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Growth of Extremely Low Birth Weight Infants (ELBW) born at a Tertiary Hospital: Statural catch-up growth continues during the 3rd year of life

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Abstract

Background: Extremely low birth weight (ELBW) infants, with birth weights less than 1000 g, often experience challenges in postnatal growth. This study aimed to assess the growth patterns of ELBW infants over a 3-year period, focusing on statural catch-up growth.

Methods: Anthropometric measures (z-scores) were obtained at birth, 2, 4, 6, 12, 18, 24, and 36 months for 87 ELBW infants born between September 2016 and September 2018. Their growth data was compared to WHO growth standards without adjusting for gestational age. All preterm infants received preterm formula for an average of 4-6 months.

Results: ELBW infants showed significant catch-up growth in weight-for-age (WAZ) and length-for-age (LAZ) during the first two years of life, while weight-for-length (WLZ) showed an initial increase followed by a mild decline. By age 3, a substantial proportion of infants achieved normal growth parameters. Specifically, 78% had normal WAZ, 90% had normal LAZ, 87% had normal WLZ, and 91.5% had normal head circumference z-scores (HCZ). Overweight was observed in 7.4% of ELBW infants at age 3.

Conclusion: ELBW infants fed preterm formula for 4-6 months demonstrated significant catch-up growth during the first 12-18 months of life, with continued catch-up in LAZ during the third year. A high percentage of these infants achieved normal growth parameters by age 3, emphasizing the effectiveness of early interventions in improving postnatal growth in ELBW infants.

Keywords: Extremely low birth weight; Catch-up growth; Postnatal growth; Preterm infants; Growth patterns.

1. Introduction

Extremely low birth weight (ELBW) infants, characterized by birth weights less than 1000 grams (g), represent one of the most vulnerable populations in the realm of neonatal medicine. The challenges faced by these infants extend far beyond their immediate survival, as their postnatal growth and long-term developmental outcomes are subjects of profound concern for healthcare providers, parents, and researchers. Extrauterine growth restriction (EUGR) is common in extremely low birth weight (ELBW) infants (<1000 g) despite 'aggressive' nutritional regimens that aimed

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at achieving intrauterine growth rates. ELBW infants exhibit distinctive growth patterns and developmental trajectories that demand close attention. (1-5)

The significance of studying the postnatal growth of ELBW infants is underscored by a body of research that highlights the distinctive features of their growth patterns, nutritional requirements, and long-term consequences. Various studies have shed light on the challenges associated with ELBW infants' growth and the interventions aimed at mitigating them. These studies have reported on the dynamics of weight, length, and head circumference growth in ELBW infants, demonstrating their early growth deficits and the potential for catch-up growth. Researchers have also explored the impact of nutritional strategies, including the use of preterm formula, on improving growth parameters in ELBW infants. (6-9)

Additionally, investigations have revealed the relationship between postnatal growth and long-term neurodevelopmental outcomes in ELBW infants, emphasizing the lasting consequences of growth challenges. (10-14)

Variable degrees of catch-up were reported by different authors at different times postnatally. For instance, Raaijmakers et al conducted a comprehensive study that examined the postnatal growth patterns of ELBW infants for 11 years and identified that Catch–up growth (i.e., ΔZ–score >0.67 SDS) for weight was achieved during the first two years of life in only 9.9% of cases, for length in 13.7% of cases and for head circumference in 14.1% of cases. During childhood (2 years– 11 years) another 73.2% of cases showed catch–up growth for weight, 59.7% for length and 4.6% for head circumference. (15)

Gonzalez et al studied postnatal growth of 92 infants with very low birth weight (VLBW). At 2 years of age only 15% had short stature (SD <-2) and only 2% had BMISDS <-2. They observed a direct relationship between daily weight gain in the first 28 days and the risk of short stature at 2 years.(16) Westerberg et al observed significant catch-up growth for weight and length in 118 VLBW infants during the first year with mean gain in z-score SD of 0.40 (1.05) and 1.01 (1.25) respectively. However, the VLBW infants remained lighter and shorter than full-term peers until 12 months corrected age with mean z-score of -0.93 (1.09) and -0.48 (1.06) respectively. (17) Deng et al studied growth of 114 VLBW infants with mean birth weight 1.27 kg and reported that at 1 year of age only 4.7% had LSDS<-2 and 9.3% had wasting (WLZ <-2). (18)

