RESEARCH BRIEF

Longitudinal Growth and Post-discharge Mortality and Morbidity Among Extremely Low Birth Weight Neonates

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Objectives: To study post-discharge growth, mortality and morbidity of extremely low birth weight neonates at corrected age of 2 years. **Methods***:* Weight, length and head circumference were compared on WHO growth charts at corrected ages 3 (*n*=54), 6, 9, 12 (*n*=51) and 24 months (*n*=37); rates of underweight, stunting, microcephaly and wasting were calculated. **Results**: The mean Z-score for weight, length, head circumference and weight-for-length significantly improved from 3 to 24 months (*P*<0.001); a significant proportion remained malnourished at 2 years. Nine infants (11%) died and 35 (44%) required re-admission during first year of age. **Conclusion**: Extremely low birth weight neonates remain significantly growth retarded at corrected age of 2 years.

Keywords: *Low birth weight, Neonate, Outcome, Protein energy malnutrition.*

Recent advances in neonatal care have resulted in improved survival of extremely low birth weight (ELBW) neonates. These babies are prone for significant growth failure during infancy [1,2]. An ELBW Taiwan cohort reported significant delay in weight, length and head circumference (HC) till corrected age of 2 years [3]. Sharma, *et al*. [4] reported a subgroup of ELBW neonates who were undernourished and microcephalic; two-thirds remained stunted at corrected age of 18 months [4]. We previously reported poor growth among VLBW infants with two-thirds being underweight and stunted, and nearly 50% having microcephaly and wasting at 1 year of corrected age [5]. In addition, ELBW infants have significant post-discharge morbidities and mortality [6]. Indian data on growth as well as post-discharge death and readmission rate are lacking.

METHODS

This study was conducted over a period of 4 years in the follow-up clinic of a level III neonatal unit in Northern India. All consecutively born ELBW neonates (birth weight <1000 g) between 2009-2011, who were discharged alive from the hospital were enrolled after written informed consent from parents, and followed up till 2 years of corrected age. Infants with major congenital malformations and chromosomal abnormalities were excluded. The morbidities during hospital stay and survival till discharge of this cohort have been previously published [7]. This cohort was followed up at corrected age of 3, 6, 9, 12 and 24 months. During each visit, growth (weight, length and HC) was assessed. All anthropometric parameters were plotted on the WHO multi-center growth reference study (MGRS) charts using the WHO software and their Z-scores were calculated [8]. Underweight was defined as weight <-2SD, stunting as length <-2SD, microcephaly as HC <-2SD and wasting as weight-for-length <-2SD. In lost to follow-up cases, we tried to contact through telephone and our research staff made home visits to local families. Institutional Ethics committee approved the study.

Accompanying Editorial: Pages 699-700.

Small for gestational age (SGA) status was assigned using Lubchenco's intrauterine growth charts [9]. Bronchopulomonary dysplasia (BPD) was defined as the need for oxygen for ≤28 days. Necrotizing enterocolitis was classified using modified Bell's criteria [10]. Diagnosis at readmission in our hospital was as per standard protocol, and for admissions outside the hospital, the diagnosis was obtained from patients' records.

Primary outcome was proportion of underweight at corrected age of 2 years. Secondary outcomes were proportion of stunting, microcephaly and wasting at corrected age of 2 years, and mortality and morbidity during first year of age.

Student *t*-test was used to compare means and chi-square test to compare the proportions. Demographic and growth variables till 3 months were compared between those who had poor growth and those with normal growth at chronological age 1 year. The factors which emerged significant ($P<0.01$) on univariate analysis were then entered in to a multivariate binomial logistic regression model using forward LR, stepwise fashion to identify factors predictive of malnutrition at corrected age of 12 months. A *P* value of <0.05 was considered significant.

