

## Neurodevelopmental Outcome of Extremely Low Birth Weight Children at Corrected Age of Two Years

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**Objective:** To assess the neurodevelopmental, cognitive and behavioral function of extremely low birth weight babies (ELBW) till corrected age of two years.

**Methods:** 79 ELBW babies were enrolled and followed at 1 year ( $n=50$ ), 18 months ( $n=47$ ) and 2 years ( $n=36$ ). Adverse composite outcome was defined as death or moderate-to-severe neurodevelopmental impairment (defined as either cerebral palsy or DQ score  $<70$  or deafness or blindness).

**Results:** At 1 year, 24% were neurologically abnormal. At 18 months, average score ( $>85$ ) was seen in 25 (54%) children in motor and 8 (17%) in mental development. Abnormal behavioral score ( $\geq 12$ ) was seen in 89% children. Adverse composite outcome was present in 28 (35.4%) babies.

**Conclusion:** ELBW neonates are at a high risk of neurodevelopmental and behavioral impairment.

**Keywords:** Behavior disorders, Cerebral Palsy, Neurological disorders, Preterm, Prognosis.

Availability of advanced neonatal care has led to increasing survival of extremely low birth weight (ELBW) babies. Several studies have reported adverse long term neurodevelopmental outcome of these infants [1-3]. However, there is paucity of data from developing nations on outcome of these infants. In developing countries including India, a high proportion of ELBW babies are small for gestational age (SGA). Outcome of this population may not be comparable to reports from the developed world. Accurate knowledge of outcomes would be helpful in parental counseling and decision-making in our resource-limited scenario. We report the neurodevelopmental outcome in a cohort of ELBW graduates from a NICU of a tertiary-care center.

### METHODS

All consecutive ELBW neonates born between January 2009 and March 2011 in our center and discharged alive were prospectively followed up till corrected age (CA) of 2 years for their neurodevelopmental and behavioral outcome. Institute research ethics committee approved the study and informed consent was obtained from the parents. They were followed up 3-monthly till CA 1 year and then 4-6 monthly till CA 2 years. At each visit, developmental screening was done by Denver

Developmental Screening Test (Denver II) (DDST) [4] and neurological status assessed by Amiel-Tison scale [5] by the consultant neonatologist. DDST was interpreted as 'normal' or 'suspect' as per the manual. Neurological examination was categorized as either abnormal (hypertonia or hypotonia) or normal. Babies with hypertonia were labeled as spastic Cerebral Palsy (CP). Developmental Assessment Scale for Indian Infants (DASII) [6] was conducted by a trained neonatologist at CA 18 months. DASII scores  $<70$ , 70-85 and  $>85$  were defined as delay, borderline and average, respectively. Behavior was assessed by Preschool Behavior Check List (PBCL) [7] at CA 2 years, and a score of  $\geq 12$  was considered high. Moderate to severe neurodevelopmental impairment (NDI) was defined as either CP, or DQ  $<70$  in DASII scale, or blindness, or deafness requiring hearing aids. Adverse composite outcome included the above or death. Mild NDI was defined as mild hypotonia or DQ between 70-85 [8]. Statistical analysis was done using SPSS version 18. Quantitative variables are reported as mean (SD) and qualitative variables as proportions. Comparison was made using student t test or chi square test, as appropriate.

### RESULTS

Of the 255 live births during the study period, 36 babies were followed till 2 years of age (**Fig. 1**).

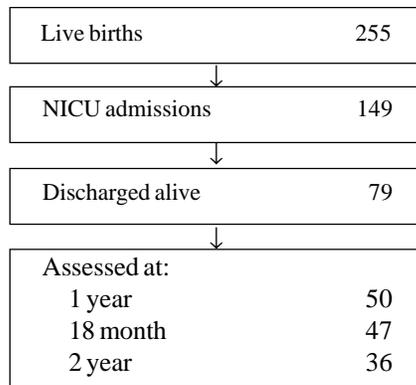


FIG. 1 Study flow chart.

**TABLE I** MOTOR AND MENTAL DEVELOPMENT QUOTIENT IN ELBW CHILDREN AT CORRECTED AGE OF 18 MONTHS (N=47)

Development Quotient	MoDQ, n (%)	MeDQ, n (%)
<70	12(25%)	15(32%)
70-85	10(21%)	24(51%)
>85	25(54%)	8(17%)

Values are expressed as n (%); Mo and Me are motor and mental DQ, respectively.

The mean (SD) birth weight and gestation of the babies who were discharged alive were 874 (81) g and gestation 29.9 (2.2) weeks, respectively and 48 were SGA (62.3%).

