RESEARCH PAPER

Growth of Very Low Birth-Weight Indian Infants During Hospital Stay

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Objectives: To evaluate the growth pattern of Very Low Birth Weight (VLBW) infants (birthweight <1500g) during hospital stay and to compare the growth of Small for gestational age (SGA) and Appropriate for gestational age (AGA) infants.

Study design: Prospective observational study.

Setting. Level III Neonatal Intensive Care Unit (NICU) in Northern India.

Participants: A cohort of 97 VLBW infants, admitted to NICU at Sir Ganga Ram Hospital, from 1 January, 2007 to 31 July, 2008.

Intervention/Measurement: Weight, length and head circumference (HC) were serially measured from birth till discharge and respective *Z* scores were calculated as per data from Fenton's references. Growth was also assessed by superimposing these trends on Ehrenkranz's postnatal growth charts.

Results: The mean *Z* scores for weight, length and HC at birth were –1.17, –1.09 and –0.54, respectively. These decreased to –2.16, –2.24 and –1.35, respectively by discharge. Both SGA and AGA infants exhibited a decrease of approximately 1 *Z* score in all parameters. On postnatal charts, growth of infants remained at or above respective reference lines, except in those below 1000g at birth. Average daily weight gain after regaining birth weight was 15.18 ± 1.7 g/kg/d, whereas the increase in HC and length were 0.48 ± 0.2 cm/week and 0.60 ± 0.4 cm/week, respectively. These increments when compared to the intrauterine growth rates, indicated discrepant growth trends.

Conclusions: VLBW infants suffered significant growth lag during NICU stay and exhibited disproportionately slow growth of HC and length.

Key words: *VLBW infants, Growth, Z score, Weight, Length, Head circumference, India.*

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Postnatal growth of Very Low Birth Weight (VLBW) infants (birthweight <1500g) remains a subject of concern for neonatologists. Infants born VLBW are at increased risk for impaired growth, due to certain factors during intrauterine life, exposure to hostile ex-utero environment and poorly understood nutritional needs. Despite improvement in care of VLBW infants, they continue to suffer growth lag during neonatal period and early infancy. Most of these infants experience catch up growth much later, by 8-20 years(1). Poor postnatal growth has been associated with subnormal long-term physical growth and neurodevelopment outcomes (2-4). The postnatal growth pattern in VLBW infants during hospital stay and beyond has not been reported from this subcontinent.

We conducted this study to document and describe the growth patterns of VLBW infants during NICU stay and to analyze the difference, if any, between those born appropriate or small for gestational age (AGA or SGA).

METHODS

VLBW infants admitted to neonatal intensive care unit at Sir Ganga Ram Hospital, New Delhi from 1st January 2007 to 31st July 2008 were followed

prospectively from birth till discharge. Infants who stayed in the hospital for less than 10 days or those admitted after 24 hours of birth or with major congenital malformations were excluded. This study was approved by the Institutional Review Board and hospital Ethics Committee. Parental consent was obtained at the time of enrolment. Gestational age was recorded as per obstetrical estimates based on first trimester ultrasonography or if not available, by date of last menstrual period.

Weight was taken by an electronic weighing scale, which was calibrated at regular intervals. It was recorded every day till birth weight was regained and then every week till discharge. Length and head circumference (HC) were recorded using standard techniques between 12 to 24 hrs initially and then every week till discharge. The minimum range for recording weight was 10 gms and, 1 mm for length and HC. All the measurements were taken twice and average of these observations was recorded. However, if there was a large discrepancy between two readings (defined as more than 5%), repeat measurements were taken. The maximum weight loss was calculated from the difference of minimum weight and birth weight. The age at maximum weight loss and time taken to regain birthweight were also calculated. For calculation of daily weight gain, period from regaining birthweight to discharge was used as denominator.

Fluid and nutrition policy: VLBW infants were started on 80 mL/kg/d (60-120 mL/kg/d) of fluid on first day of life. The total fluid intake was regulated to allow physiological weight loss. Enteral feeds were initiated as soon as possible, preferably on first day of life, if haemodynamically stable. Increments of 20-30 mL/kg/d were made as tolerated. Human milk was preferred and once infants reached an enteral intake of 100mL/kg/d, human milk fortifier (Lactodex HMF, manufactured by Raptakos, Brett & Co, with 6.5 Calories, 0.2 g protein and 0.1 g fat in each sachet) were added to increase the calories to 80 kcal/100ml with an additional protein intake of 0.6g/kg/d. However if human milk was not available, a low birth weight infant formula (Dexolac special care, manufactured by Wockhardt Ltd, Mumbai, India) was used with a calorie content of 80 kcal/100ml and 2.67g of protein in 100ml of reconstituted formula. Infants who were not expected to be on total enteral feeds within first 5 days of life, were started on parenteral nutrition (PN) on first day with protein and lipid intake of 1g/kg/d. Daily increments of 1g/kg/d were made with a maximum intake of 3 g/kg/d, targeting a parenteral calorie intake of 90 kcal/kg/d.