TABLE I GESTATIONAL AGE WISE GROWTH OF ELBW NEONATES TILL 2 YEARS OF CORRECTED AGE

Variables	*Gestational age category (wk)*		
	<28	*28-29*	*>30*
Live births (*n*)	42	46	61
Discharged alive (*n*)	10	26	43
Gestational age (wks)	26.2 (0.8)	28.7 (0.5)	31.6 (1.6)
SGA (*n*, %)	2 (20%)	10 (39%)	39 (91%)
3 mo (*n*=54) *Z* scores			
WFA	-3.4 (1.1)	-3.4 (1.2)	-4.4 (1.2)
LFA	-3.0 (1.5)	-3.5 (1.7)	-4.4 (1.3)
HFA	-2.6 (1.0)	-2.2 (0.9)	-2.9 (1.3)
WFL	-1.2 (0.9)	-0.4 (1.6)	-0.8 (1.9)
6 mo (*n*=51) *Z* scores			
WFA	-2.9 (1.0)	-2.3 (1.3)	-3.3 (1.4)
LFA	-2.8 (1.2)	-2.5 (1.3)	-3.6 (1.4)
HFA	-2.3 (0.9)	-1.7 (0.9)	-2.2 (1.3)
WFL	-1.6 (1.2)	-0.8 (0.9)	-1.2 (1.4)
9 mo (*n*=51) *Z* scores			
WFA	-2.7 (1.1)	-2.1 (1.3)	-2.6 (1.5)
LFA	-2.6 (0.9)	-2.2 (1.1)	-2.6 (1.4)
HFA	-2.0 (0.7)	-1.7 (1.1)	-1.9 (1.2)
WFL	-1.6 (1.1)	-1.1 (1.1)	-1.7 (1.5)
12 mo (*n*=51) *Z* scores			
WFA	-2.2 (0.9)	-2.0 (1.1)	-2.3 (1.7)
LFA	-2.1 (1.2)	-2.1 (1.0)	-2.5 (1.2)
HFA	-1.9 (0.7)	-1.7 (1.1)	-1.9 (1.2)
WFL	-1.6 (0.4)	-1.4 (1.5)	-1.4 (1.7)
24 mo (*n*=37) *Z* scores			
WFA	-1.5 (0.4)	-1.6 (1.2)	-2.1 (1.4)
LFA	-2.6 (0.5)	-2.2 (1.1)	-2.5 (1.3)
HFA	-0.8 (0.8)	-1.7 (1.2)	-1.7 (1.1)
WFL	-0.1 (0.2)	-0.6 (1.1)	-1.1 (1.4)

Values are expressed as Mean (SD) unless specified; SGA-small for gestational age, WFA-weight for age, LFA-length for age, HFA-head circumference for age, WFL-weight for length.

RESULTS

Of the 149 ELBW neonates admitted to the NICU, 79 were discharged alive. Mean gestational age and birth weight were 29.9 (2.3) weeks and 872 (82) g, respectively. Fifty-one (64.5%) were SGA and 41 (52%) were males. The mean (SD) postnatal age and weight at discharge were 46 (19) days and 1440 (289)g, respectively, and the post-conceptional age was 36.9 (2.3) weeks. Follow-up could be completed in 54 children at 3 months (±1 week), 51 at 6, 9 and 12 months (±2 weeks) and 37 corrected age of 24 months (±1 month) (14 lost). The growth pattern as per gestation subcategories is shown in ***Table* I**. At corrected age of 1 year, growth was below 3rd centile in 60% infants for weight, 49% for length and 61% for HC. Overall, Z-scores for weight and HC improved significantly from 3 months to 2 years whereas that for length improved from 3 to 12 months, but had a slight decline at 24 months. Weight-for-length scores declined from 3 to 9 months, plateaued between 9 and 12 months, and thereafter increased till 2 years (***Fig.* 1**). At corrected age of 2 years, 41%, 68%, 32% and 19% children remained underweight, stunted, microcephalic and wasted, respectively. There was no difference between growth of SGA and appropriate for gestational age (AGA) children (***Table* II**).

Forty-four percent (35 of 79) children required readmission during first year (21 once, 9 twice and 5 thrice). Reasons for readmissions were anemia (10, 19%), sepsis (8, 15%), pneumonia (8, 15%), acute gastroenteritis (6, 11%), bronchiolitis (3, 6%), laser treatment of retinopathy of prematurity (3, 6%), inguinal hernia (6, 12%) and fever (3, 6%). Nine children (11%) died during first year (sepsis 6, pneumonia 3).

We created a prediction model for underweight infants at corrected age of 1 year. Univariate analysis revealed BPD, intraventricular hemorrhage (IVH), grade III /IV and Z-score for weight at 3 months to be significant predictors of underweight at 1 year. Regression analysis revealed Z-score at 3 months (OR 0.4, 95% CI: 0.2-0.8; P=0.006) and IVH grade III/IV (OR 11.1, 95% CI: 1.04-118.1; P=0.046) as independent predictors of underweight at corrected age of 1 year. Overall, this model had an accuracy of 80% for predicting underweight at 1 year.

DISCUSSION

Our results showed that a significant proportion of ELBW neonates remained growth retarded at 1 and 2

