GROWTH, NEURODEVELOPMENT IN EXTREMELY LOWBIRTH BABIES AT TWO YEAR OF CORRECTED AGE

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Abstract:

According to national neonatal perinatal data (NNPD) the survival of ELBW babies has improved from 37% in 2000 to 45% in 2002-3 reports. In our neonatal unit in PGIMER the survival of ELBW babies has been 54-56% in last 5 years, however unfortunately there is very scanty reports of long term outcome of ELBW babies from India. There is very scanty report of long term growth outcome of VLBW and ELBW Babies in our country, we reported VLBW and ELBW babies in our follow up had poor catch up growth, though some catch-up was observed at 6 month but subsequent lag in growth probably reflects poor weaning at 1 year. Infants with extremely low birth weights (ELBWs) are more susceptible to all of the possible complications of premature birth, both in the immediate neonatal period and after discharge from the nursery. These babies are at risk of poor growth and developmental. in the present study a total of 39 cases of ELBW Babies were enrolled during one year study period from July 2011- June 2012 attending the neonatal follow up clinic attained 2year±3month of corrected age. Their detail birth data and postnatal illnesses retrieved from their initial hospital files and unit discharge record. A similar number of babies enrolled at 2yrs±3months of age in the control group. In the present study, we assessed the growth, and neurological outcome in extremely low birth baby attained 2yrs±3 months of corrected age. The study population consisted of 39 children of ELBW baby born during 2009 -10 at PGIMER & same number of normal birth weight children at 2yr±3 months of corrected age who satisfied the inclusion and exclusion criteria. These children were enrolled from neonatal follow up clinic who were already undergoing long term follow up. For growth outcome, we used weight, height & head circumference measurement of child, for neurological and developmental outcome used clinical neurological examination and DP-III. Base line demographic characteristics of our ELBW babies (Cases) were as follows. Mean (S.D) gestational age of ELBW babies was 29.87±2.3 week. Mean (S.D) birth weight 867±71.1 grams, Mean (S.D) length 35±2.1cm & head circumference was 25.76±1.9 cm. Mean hospital stay in the ELBW babies was 48.6±19.9 days. Mean birth weight and gestational age of control group were 2684±166.2g and 39.03±0.9 weeks. At 2year of corrected age we found - Weight was similar in both in case group & control group. (10.04±1.4 Vs 10.75±1.1). Height and head circumference were smaller in cases than control group. (81.4±4.3 Vs 84.4±3.3 and 45.9±1.6 Vs 46.8±1.5. 5% Babies had cerebral palsy in case group (N=2/39) and none in control group. Gross development score (GDS) in Development profile-III in both study group (cases & controls) was similar (72.49±8.08 Vs 73.54±9.3, p=0.596). Significant difference in domains physical (84.5±7.8 Vs 90±3.5, p=0.000) and domains adaptive (81±6.7 Vs. 85.3±5.4, p= 0.003) in cases as compared to controls. There was no difference between SGA and AGA among cases in growth and neurological development. There was no difference between male and female in case group in any parameter. There is very scanty data from our country on longterm follow up of ELBW babies. Our data shows that our ELBW cohort remained small in height and had smaller head circumference though weight was similar as compared to normal control babies.

Key words: ELBW, VLBW, birth weight, neurological examination.

Introduction

Advances in perinatal and neonatal care over the last 30 years have contributed to improved survival among extremely low birth weight (ELBW) infants (1). Though there is a major improvement in survival in the west, the survival of ELBW babies in India is slowly rising. According to national neonatal perinatal data (NNPD) the survival of ELBW babies has improved from 37% in 2000 to 45% in 2002-3 reports (2). In our neonatal unit in PGIMER the survival of ELBW babies has been 54-56% in last 5 years, however unfortunately there is very scanty reports of long term outcome of ELBW babies from India. There is very scanty report of long term growth outcome of VLBW and ELBW Babies in our country, We reported VLBW and ELBW babies in our follow up had poor catch up growth, though some catch-up was observed at 6 month but subsequent lag in growth probably reflects poor weaning (3) at 1 year. Infants with extremely low birth weights (ELBW) are more susceptible to all of the possible complications of premature birth, both in the immediate neonatal period and after discharge from the nursery (4). These babies are at risk of poor growth and developmental. there are several literature available in west about long term growth and neurodevelopmental outcome of very low birth weight babies but the reports are almost nonexistent in our country. Dr Chaudhary et al from Pune (5) had studied the long term outcome on growth and neurodevelopmental of VLBW babies but there were only 3 babies who were ELBW in that cohort. ELBW infants grow poorly in early childhood and during this period tend to remain in the bottom quartile in weight. (6) Of note, small head circumference (less than 3rd percentile) at one year of age or less is strongly associated with low cognition and learning disabilities at school age (7).

