RESEARCH PAPER

Growth and Neurodevelopmental Outcomes of Very Low Birth Weight Infants From Southern India at Corrected Age of One Year

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Objective: To assess the growth and neurodevelopmental outcome of very low birth weight (VLBW) infants at corrected age of one year. **Methods:** This prospective cohort study enrolled VLBW infants delivered in a tertiary care hospital, and followed up till one-year corrected age. The WHO Anthropo version 3.2.2 software was used to calculate weight for age, length for age, and head circumference *z*-score during follow up. Neuro-developmental assessment was done using Developmental Assessment Scale for Indian Infants (DASII) at the age of one year. **Results:** The mean (SD) *z*-scores at one-year for weight for age, length for age and head circumference were -2.1 (1.1), -1.4 (1.03) and -2.2 (1.2), respectively. The mean (SD) DASII motor and mental scores were 90.8 (13.4) and 96.5 (13.2), respectively. Major and minor developmental abnormalities were noted in 9.4% and 18.2%, infants, respectively. Cerebral palsy was noted in 5.8% infants. **Conclusion:** VLBW infants showed impaired growth and significant developmental abnormalities at the corrected age of one year.

Keywords: *Cerebral palsy, Development quotient, High risk follow up*.

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VLBW neonates contribute to 1.4- 2.1% of total live births [1,2]. With an increase in the incidence of prematurity and better neonatal care, the number of very low birth weight (VLBW) survivors is increasing, who are prone to short term adverse outcomes and long-term neurodevelop-mental problems [3]. In the earlier Pune study [4], preterm small for gestational age infants and VLBW infants had the poorest cognition at the age of 12 years. There is paucity of literature from southern India related to long-term out-comes of VLBW infants. This study was done to assess the growth and neurodevelopmental outcomes of VLBW infants at corrected age (CA) of one-year.

METHODS

This prospective cohort study was conducted at a tertiary care teaching hospital in southern India from January, 2017 to December, 2018 after approval from institutional ethics committee. All VLBW inborn neonates delivered in the hospital during the study period were enrolled after obtaining informed consent from the parents. Neonates with one or more of the following were excluded: *i*) birth weight <500 g and/or gestational age (GA) less than 25 weeks; *ii*) presence of lethal congenital malformations, and *iii*) death within 6 hours of life. All neonates were managed as per standard neonatal intensive care unit (NICU) protocols.

Relevant antepartum and intrapartum details including mother's age, parity, associated medical or pregnancy related complications, ultrasound findings, antenatal steroid use, fetal distress, and mode of delivery were recorded from maternal case records on a pre-structured form. Gestational age was determined by first trimester scan findings or new Ballad score. In case of discrepancy between these two methods, first trimester scan findings were preferred. Neonatal data including gender, birth weight, resuscitation details and Apgar scores were recorded. Co-morbidities observed during the NICU stay were also recorded. Enrolled infants were assessed within 24 hours of birth, at discharge, 40 weeks of CA, and subsequently at CA of 3, 6, 9 and 12 months with time tolerance limit of ± 7 days on the day of assessment at high risk follow up clinic.

Invited Commentary: Pages 15-16.

At each visit to the clinic, the infant was evaluated for anthropometric measurements, clinical assessment of vision and hearing, neurological examination and develop-mental assessment. Vision was assessed by the ability to fix and follow a target and hearing was checked using a bell. Screening for retinopathy of prematurity (ROP) was done first at 3 weeks of CA in eligible neonates and was classified according to the International Classification of

Retinopathy of Prematurity (ICROP) [5]. Hearing screening was done by oto-acoustic emission (OAE) (Interacoustics Titan TEOAE 440) at 34 weeks of gestation or prior to discharge, whichever was later. Infants who failed on OAE were further assessed by brain evoked response auditory (BERA) in the Ear Nose and Throat (ENT) department of the Institute. Cranial ultrasonography was done as per the unit protocol.