TABLE II GROWTH OF ELBW NEONATES TILL 2 YEARS OF CORRECTED AGE IN SGA *VS* AGA

Variables	*SGA (N=51)*	*AGA (N=28)*	*P value*
3 mo	*n*=36	*n*=18	
WFA z score	-4.1 (1.3)	-3.9 (1.3)	0.68
LFA z score	-4.2 (1.5)	-3.5 (1.4)	0.19
HFA z score	-2.6 (1.1)	-2.6 (1.3)	0.99
WFL z score	-0.7 (1.7)	-0.5 (1.7)	0.67
6 mo	*n*=31	*n*=20	
WFA z score	-3.1 (1.7)	-3.1 (1.0)	0.94
LFA z score	-3.1 (1.6)	-3.2 (1.1)	0.89
HFA z score	-2.0 (1.1)	-2.1 (1.1)	0.71
WFL z score	-1.3 (1.2)	-1.3 (1.0)	0.91
9 mo	*n*=32	*n*=19	
WFA z score	-2.4 (1.5)	-2.8 (1.1)	0.35
LFA z score	-2.5 (1.2)	-2.6 (0.8)	0.73
HFA z score	-2.0 (1.0)	-2.1 (1.0)	0.67
WFL z score	-1.4 (1.5)	-1.7 (0.9)	0.58
12 mo	*n*=31	*n*=20	
WFA z score	-2.2 (1.5)	-2.6 (1.0)	0.40
LFA z score	-2.4 (1.2)	-2.3 (1.1)	0.77
HFA z score	-1.9 (1.0)	-2.1 (1.1)	0.63
WFL z score	-1.3 (1.6)	-1.9 (0.9)	0.20
24 mo	*n*=23	*n*=14	
WFA z score	-1.9 (1.5)	-1.7 (1.2)	0.78
LFA z score	-2.5 (1.4)	-2.4 (1.0)	0.90
HFA z score	-1.6 (1.0)	-1.7 (1.3)	0.98
WFL z score	-0.8 (1.4)	-0.7 (1.1)	0.80

Values are expressed as Mean (SD); SGA-small for gestational age, WFA-weight for age, LFA-length for age, HFA-head circumference for age, WFL-weight for length. P<0.05 considered significant.

years despite improving trend in their Z-scores. Weight at 3 months and major IVH were significant predictors of underweight at 1 year. Nearly half of ELBW infants required readmission and 11% died during follow-up of one year.

The main limitation of our study is high rate of loss to follow-up which probably underestimated deaths and admissions. There is also a possibility of failure to recall all admissions and morbidities. Moreover, sample size was small and post-discharge dietary details were not recorded adequately, which could have helped us to determine the cause for persistent poor growth.

Lin, *et al*. [3] found that 30-40% of their ELBW infants had delay in weight, length and HC at 6, 12 and 24 months, which remained more or less constant. The

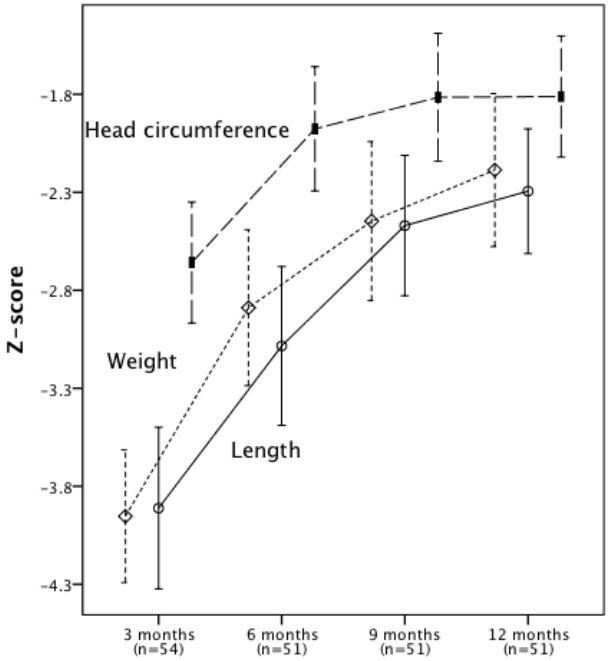

FIG. 1 *Pattern of growth in terms of weight, length and head circumference of ELBW neonates.*

Z-scores for the growth were significantly lower than term babies at 2 years. Sharma, *et al*. [4] also reported that 60% of their ELBW neonates had undernutrition, 75% were stunted, 60% had microcephaly and 18% had wasting at corrected age of 18 months. Modi, *et al*. [11] reported significantly lower *Z*-scores for weight, length and HC at 1 year in VLBW babies. ELBW babies develop a large protein and calorie deficit in the initial postnatal period which later on becomes difficult to compensate. In addition, inadequate complementary feeding along with recurrent illness and hospitalizations add to poor growth during childhood.

Sharma, *et al*. [4] reported 9% readmissions and 8% death during their 18 month follow-up period, though only a small proportion were ELBW and this might have probably underestimated their re-admission and death rates. An Australian study [12] showed that their cohort of 63 ELBW babies required frequent hospitalizations due to ill-health.

We conclude that ELBW babies continue to improve their growth but a sizeable proportion remains growth retarded at 2 years. Hence it is important not only to emphasize on their immediate postnatal nutrition but also continued monitoring of their diet and growth during follow-up, appropriate timely intervention and adequate pre-discharge counseling to prevent mortality and morbidities. Studies with larger sample size and longer duration of follow-up are

WHAT THIS STUDY ADDS?

- A significant proportion of ELBW neonates remain growth retarded at 2 years and suffer from significant post-discharge mortality and morbidities.

needed from diverse settings in developing countries.

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