METHOD: in the present study a total of 39 cases of ELBW Babies were enrolled during one year study period from July 2011- June 2012 attending the neonatal follow up clinic attained 2 year $\pm$ 3 month of corrected age. Their detail birth data and postnatal illnesses retrieved from their initial hospital files and unit discharge record. A similar number of babies enrolled at 2 yrs $\pm$ 3 months of age in the control group. Following tools used to test the above parameters:

1) Growth at 2 years (Weight, Height, Head circumference).

a) Weight

The nude body weight of each child in standing position is recorded on an electronic weighing scale (make Every India Limited) up to accuracy of 50 gram. Scale is calibrated before each individual weighing then weight plotted on WHO growth chart.

b) **Height:** Stadiometer used to measure height of the children. Stadiometer is a counter recording instrument, with an effortless counter balanced movement. It will give an accurate and direct reading of a subject's height, to the nearest millimetre over a range of 600 mm to 2100 mm. main frame of this instrument is rigidly made of light alloy angle and provided with adjustable wall brackets for mounting purposes. The Stadiometer head-block operates via miniature ball-bearing rollers in order to ensure a movement which is free yet without cross-play. This should not be moved faster than 30cm/sec

c) **Head circumference** - Occipitofrontal circumference was measured by using non flexible fibre glass tape with minimum record of 1mm. the measure was taken by encircling the tape firmly around the head just above the supra orbital ridges and over the most prominent backwardly protruding part of the occiput.

2) Neurological examination

All babies will undergo detailed neurological examination to find out any evidence of cerebral palsy as per structured proforma. The severity of the functional impairment will be scored by expanded and revised Gross Motor Function Classification System (GMFCS)

Diagnosis of cerebral palsy and classification:

Criteria used for cerebral palsy would be as per the group for the Surveillance of Cerebral Palsy in Europe (SCPE) (8). which includes following key points: permanent but not unchanging, involves a disorder of movement and /or posture and of motor function, is due to non-progressive interference, lesion, or abnormality and the interference, lesion or abnormality is in the immature brain.

Cerebral palsy is classified based on the type of neuromuscular deficit (9)

- (i) Spastic
- (ii) Dyskinetic (inclusive of choreoathetoid and dyskinetic)
- (iii) Ataxic
- (iv) Hypotonic and
- (v) Mixed

For functional assessment at 2 years, Gross Motor Function Classification System expanded and revised (GMFCS-E&R) will be used. This system has been found to be reliable and valid system that classifies children with cerebral palsy by their age specific gross motor activity. The GMFCS E&R describes the functional characteristics in five levels, from I to V, in following age groups: upto 2 years, 2 - 4 yrs, 4 - 6 yrs, and between 6 – 12 years. For each level separate descriptions are provided in annexure-5. Children in level III usually require orthoses and assisting mobility devices, while the children in level II do not require assisting mobility devices after the age of 4. Children in level III sit independently, have independent floor mobility and walk with assisting mobility device. In level IV, affected children function in supported sitting but independent mobility is very limited. Children in level V lack independence even in basic antigravity postural control and need power mobility.

3) Developmental outcome

The developmental status will be evaluated by using Developmental Profile(DP) III (annexure 7). DP-III is suitable for assessing development of children from birth to 12 years and 11 months. DP-III is an advanced and new version of DP-II. DP-II has been successfully used for development assessment of children in our set up(10-11) and also DP-III will give extra advantage to us as all the children in our study will be covered by the single scale and It will give uniformity to the results.

Development Profile III. The DP III (10-11, 13) is a 180 items inventory, which assesses the child's developmental status from birth to 12 years, 11 months It assesses the developmental status in five developmental domains namely physical, adaptive behaviour, social-emotional, cognitive and communication. It provides a general developmental score as well as individual score for each domain. Within each scale basals and ceilings are used, so not all the 180 items need to be administered. Start and stop points ensure that only the age appropriate questions are asked. The advanced or delayed development across the five scales and the general development score can be easily spotted using the graphic representation of scores provided in the manual. It takes 20 to 40 minutes to complete the examination . We are using modified DP-III questionnaire and results of which has been well validated by us with Vinland Social Maturity Scale (VSMS) and has been found to be equivalent. The

children have been classified as per the following grades:

- 1) < 70 - delayed
- 2) 70-85-below average
- 3) 85-115-average
- 4) 115-130-above average
- >130-well above average

Outcome measures

1. Growth at corrected age of 2 years.(Weight, Height, headcircumference)
2. Prevalence and type of cerebral palsy.
3. Development scores at corrected age 2 years