At CA 1 year, 38 (76%) were neurologically normal and 12 (24%) were abnormal (7 hypotonic and 5 hypertonic). According to Denver II assessment, 36 (72%) were normal and 14 (28%) were suspect. Adverse composite outcome (moderate to severe NDI including death) was diagnosed in 35.4% (28) at CA 18 months. In

followed up cases (n=57), adverse composite outcome was seen in 49% (28) and in 38% (18, if death excluded). Minor NDI was diagnosed in 45.6% (26). Only 3 children were normal at corrected age 18 months. Mean (SD) of MoDQ, MeDQ and PBCL were 83.1 (16.1), 72.7 (16.1) and 19.4 (4.1), respectively. Thirty two (89%) had high PBCL (score ≥12).

**Table I** depicts the mental (MeDQ) and motor developmental quotients (MoDQ) and PBCL and their subcategories. Overall MeDQ score was lower than MoDQ scores. We did not find any significant effect of any risk factor on the adverse composite outcome (**Table II**).

## DISCUSSION

We assessed an ELBW cohort by using three different tests to detect neurodevelopmental impairment. Neurological abnormality was seen in 24%, Denver II was suspect in 28% and delay (DQ < 70) was in 25% and 32% in MoDQ and MeDQ, respectively.

The major limitation of our study was a very small sample size due to lower rates of survival of ELBW babies [9,10] and limited duration of study. Hence it was difficult to calculate associations of various risk factors to abnormal outcome. Another limitation was high drop-out rate as patients came from very far-off places.

Most of the outcome studies of ELBW are reported in less than 25-26 weeks of gestation [1,11]; however, the mean gestation of our babies was ~29 weeks and proportion of growth retarded babies was higher. Rates of severe NDI has been reported as 17-59% at 18-36 months in ELBW babies [1,11] and gestation is an important variable in calculating risk of NDI. Our higher NDI rates in spite of higher gestation probably can be explained due to high sepsis rate, high SGA proportion and poor postnatal growth [10].

**TABLE II** RISK FACTORS FOR DEATH OR NEURODEVELOPMENTAL IMPAIRMENT (NDI) IN ELBW BABIES

Variables	Death and Moderate to severe NDI (n=28), No. (%)	No (n=3) and Mild NDI (n=26), No. (%)	OR (95% CI)	P value
Ventilated	14 (50)	13 (45)	1.2 (0.4-3.4)	0.78
Male	18 (64)	13 (45)	2.1 (0.7-6.5)	0.17
Small for gestational age	14 (50)	8 (27.5)	0.5 (0.2-1.6)	0.27
Culture positive sepsis	12 (43)	10 (34)	0.7 (0.2-2.2)	0.59
Apnea	15 (53.5)	13 (45)	1.3 (0.5-3.9)	0.55
Hypoglycemia	8 (28.5)	6 (21)	1.5 (0.4-5.1)	0.53
Abnormal USG head (IVH/PVL)	10 (36)	13 (45)	0.6 (0.2-1.9)	0.41
Bronchopulmonary dysplasia	8 (28.5)	9 (31)	0.8 (0.25-2.51)	0.70

IVH: Intraventricular haemorrhage; PVL: Periventricular leucomalacia.

**WHAT THIS STUDY ADDS?**

- Extremely low birth weight babies are at a high risk of neurodevelopmental and behavioral abnormalities; Mental development is affected more than motor development in these babies.

Cerebral palsy was diagnosed in 3.7% and low DQ (70-85) was seen in one-third of babies in a South African study with mean gestation of 30 weeks and birth weight of 1182 grams [12]. A similar rate of NDI was reported by NICHD nearly 2 decades ago in babies with gestational age of 27-32 weeks, in which NDI ranged from 28-40% and only 21% ELBW babies were reported as normal [8]. The Epicure study reported severe impairment in 13.4% and moderate impairment in 11.8% and CP in 14%. Risk factors of CP were male sex, intrauterine growth restriction, surgery, postnatal steroids and high frequency ventilation [2].

Our Mean DQ was comparable to NICHD reports of a mean of 76 [3] and varied from center to center between 70-83 [13]. However, their mean gestation was 26 (2) weeks as opposed to our higher mean gestation. Similar to our data, mean DQ of <70 was seen in 23-30% babies in a cohort of babies who were less than 32 weeks of gestation [8]. High rates of behavioral abnormalities is also a well-recognized feature of ELBW babies, which was also observed by us [14].

We had nearly 30% drop out at 18 months CA. Most of the follow-up studies report a dropout rate of 5-30% [11], and a high dropout rate attributes to a biased higher NDI due to higher reporting of NDI in followed-up cases than non-followed up cases and this issue has been highlighted in a systematic review [15].

With high rates of NDI in ELBW babies, early intervention facilities must be developed across all neonatal intensive care units in our country. For greater generalizability, a multicentric study with a large number of cases and at least 80- 90% follow up rate is desirable.

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