Kwinta et al studied growth of 88 babies with VLBW ≤1000 g and found that The ELBW children in the 7th year of life were shorter (z-score: -1.06±1.4 p<0.001), had lower body mass (z-score: -0.57±0.9; p=0.01), smaller head circumference (z-score: -1.2±1.3; p<0.001), and lower BMI (z-score: -0.99±1.6; p<0.001) as compared to their peers. (19) Wang et al studied growth of 126 children born VLBW. 89% of these babies reached normal height and weight by the age of 2 years, and more than 89% maintained normal growth at 5 years of age. At 5 years of age 10.3% had underweight, 8.7% were short (HAZ <-2) and 16.0% had small head size (HCZ <-2). However, the VLBW children remained lighter and shorter compared to their normal controls at age 5. (20)

Farooqi et al studied 83 VLBW children showed a sharp decline in weight and height z scores up to 3 months' corrected age, followed by catch-up growth in both weight and height up to 11 years. (9) The mean BMI z scores increased significantly from 1 to 11 years in both groups. Durá-Travé et al reported a gradual catch up in their VLBW infants from birth till the age of 8. Complete height catches up occurred in 66 % of their ELBW and 90% VLBW infants at the age of 8 years. (21). However, Ford et al, followed 80 ELBW infants till adolescence and reported that VLBW children experienced late catch-up growth to age 14 years but remain smaller than their normal birth weight peers (22). A systemic review of 17 studies consistently reported that former VLBW neonates experience a period of accelerated postnatal growth, but they achieve lower anthropometric parameters than normal birth weight children. (23)

Considering these studies and the collective body of research on ELBW infants, it appears that postnatal growth in this population is a multifaceted issue with far-reaching implications.

This research seeks to investigate the postnatal growth patterns of ELBW infants, focusing on the dynamics of weight, length, weight-for-length, and head circumference growth, in relation to their nutritional strategies.

2. Methods

This retrospective cohort study included 87 ELBW infants born between September 2016 and September 2018 at a tertiary hospital. Anthropometric measures, represented as z-scores, were collected at various time points, including birth, 2, 4, 6, 12, 18, 24, and 36 months.

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 at birth, on electronic weighing scale with accuracy of ± 5 gram, with baby being unclothed. Length and head circumference (HC) were taken within 12 hrs of age using standard techniques. Subsequently, measurements were repeated at discharge and then at 3, 6, and 12, 18, 24 and 36 months of corrected age. To improve follow up, periodic reminders were sent to parents through telephonic calls and Phone Short Message Service (SMS) .

Growth data was compared to the World Health Organization (WHO) growth standards without adjusting for gestational age. All preterm infants in the study received preterm formula for an average of 4-6 months. Full enteral feeds (150 ml/kg) were reached by Day 10-14 with energy >100 Kcal/kg/day from Day 10, and protein >3.5 mg/kg/day from Day 14, onwards.

All infants had birth weight < 1000 grams and all with a birth weight > 750 grams. All ELBW infants were started on enteral feeds at 15–20 mL/kg/day and increased by 15–20 mL/kg/day. When the feeds were tolerated for around 2–3 days, faster increase was adopted. Enteral feeds were increased gradually to a volume of 180 mL/kg/day. LBW formula was used. Once infant reached 100 mL/kg/day of enteral feeds, expressed breast milk was fortified with human milk fortifier to make caloric content of 80 Cal/100 mL, to achieve a target calories 110-130 cal/kg/day. Developmentally supportive care was routinely provided to all the neonates. Special care was taken for environment including noise level, light, positioning, and nesting. Kangaroo mother care was offered, once infants were hemodynamically stable. Early stimulation and intervention tailored to the infant's need was provided during NICU stay and during follow up. (24)

2.1. Statistical analysis

Weight, length and HC were converted to Z-scores for gender and the chronological age (CA) based on the WHO Child Growth Standards. [WHO Anthro (version 3.2.2, January 2011), https://www.who.int/childgrowth/software/en/]

The CA was calculated by subtracting the difference between term birth and the GA at birth from the child's chronological age. Anthropometric data are presented as Z-scores based on the WHO growth charts.

