21	3.1	3.2	3.4
	Day 28	3.1	3.2	3.5
Fat (g/kg/day)				
	Day 1	0	0	0
	Day 3	1.2	1.4	1.2
	Day 7	2.7	3.1	3.0
	Day 14	3.5	4.1	3.5
	Day 21	4.3	4.8	4.0
	Day 28	5.1	5.4	4.7
Carbohydrate (g/kg/day)				
	Day 1	4.3	4.4	4.5
	Day 3	7.1	7.8	7.6
	Day 7	8.0	9.3	9.6
	Day 14	9.2	10.0	10.5
	Day 21	10.1	10.6	10.9
	Day 28	10.8	10.9	11.0
Total calories (kcal/kg/day)				
	Day 1	25	26	26
	Day 3	55	59	57
	Day 7	70	79	84
	Day 14	84	92	92
	Day 21	93	101	100
	Day 28	103	105	104

$$GV = [1000 \times ((wt_{28} - wt_7) / wt_7) / 21]$$

Table 2

Median values of nutrient intakes (from both parenteral and enteral routes) in strata defined by GA and birth weight Z-score.

Nutritional characteristic	Gestational age (weeks)			Birth weight Z-score		
	23-24	25-26	27	<-2	≥2, <-1	≥1
Protein (g/kg/day)						
Day 3	3.0	3.0	3.1	3.0	2.7	3.0
Day 7	3.5	3.5	3.7	3.5	3.5	3.6
Day 14	3.5	3.5	3.4	3.5	3.5	3.5
Day 21	3.4	3.3	3.2	3.5	3.2	3.2
Day 28	3.4	3.2	3.2	3.5	3.2	3.2
Fat (g/kg/day)						
Day 3	1.0	1.3	1.5	1.1	1.2	1.4
Day 7	2.6	3.0	3.2	2.8	2.7	3.1
Day 14	3.1	3.7	4.5	3.2	3.6	3.8
Day 21	3.2	4.6	5.3	4.0	4.3	4.6
Day 28	4.3	5.0	5.8	4.6	5.3	5.2
Carbohydrate (g/kg/day)						
Day 3	6.9	7.8	7.8	6.8	6.9	7.8
Day 7	7.8	9.0	10.6	8.0	8.2	9.3
Day 14	8.6	9.9	10.6	10.0	9.4	10.0
Day 21	9.6	10.6	10.8	10.8	10.4	10.5
Day 28	10.6	10.8	11.1	11.2	10.8	10.9
Total calories (kcal/kg/day)						
Day 3	54	58	61	53	53	58
Day 7	67	77	85	70	71	79
Day 14	78	89	99	86	86	91
Day 21	83	99	104	95	97	100
Day 28	99	103	108	96	104	104

Table 3

Median GV within strata of GA and birth weight.

	Gestational age					
	23	24	25	26	27	N
Birth weight						
≤ 750	19	18	18	20	19	443
751 - 1000	20	17	17	18	20	517
1001 - 1250	--	--	18	18	18	209
> 1250	--	--	--	17	15	18
Birth weight Z-score						
□ < -2	33	15	22	21	18	65
□ < -1	34	22	19	19	18	154
-1 to 1	18	18	17	18	19	832
> 1	22	15	17	18	19	117
> 2	15	--	18	20	13	19
N	57	192	250	301	387	1187

$$GV = [1000 \times ((wt_{28} - wt_7) / wt_7) / 21]$$

Table 4

Median GV associated with quartiles of each nutrient intake.

Nutritional characteristic		Quartiles of each nutritional practice		
		25 th	50 th	75 th
Protein (g/kg/day)				
	Day 3	17	18	20
	Day 7	17	18	20
	Day 14	18	18	19
	Day 21	17	19	19
	Day 28	18	18	20
Carbohydrate (g/kg/day)				
	Day 3	17	18	19
	Day 7	16	18	20
	Day 14	17	18	20
	Day 21	17	18	20
	Day 28	18	18	19
Fat (g/kg/day)				
	Day 3	19	18	18
	Day 7	17	18	19
	Day 14	18	18	18
	Day 21	17	18	17
	Day 28	17	18	18
Total calories (kcal/kg/day)				
	Day 3	17	18	20
	Day 7	16	18	20
	Day 14	17	18	19
	Day 21	17	18	19
	Day 28	18	18	19

$$GV = [1000 \times ((wt_{28} - wt_7) / wt_7) / 21]$$

Median GV for infants who maintained or exceeded their birth weight Z-score at 28 days of life within strata of GA and birth weight.

Table 5

	Gestational age								N
	23	24	25	26	27	28	29	30	
Birth weight	26	30	24	23	21	142			
≤ 750	---	---	---	---	---	---	---	---	---
751 - 1000	---	---	---	---	---	---	---	---	---
1001 - 1250	---	---	---	---	---	---	---	---	---
> 1250	---	---	---	---	---	---	---	---	---
N	18	24	32	67	39	180			

$$GV = [1000 \times ((wt_{28} - wt_7) / wt_7) / 21]$$

Table 6

Odds ratios (95% confidence intervals) for the lowest quartile of GV predicted by the lowest quartiles of nutrient intakes at each week adjusted for birth weight Z-score (< -2 , ≥ -2 to < -1 , ≥ -1), GA (23-24, 25-26, 27 weeks), SNAP-II score (< 30 , ≥ 30), total fluid intake (mL/kg/day), and all the other nutrition variables for that day.

Lowest quartile	OR (95% CI) for lowest quartile of GV		
	Day 7	Day 14	Day 21
Total protein (g/kg/day)	1.4 (1.02, 2.0)	1.0 (0.7, 1.4)	1.3 (0.9, 1.7)
Total carbohydrate (g/kg/day)	2.1 (1.4, 3.1)	1.5 (0.97, 2.2)	1.5 (1.02, 2.2)
Total fat (g/kg/day)	1.7 (1.2, 2.3)	1.1 (0.8, 1.6)	0.8 (0.6, 1.2)
Total calories (kcal/kg/day)	1.1 (0.7, 1.7)	1.2 (0.7, 1.9)	1.2 (0.8, 1.9)

$$GV = [1000 \times ((wt_{28} - wt_7) / wt_7) / 21]$$