Statistical methods: The *Z* scores for weight, length and HC for each gestation were calculated based on means and standard deviations from Fenton's reference data(5,6). Infants were classified SGA if the birth weight was below 10th centile as per Fenton's growth charts. Mean *Z* scores for weight, length and HC of the whole cohort, were compared at birth and discharge. Similar comparisons were made between SGA and AGA infants. For further analysis, the cohort was classified into three gestational age groups; less than 30 weeks, 30-34 weeks and more than 34 weeks. The infants were also categorized by 100g birthweight intervals and their weight, length and HC during the hospital stay were plotted on the Ehrenkranz growth curves for comparison(7). SPSS version 13.0 was used for statistical analysis. Continuous variables were compared using student t test or Mann Whitney U test as per the distribution of data. Paired observations were compared by paired t test or equivalent non parametric test, as applicable.

RESULTS

Enrolment and characteristics of the study population including prenatal factors and neonatal morbidities are depicted in ***Fig.* 1** and ***Table* I,** respectively. ***Table* II** depicts the average increase in weight, length and HC for different gestational age categories.

The mean *Z* scores for weight, length and HC at birth in all subjects as calculated from the data from Fenton's references, were –1.17, –1.09 and –0.54, respectively. These decreased to –2.16, –2.24 and –1.35, respectively by discharge (***Fig.* 2**). The mean fall in *Z* scores for each parameter from birth to discharge were significantly lower in SGA as compared to AGA infants ($P<0.01$).

Infants were categorized by 100 g birth weight intervals. Their gestation, birth weight, and growth velocity in each of these categories is depicted in

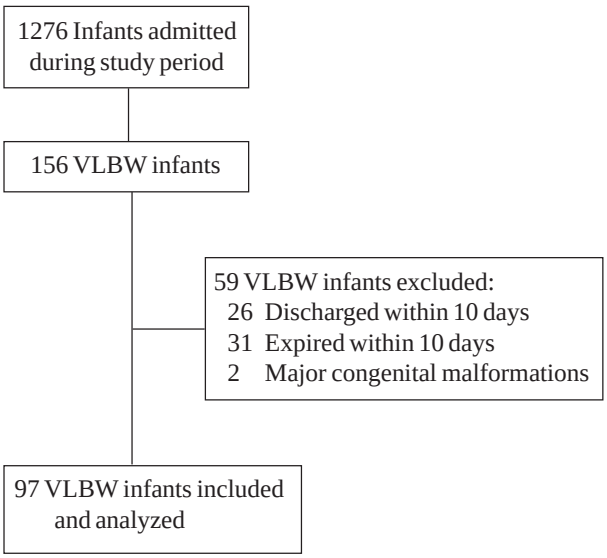


FIG. 1 *Study flow chart.*

Table* III**. Maximum weight loss, time taken to regain birth weight and later weight gain pattern followed the Ehrenkranz postnatal growth curves except in infants with birth weight below 1000 g who experienced slower growth (Fig.* 3**)(7). The length and HC in this cohort were higher at birth and fell well below respective reference lines by discharge, except in infants with birthweight more than 1200g.

TABLE I CHARACTERISTICS OF VLBW INFANTS (*N* = 97)

Maternal factors	
gestational hypertension, *n* (%)	52 (53.6)
gestational diabetes / IDM, *n* (%)	3 (3.1)
Birth weight, mean (SD) g	1257 (190.7)
Gestational age, mean (SD) wk	31.7 (2.35)
Male, *n*(%)	57 (58.8)
Infants < 30 weeks (*n*=25): AGA, *n*(%)	25 (100)
Infants 30-34 weeks (*n*=56)	
AGA, *n* (%)	25 (44.6)
SGA, *n* (%)	31 (55.4)
Infants >34 weeks (*n*=16); SGA, *n* (%)	16 (100)
Respiratory distress, *n* (%)	58 (59.7)
Culture positive sepsis, *n* (%)	28 (28.9)
Weight at discharge, mean (SD) g	1695 (158.9)
Gestation at discharge, mean (SD) wk	36.35 (2.45)
Hospital stay, median (range) d	27 (11-105)