Z-score means were calculated as follows: (observed value minus the median value of the reference population) /standard deviation (SD). SGA was defined as a birth weight below the 10th percentile for GA based on Fenton's growth chart for 22–50 weeks (25) . Stunting was defined as a length-for-age Z-score (LAZ) < − 2 SD; microcephaly was defined as an HC-for-age Z-score (HCZ) < − 2 SD; and wasting was defined as a weight-for-length Z-score (WLZ) was < − 2 SD.

Statistical analysis was done using SPSS version 17.0. Comparisons were made using independent t test, paired t test and repeated measure ANOVA, as applicable. A Nonparametric Wilcoxon test was used when the data was not normally distributed. The ethical Committee of Hamad General hospital approved the protocol of the study (IRB number MRC 01-21-277)

3. Results

The ELBW infants in our study had a gestational age (GA) at delivery ranging from 23 to 27.5 weeks. At birth, they exhibited severe growth restriction, with weight z-score (WAZ) = -7.7 ± 0.14, length z-score (LAZ) = -8.8 ± 0.25, weight-for-length z-score (WLZ) = -5.6 ± 0.39, and head circumference z-score (HCZ) = -8.8 ± 0.3. (Table 1)

During the first 24 months of life, ELBW infants displayed a progressive gain in WAZ, improving from -7.7 to -0.52. The catch-up growth in WAZ, however, ceased during the third year of life (Figure 1). Similarly, LAZ demonstrated consistent catch-up growth over 3 years, improving from -8.8 to -0.34 (Figure 1) . WLZ increased significantly during the first year, with a peak gain during the first 6 months, followed by a mild decline over the subsequent two years. (table 1)

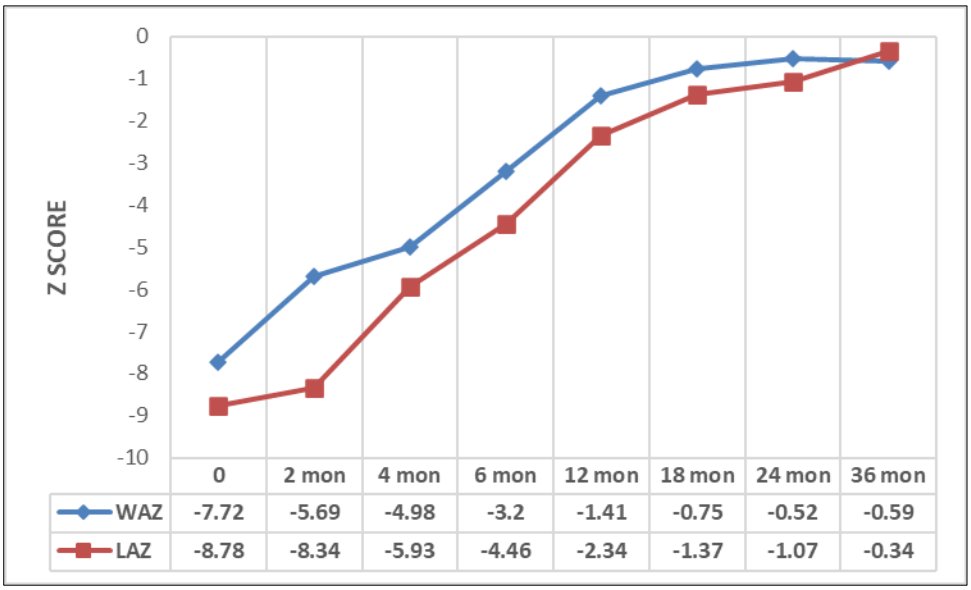

Figure 1 WAZ and LAZ in ELBW during the first 3 years of life

Table 1 Postnatal growth data for infants born with ELBW (for 3 years)