Weight, length and head circumference were measured using infant weighing scale, infantometer and non-stretchable tape, respectively. All equipment were calibrated and standard precautions were taken during measurements by the first author. Growth was assessed by measuring weight for age, length for age and head circumference for age. Growth was plotted on Fenton charts for boys and girls till 40 weeks of CA, after which WHO child growth standards were used till one-year CA. Growth parameters were entered in WHO Anthropo version 3.2.2 to calculate the *z*-score. A single trained researcher carried out all the neurological and anthropometric evaluations.

The neurodevelopmental assessment was done at one-year CA using Developmental Assessment Scale for Indian Infants (DASII), which is an Indian adaptation of Bayley scales of infant development (BSID) [6]. Development score less than 70 was considered as severe delay [7]. Major neurodevelopmental abnormality was defined if at least one of the following was present *i*) Cerebral palsy, *ii*) development quotient less than 70% in DASII (either mental or motor assessment), *iii*) vision impairment, or *iv*) hearing impairment. The motor ability of infants with cerebral palsy was graded using the Gross Motor Function Classification System (GMFCS). A GMFCS level ≥II was considered as functionally impaired. Visual impairment was defined as blindness with no functional vision in at least one eye [8]. Hearing impairment was defined as the need for sound amplification. Hearing loss was defined as hearing loss greater than 30 dB in the better hearing ear [9]. Minor neurodevelopmental abnormality was defined as the presence of any morbidity less than that classified as major neurodevelopmental abnormality. Intraventricular hemorrhage (IVH) was detected by ultrasonography, and graded according to Papile classification.

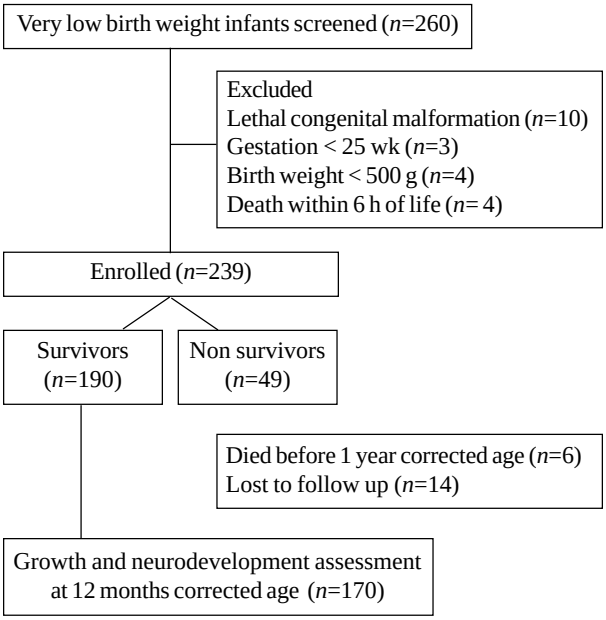

Fig. 1 Flow of participants in the study.

Statistical analysis: Comparisons were made using independent *t* test, paired *t* test and repeated measure ANOVA, and chi-square test as applicable. Statistical analysis was done using Stata version 14. A value of $P<0.05$ was considered statistically significant.

RESULTS

A total of 260 VLBW infants were screened for eligibility at the time of birth and 170 infants were included in the final analysis (**Fig.1**). The baseline characteristics and morbidity profile of the VLBW cohort is described in **Table I**. The mean (SD) motor and mental scores of the babies were 90.8 (13.4) and 96.5 (13.2), respectively. A DASII score below 70% (borderline intellectual functioning) was seen in 13 (7.6%) and 10 (5.8%) babies for the motor and mental domain, respectively. The serial anthropometric parameters and neurodevelopmental parameters at one-year CA are shown in **Table II**.

Major and minor developmental abnormalities were found in 16 (9.4%) and 31(18.2%) infants, respectively. Ten (5.8%) infants developed cerebral palsy at follow up. One infant was diagnosed to have moderate to severe hearing impairment. No infant was noted to have vision loss.