DISCUSSION

Infants in our study were smaller at birth in all three parameters as compared to Fenton's intrauterine growth references. This difference could be due to racial and ethnic factors or due to nutritional and life style differences in this population. Lower birth *Z* scores for weight and length as compared to HC suggest brain sparing growth restriction in this cohort. These infants exhibited slow growth during hospital stay as indicated by a fall of approximately one *Z* score in each of the three parameters from birth to discharge. This observation is similar to the decline reported by Hack, *et al*.(1) in VLBW infants from birth to 40 weeks.

With the nutritional practices used in this study, our infants experienced a daily weight gain of 15.18±1.7 g/kg/d, which is comparable to intrauterine growth rate and other reports. However, the weekly increments in HC and length were almost half of the intrauterine growth expectations and other reports(7-9). This discrepant growth could be due to relatively more accumulation of body fat as compared to muscle mass and bone growth. Larger proportion of SGA infants in this study may have contributed towards this trend. Whether this is due to variation in quality and composition of low birthweight feeding-formula, human milk fortifiers, or due to poor growth potential of SGA infants in this ethnic group, needs to be investigated.

Since most VLBW infants do not achieve intrauterine growth rates during postnatal life, it seems more appropriate to monitor their growth on postnatal charts. When we plotted the growth of our infants on Ehrenkranz's charts, it matched reference lines for each 100g category, except in those below 1000g at birth(7). This could be due to higher morbidity in extremely low birth weight infants in the present setting. Growth comparable to these references in infants above 1200g is possibly due to better maturity and feed tolerance, and lesser neonatal morbidity. Higher length and HC at birth in each 100g category could be due to higher gestational age in our cohort as compared to NICHD data(7). However, even in these parameters, weekly increments were less than expected(5,7).

TABLE II GROWTH PATTERN IN VLBW INFANTS DURING HOSPITAL STAY

	< 30 wk	30 – 34 wk		> 34 wk	Total	
	(all AGA) (*n*=25)	AGA (*n*=25)	SGA (*n*=31)	(all SGA) (*n*=16)	AGA (*n*=50)	SGA (*n*=47)
Maximum weight loss (%)	7.3 (4.5)	6.8 (3.2)	6.6 (3.7)	5.24 (3.07)	7.1 (3.8)	6.1 (3.5)
Age to regain birthweight (d)	10.2 (4.4)	9.8 (3.1)	8.8 (3.5)	8.56 (3.72)	10.0 (3.7)	8.7 (3.5)
Weight gain (g/kg/d)	16.0 (20.3)	14.8 (4.6)	13.3 (7.9)	18.30 (6.6)	15.3 (14.6)	14.9 (7.8)
HC increment (cm/wk)	0.45 (0.21)	0.45 (0.24)	0.50 (0.30)	0.53 (0.29)	0.45 (0.22)	0.51(0.29)
Length increment (cm/wk)	0.53 (0.33)	0.59 (0.46)	0.70 (0.45)	0.51(0.32)	0.56 (0.39)	0.63 (0.42)

** VLBW: very low birth weight; AGA: appropriate for gestational age; SGA: small for gestational age;* *Difference *between AGA and SGA infants for all parameters was not significant (P > 0.05); All values are show as mean (SD); HC: head circumference.*

SGA infants are at double jeopardy; in addition to intrauterine growth restriction, many are born prematurely(10). They continue to grow slow during early postnatal life(11,12). We noted that both AGA and SGA infants had a significant drop in their growth *Z* scores during hospital stay. Even though SGA infants experienced lesser fall in their growth parameters as compared to AGA, they did not exhibit desired catch up growth during hospital stay and continued to grow at a lower trajectory. Both SGA and AGA VLBW infants in our study had comparable growth velocity during hospital stay. This is in contrast to an earlier observation which reported faster weight gains in SGA infants(7). This could possibly be due to more growth restriction or poor growth potential of SGA infants in our study population. Further analysis of a category of infants between 30-34 weeks, which had comparable number of SGA and AGA infants, revealed similar growth trends.