		0.00	**2 mon**	**4 mon**	**6 mon**	**12 mon**	**18 mon**	**24 mon**	**36 mon**
WAZ	mean	-7.72	-5.69	-4.98	-3.20	-1.41	-0.75	-0.52	-0.59
	SE	0.14	0.19	0.19	0.17	0.14	0.13	0.14	0.15
LAZ	Mean	-8.78	-8.34	-5.93	-4.46	-2.34	-1.37	-1.07	-0.34
	SE	0.25	0.20	0.28	0.23	0.17	0.15	0.14	0.15
WLZ	Mean	-5.60	-3.21	-1.00	-0.02	-0.19	-0.10	-0.42	-1.10
	SE	0.39	0.39	0.21	0.17	0.17	0.13	0.15	0.21

Proportions of infants with z-scores below -2 decreased over time, indicating significant catch-up growth. By age 3, 10% of infants had LAZ < -2, 19% had WAZ < -2, and 7.4% had WLZ < -2. Additionally, 14.8% of infants had WLZ between 1 and 2, and 7.4% had WLZ greater than 2, reflecting improved growth. (table 2)

Head circumference z-scores (HCZ) showed an interesting trend, with 98.5% of infants having HCZ < -2 at birth, which improved significantly, with only 8.5% having HCZ < -2 at age 3, indicating favorable brain growth. (table 2)

Table 2 Proportions of abnormal postnatal growth (%) in infants born With ELBW at different ages.

	% at birth	**% at 18 mon**	**% at 24 mon**	**% at 36 mon**
WAZ <-2	97%	16.67%	14.00%	22.00%
WAZ <-1	100%	35.00%	34.00%	40.00%
WAZ >2	0	5.00%	14.00%	2.00%
WAZ >1	0	11.67%	38.00%	12.00%
LAZ < -2	96%	18.75%	14.00%	10.00%
LAZ <-1	98.5%	53.13%	38.00%	20.00%
WLZ <-2	98.5%	6.00%	17.14%	19.00%

WLZ < -1	100%	24.00%	28.57%	29.00%
WLZ >2	0	5.00%	5.71%	7.41%
WLZ >1	0	16.67%	14.29%	14.81%
HCZ <-2	98.5%	18.00%	8.5%	ND
HCZ <-1	100%	56.00%	31.43%	ND

4. Discussion

The results of our study on postnatal growth in extremely low birth weight (ELBW) infants provide valuable insights into the growth trajectories of this vulnerable population. To contextualize our findings and gain a more comprehensive understanding, we will compare our results with those of different authors who have investigated similar aspects of ELBW infant growth.

Our study revealed that ELBW infants, with a wide range of gestational ages at delivery (23 to 27.5 weeks), exhibited severe growth restriction at birth. This is consistent with findings from González-García et al who reported similar growth deficits in ELBW infants at birth. In addition, early catch up growth in WAZ and WLZ occurred in our infants, however the majority (85 and 79%) were still having WAZ <-2 on the 2nd and 4th months postnatally. In Gonzalez et al study, 76.6 % of ELBW babies had WAZ <-2. (25)

During the first 24 months of life, our ELBW infants displayed progressive catch-up growth in weight-for-age (WAZ) and length-for-age (LAZ), showing significant improvements from their initial z-scores. This finding aligns with other studies reported a similar pattern of catch-up growth in WAZ in ELBW infants during the first two years. (9, 17, 18, 20,22)

At ages 2 and 3 years, 86 and 90% of our ELBW infants had normal height (HAZ >-2) which goes with the finding of González-García et al who reported normal height At age 2, and 4 in 49.4%, 78.9% of their children with ELBW.

However, the catch-up growth in WAZ plateaued during the third year of life in our ELBW infants. 40 % of our VLBW children had WAZ < -2 at 3 years of age. The implications of this plateau in WAZ warrant further investigation, as it may indicate a need for continued nutritional support beyond the initial two years.