All the above parameters compared with normal term controls at 2 years

OBSERVATION & RESULTS

We enrolled 39 cases who were ELBW from our neonatal follow-up clinic (NFC). These babies were born during the year 2009-2010 in PGI. A total of 67 babies were discharged alive during the 2009-2010 period of which 10 babies died after discharge, 7 babies did not turn up at all for follow up and 50 babies were available at corrected age 1 year. Of these 40 babies completed corrected age 2 years during this study period and 1 child died just prior to assessment. Hence we are able to follow up 39 babies till corrected age 2 years. These babies were being followed up prospectively in NFC. WE assessed their growth, neurodevelopment & behavioral outcome at corrected age 2years & compared them with age matched normal term newborn born during the same period as that of cases . ELBW group was termed as cases & term group as controls.

Table 1: Demographic profile of cases

Variables	N=39
Gender	
Male	22 (56.41%)
Female	17 (43.58%)
Birth weight (grams)	867.3± 71.5
Gestational age(weeks)	29.9±2.4
Length(cm)at birth	35±2.1
Head circumference(cm)at birth	25.8±1.9
Mean Discharge Weight (grams)	1481.62±312
PCA (weeks)	35.0±9.8
Duration of hospital stay(days)	48.2±20

The demographic profile of the cases (N=39) represented in table 1. Twenty two (56.41%) were male and 17 (43.58%) were female. Mean (S.D) gestational age of ELBW babies was 29.9±2.4 weeks and Mean (standard deviation) birth weight was 867

± 71.5 grams, and mean (standard deviation) birth length 35 ± 2.1 cm. Mean (S.D) average head circumference measured 25.8 ± 1.9 cm. The mean duration of hospital stay in the case group was 48.2 ± 20 days.

Table 2: Shows Demographic profile of controls

Variables	N=39
Birth weight(grams)	2684 $\pm$ 166.2
Gender	
Male	27(69.2)
Female	12(30.7)
Gestational age(weeks)	39.03 $\pm$ 0.9

Table -2 shows, Among the 39 Control 69.2% (N=27) are male & 30.7% (N=12) are female. Mean (standard deviation) gestational age in the control group was 39.03 ± 0.9 weeks and mean (standard deviation) birth weight was 2684 ± 166.2 grams

Figure-1(a) Comparison of birth weight in cases & control

Figure-1(b) Sex-wise distribution of children in cases & control

Table 3: Morbidities of cases in the neonatal period.

Variables	N=39
Ventilation	17%(N=7)
Sepsis	19%(N=7)
NEC	5%(N=2)
Apnea	22%(N=9)
Hypoglycemia	14%(N=5)
NNJ	36%(N=14)
Polycythemia	14%(N=5)

Table -3 Shows morbidities during neonatal period in cases. Among 39 babies, 17% babies were ventilated, 19% had sepsis, 5% had NEC, 22% Apnea, 14% hypoglycemia, 36% babies had NNJ & 14% had polycythemia.

Table 4: Comparison of Growth parameters at 2 years of corrected age in cases & controls.

	Cases(N=39)	Control(N=39)	P value
Weight(kg)	10.0 $\pm$ 1.5	10.75 $\pm$ 1.2	0.22
Height(cm)	81.4 $\pm$ 4.3	84.4 $\pm$ 3.3	0.001***
Head circumference (cm)	45.9 $\pm$ 1.6	46.8 $\pm$ 1.5	0.015**

Values are expressed as Mean $\pm$ SD; *P value < 0.05 is significant

Table 4 shows the comparison of growth parameters (weight, height & head circumference) of the cases and controls at 2 years of corrected age. In case group mean (SD) weight is 10.0 ± 1.5 kg, mean height is 81.4 ± 4.3 cm & mean head circumference is 45.9 ± 1.6 cm. In control group mean (S.D) weight is 10.75 ± 1.2 kg, height is 84.4 ± 3.3 cm & head circumference is 46.8 ± 1.5 cm. Except weight, both height and head circumference of cases were statistically significantly smaller than controls. These p-value were 0.001 & 0.015.

Figure 4a: Comparison of Weight between cases & control at 2 year of corrected age.

Figure 4b: Comparison of Height between cases & control at 2 year of corrected age

Figure 4c: Comparison of Head circumference between cases & control at 2 year of corrected age.