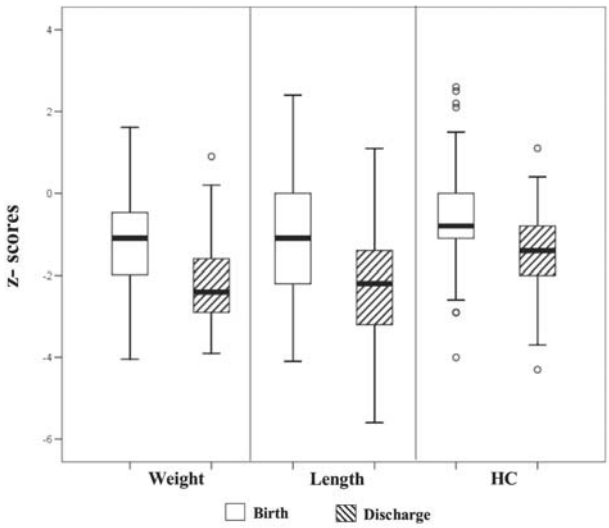


FIG. 2 *Box and Whisker plot for z scores for weight, length and HC in VLBW infants. Solid line in the box shows median, top and bottom of the box are the interquartile range with the range of the data.*

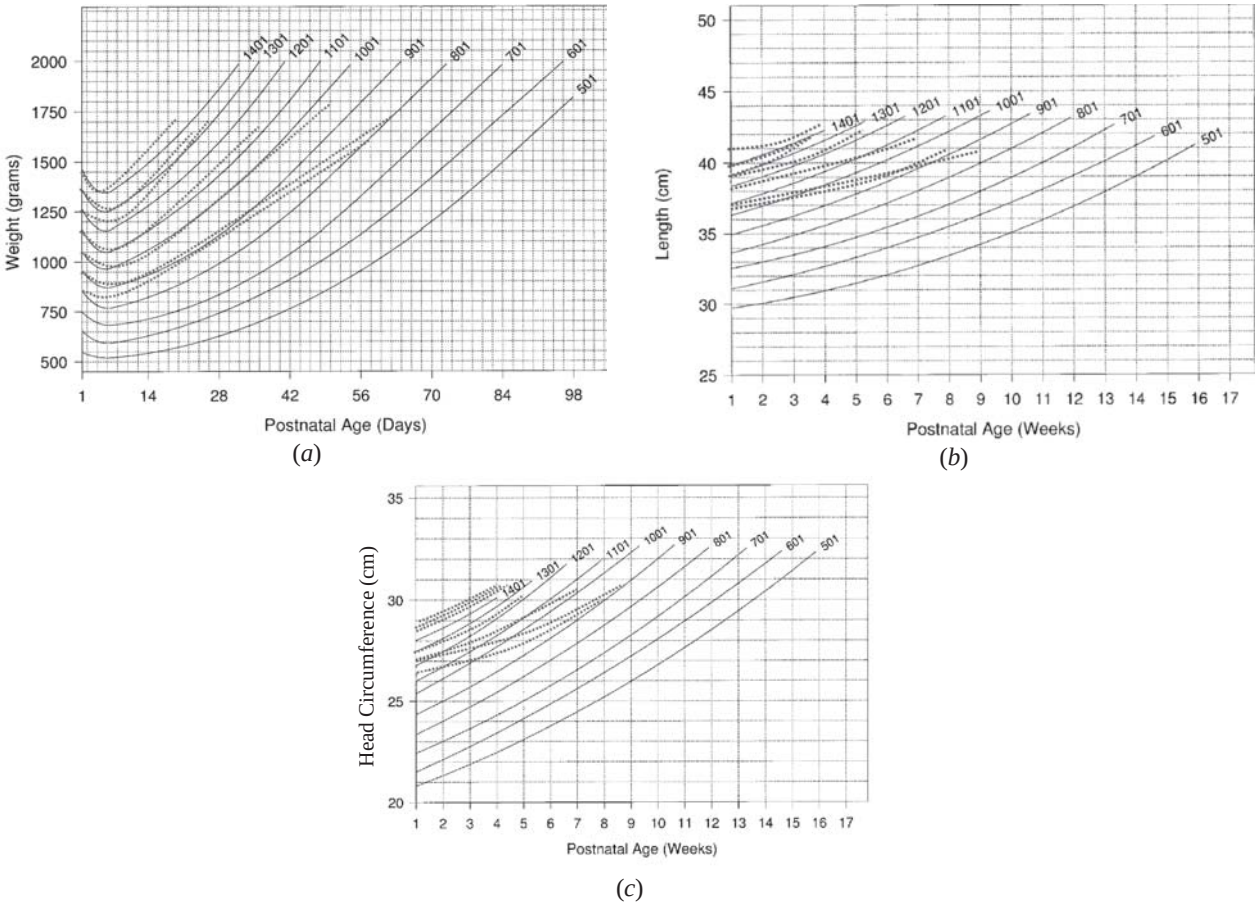
Slower brain growth during infancy is a predictor of poor neurodevelopment outcome and has been shown to be associated with poor school performance(13,14). Smaller increments in HC during hospital stay in this cohort is a cause for concern and there is a need for continued follow up of these infants to monitor for catch up in head growth, along with their cognitive and learning abilities. VLBW infants in this study also experienced slower linear growth during hospital stay. They need a long term follow up for catch up, as poor growth during early infancy has been shown to be associated with persistent stunting in later life(15).