Consistent catch-up growth in LAZ over three years, as observed in our study, is an encouraging finding. This observation is in line with other studies reporting progressive catch up in LAZ up to the age of 8- 11 years. It highlights the potential for ELBW infants to achieve improved length growth, even after severe growth restriction at birth. (9, 21)

Mukhopadhyay et al reported significantly improved WAZ (from -2.3 ± 1.2 to -1.7 ± 1.4) and LAZ (from -2.1 ± 1.5 to -1.5 ± 1.3) in 99 ELBW infants from 40 weeks to one year (26).While Deng et al followed growth in 32 ELBW, 504 LBW and 198 normal-birthweight and reported faster rates of catch-up growth for weight, length and HC at 1 year of corrected age (CA) in the first 2 groups compared to normal group. (22.6% , 29.1% and 14.6%, respectively) (18).

Weight-for-length z-score (WLZ) showed an intriguing pattern in our study, with significant increases during the first year, particularly in the first 6 months, followed by a mild deceleration in the subsequent two years . This suggests that the initial rapid improvement in WLZ may be attributed to weight gain outpacing length growth during the early postnatal period. However, the subsequent decline in WLZ could be linked to the relatively faster gain in length compared to weight, emphasizing the importance of maintaining a balanced growth trajectory.

The proportion of infants with WAZ, LAZ and HCZ below -2 decreased over time in our study, reflecting significant catch-up growth. By age 3, a notable percentage of infants achieved improved z-scores, indicating a favorable response to nutrition. This finding is consistent with the work of other authors. Matsuda et al., studied 16 ELBW infants and reported that 94% and 88% of ELBW had LAZ > −2 and WAZ >-2 at age 3 yr. Brinkis et al reported significant catch up in LAZ, WAZ, and HCZ in infants born VLBW (n= 59) during the first year of life (from −1.29 to 0.35, from −1.77 to −0.03 and from −0.97 to -0.5 respectively). these data highlighting the effectiveness of nutritional and healthcare strategies in promoting postnatal growth. (27,28)

Our study also noted a noteworthy trend in head circumference z-scores (HCZ), with a significant improvement from birth to age 3. This reflects favorable brain growth in ELBW infants. This finding is consistent with the research conducted by Michaelis et al, who reported that mean HCZ in 48 VLBW infants were initially below −1.5 , but after 6 months the z-scores were within normal limits (−0.19) and remained normal thereafter (29) While Deng et al reported HCZ catch up (Z-score gain >0.67) in 28% of their ELBW infants (n= 90) at 6 months and 33% at 12 months (18). In addition, Hong et al described significant catch up in the head size in the majority of their VLBW infants (206/253) during the first 2 years postnatally (30). These data emphasized the importance of assessing head circumference as an indicator of brain development in ELBW infants. (31,32)

Limitations of the study include the small sample size, single-centre design, and potential confounding factors not accounted for in the analysis. Future research should aim to replicate these findings in larger and more diverse populations and explore the potential impact of various nutritional interventions and additional factors that may influence growth patterns in ELBW infants.

5. Conclusion

ELBW infants who received preterm formula for 4-6 months demonstrated significant catch-up growth in weight, length, and weight-for-length during the first 12-18 months of life. Catch-up in length continued during the third year of life, highlighting the importance of early interventions in promoting growth in ELBW infants. The majority of ELBW infants achieved normal growth parameters by age 3, emphasizing the effectiveness of nutritional strategies and healthcare interventions in supporting postnatal growth.

While our findings reveal the achievement of improved growth parameters in the majority of ELBW infants, the plateau in weight growth beyond the first two years warrants further investigation to optimize long-term nutritional strategies. The finding that 7.4% of ELBW infants were overweight at age 3, necessities continued monitoring and care.

Compliance with ethical standards

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Disclosure of conflict of interest

Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Author contributions

FA and ATS shared the conception/design and coordination of the review. FA, DA, HA, MS, NA, NH, SA collected the data and followed the patients. All the Co-Authors contributed to the interpretation of data, writing the manuscript, and provided critical comments and suggestions on the manuscript for important intellectual content. All authors read the final version of the manuscript and approved it. VDS performed a critical revision and editing of the manuscript.

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