Table I Baseline Characteristics of Very Low Birth Weight Infants Enrolled in the Study (*N*=170)

Variables	*Value*
Birthweight (g) [a]	1253 (170)
Gestational age (wk) [a]	32.1 (2)
Small for gestational age	107 (62.5)
Male gender	83 (48.8)
Sepsis	52 (30.5)
Intraventricular hemorrhage	18 (10.5)
Bronchopulmonary dysplasia	8 (4.7)
Hemodynamically significant PDA	24 (14.1)
Retinopathy of prematurity	7 (4.1)

Data expressed as no.(%) or [a]mean (SD). PDA-patent ductus arteriosus.

WHAT THIS STUDY ADDS?

- Very low birth weight infants have impaired growth and significant developmental abnormalities, at one-year corrected age.

Table II Anthropometric Parameters at Different Time-points in Very Low Birth Weight Infants (*N*=170)

Timing of assessment	*WFA z-score*	*LFA z-score*	*HCFA z-score*
Birth	-1.6 (1.3)	-1.2 (1.6)	-1.5 (1.3)
At discharge[a]	-2.7 (1.1)	-1.8 (1.3)	-1.7 (1.0)
Chronological age			
3 mo	-2.9 (1.3)	-2.3 (1.3)	-2.3 (1.3)
6 mo	-2.4 (1.08)	-1.6 (1.2)	-2.5 (1.1)
9 mo	-2.2 (1.09)	-1.3 (1.0)	-2.5 (1.1)
12 mo	-2.1 (1.1)	-1.4 (1.03)	-2.2 (1.2)

Data expressed as mean (SD). [a]measurements at discharge from neonatal intensive care unit. WFA-weight for age; LFA-length for age; HCFA-head circumference for age.

DISCUSSION

The present study reported growth and neurodevelopmental outcomes of VLBW infant at one-year CA. The anthropometry showed growth impairment and a significant proportion of infants had neurodevelopmental abnormality.

The high rates of neurological and developmental problems reported among VLBW infants are of concern. Birth weight, gestational age, sex, multiple births, antenatal corticosteroid administration, neonatal infection, necrotizing enterocolitis, periventricular leukomalacia and IVH are some of the risk factors that influence both short- and long-term outcomes [11]. Local NICU data on expected mortality and adverse long-term outcomes may be useful to counsel parents of VLBW neonates. The birth weight and gestation of our cohort was comparable to other Indian studies [12,13]. VLBW mortality rate was 20% in the population studied. A birth weight <1000 g, severe grade of IVH, hyperglycemia, and respiratory distress syndrome requiring surfactant therapy were the significant predictors of mortality among VLBW neonates [14].

The mean *z*-scores at one-year CA were below the corresponding *z*-scores at birth. The mean *z*-scores of weight and length were below and farthest from the population median at 3 months CA, and subsequently improved. However, head circumference *z*-scores improved only after 9 months CA. This may suggest that somatic growth in VLBW infants recovers earlier than the neural growth. These findings are similar to an earlier Indian study [12], except that the improvement in *z*- scores for weight and length were noted after three months in our cohort. Although, our study had a larger sample size compared to the earlier Indian studies [6,7,12,13], the results are similar.

According to the Neuroprem 2 study [15], among 502 VLBW survivors who completed 24-month follow up, severe functional disability, and cerebral palsy were seen in 9.6% and 5.4%, respectively. The rates of severe functional disability and cerebral palsy were higher in neonates with a lower gestational age. In our study, the proportion of developmental abnormalities and cerebral palsy were similar. On comparing our data with the Western data, ethnicity and development assessment tools used may have affected the outcome assessment. Extra-uterine nutrition and comorbidities at birth could have influenced both growth and development of the cohort studied.

To conclude, at one-year CA, VLBW infants showed impaired growth and significant developmental abnormalities in this study. Appropriate nutritional and follow-up strategies should be implemented so that these vulnerable infants achieve optimum growth and development.

Ethics clearance: IEC (Human studies), JIPMER, Puducherry; No. JIP/IEC/2016/1145, dated Feb 16, 2017.
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