This study highlights the growth trends of VLBW infants in a setting where incidence of low birth weight and growth restriction is high. The disproportionate postnatal growth pattern observed in this study may reflect altered body composition with increased fat and lesser lean body mass, which may predispose them to metabolic syndromes(16). This observation needs further validation, to know the real growth potential of VLBW infants from this subcontinent. The limitations of this study are small sample size, recruitment from a single centre, and comparison of their growth with references from ethnically different population. Another limitation is that almost 17% of the VLBW infants were not available for follow up.

TABLE III CHARACTERISTICS AND GROWTH VELOCITY OF VLBW INFANTS AS 100 g BIRTHWEIGHT CATEGORY

Category (*n*)	Birthweight (g) mean (SD)	GA (wk) mean (SD)	Mean weight gain (SD) g/d	g/kg/d	HC increment cm/wk mean (SD)	Length increment cm/wk mean (SD)
Overall (97)	1257 (190.7)	31.72 (2.3)	22.58 (17.1)	15.18 (1.7)	0.48 (0.2)	0.60 (0.4)
701- 800 (1)	760	26.71	6.47	6.60	0.27	0.45
801-900 (3)	853.3 (45.4)	29.81 (2.4)	15.80 (2.6)	12.50 (1.88)	0.44 (0.13)	0.66 (0.27)
901-1000 (5)	951.0 (24.6)	30.09 (2.16)	15.11 (3.82)	11.42 (2.92)	0.37 (0.13)	0.40 (0.21)
1001-1100 (15)	1051.7 (27.1)	30.05 (2.12)	27.41 (36.26)	19.48 (25.73)	0.48 (0.24)	0.54 (0.24)
1100-1200 (14)	1152.7 (23.1)	31.29 (1.57)	18.60 (4.78)	13.15 (3.25)	0.45 (0.18)	0.58 (0.36)
1201-1300 (12)	1258.3 (33.8)	33.70 (2.47)	22.60 (4.42)	15.25 (2.41)	0.53 (0.20)	0.82 (0.44)
1301-1400 (16)	1351.8 (33.1)	32.06 (2.09)	19.80 (11.33)	13.11 (7.91)	0.46 (0.32)	0.54 (0.33)
1401-1500 (31)	1457.9 (31.4)	32.53 (1.96)	25.71 (13.49)	16.21 (8.59)	0.51 (0.31)	0.61 (0.53)

GA: Gestation at Birth, g/d: weight gain in gram/day after regaining birthweight, g/kg/d: weight gain/kg/day after regaining birthweight.



(*a*) (*b*) (*c*)

FIG. 3 *Postnatal growth of VLBW infants categorized by 100g birth weight superimposed on reference growth curves. Bold lines are reference lines and dotted lines are growth pattern of study subjects. Adapted from Longitudinal growth of hospitalized very low birth weight infants. (1999)(7). The lowest dotted line indicates infants with birth weight between 801 – 900g and each of above lines with 100g weight difference. a – Weight, b – Length, c - HC.*

WHAT IS ALREADY KNOWN?

- VLBW infants suffer growth lag during early postnatal period.

WHAT THIS STUDY ADDS?

- A disproportionate growth was found in the VLBW infants studied.

Contributors: SS and MM were responsible for the study idea, design, data collection and analysis. AK and AB helped in data collection and analysis. AS and PG helped in editing manuscript. NK supervised and helped in review and editing the manuscript. All authors approved the final content of the manuscript.

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Competing interest: None stated.

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