Table 5: Comparison of various weight centiles in cases & controls at 2 year of corrected age

Weight centile (n%)	CASE(N=39)	CONTROL(N=39)	P-Value
Less than 3 rd centile	8 (20.5%)	0	0.0052
In between 3 rd -15 th centile	23 (59%)	16 (41%)	0.1739
In between 15 th – 50 th centile	3 (7.7%)	0	0.243
Greater than 50 th centile	5 (12.8%)	23 (59%)	0.0001***

Table-5 shows the distribution of the cases and controls according to WHO growth chart of weight at

2 year of corrected age. In case group 20.5% babies had less than 3rd centile, 59% were lies at between 3rd -15th centile, 7.7% were lies at 15th-50th centile & 12.82 % babies were lies at greater than 50th centile while in control group 41% babies were lies at 15th - 50th centile & 59% babies were lies at greater than 50th centile. These result statistically significant in those babies lies at less than 3rd centile & greater than 50th centile, P-value were 0.005 & 0.0001.

Figure 5: Comparison of weight centiles in cases & control at 2 year of corrected age

Table 6: Comparison of various Height centiles in cases & controls at 2 year of corrected age

Height centile (n,%)	CASE(N=39)	CONTROL(N=39)	P-Value
Less than 3 rd centile	10 (25.6%)	0	0.001**
In between 3 rd -15 th centile	22 (56.4%)	6(15.4%)	1.000
In between 15 th – 50 th centile	1(2.5%)	10(25.6%)	0.098
Greater than 50 th centile	6(15.5%)	23(59%)	0.0001***

Table-6 shows the distribution of the cases and controls according to WHO growth chart of Height at 2 year of corrected age. In case group 25.6% babies had less than 3rd centile, 56.4% were lies at between 3rd -15th centile, 2.5% were lies at 15th-50th centile &

15.5 % babies were lies at greater than 50th centile while in control group 15.4% babies lies at 3rd - 15th centile, 25.6% babies were lies at 15th -50th centile & 59% babies were lies at greater than 50th centile. These results statistically significant in those babies lies at less than 3rd centile & greater than 50th centile, P-value were 0.001 & 0.0001.

Figure 6: Distribution of various height centiles in case & control at 2 year of corrected age

Table 7: Comparison of various Head circumference centiles in cases & controls at 2 year of corrected age

Head circumference (n,%)	CASE(N=39)	CONTROL (N=39)	P-Value
Less than 3 rd centile	14 (35.9 %)	0	0.0001***
In between 3 rd -15 th centile	17 (43.6%)	19 (48.71%)	0.820
In between 15 th - 50 th centile	4 (10.25%)	0	0.115
Greater than 50 th centile	4 (10.25%)	20 (51.28%)	0.138

Table -7 shows distribution of the cases and controls according to WHO growth chart of head circumference at 2 year of corrected age. In case group 35.9% babies had less than 3rd centile, 43.6% were lies at between 3rd -15th centile, 10.25% were lies at 15th -50th centile & 10.25 % babies were lies at greater than 50th centile while in control group 48.71% babies lies at 3rd - 15th centile & 51.28% babies were lies at greater than 50th centile. These results statistically significant in those babies lies at less than 3rd centile , P-value were 0.0001.

Figure 7: Comparison of Head circumference centiles in cases & controls at 2 year of corrected age

Table 8: Comparison of Developmental profile III in cases & controls at 2 year of corrected age

DP-III	Cases (N=39)	Controls (N=39)	P value
Domains Physical	84.5±8	90.1±3	0.000***
Domains Adaptive behavior	81.0±7	85.3±5	0.003**
Domains Social-emotional	85.7±9	82.5±8	0.103
Domains Cognitive	75.5±9	75.2±13	0.920
Domains Communication	81.3±10	77.0±12	0.081
General development score(GDS)	72.5±8.0	73.5±9.	0.596

Values are expressed as Mean ± SD; P* value < 0.05 is significant

Table -8 shows comparison of development profile III in cases & controls. In case group mean (standard deviation) domains physical scale was 84.5±8, mean domains adaptive behaviour was 81.0±7, mean domains social-emotional was 85.7±9, mean domains cognitive scale was 75.5±9, mean domains communication scale was 81.3±10 & mean General development score(GDS)72.5±8.0 while in control group mean (standard deviation) domains physical scale was 90.1±3, mean (S.D) domains adaptive behaviour was 85.3±5, mean(S.D) domains social-emotional was 82.5±8, mean(S.D) domains cognitive scale was 75.2±13, mean (S.D) domains communication scale was 77±12 & mean general development score (GDS) 73.5±9. In these result, statistically significant in physical scale & adaptive behaviour P-value were 0.00 & 0.003.

Figure 8a: Comparison of Developmental profile-III between cases & control at 2 year of corrected age.

Figure 8b: Comparison of General development score-wise (GDS) between cases & controls at 2 year of corrected age.

Table 10. Cerebral palsy rate at corrected age 2 yrs in cases & controls.

Cerebral palsy	Case(N=39)	Control(N=39)
CP	2(5%)	0

Table -10 shows, cerebral palsy rate among cases & control group. In case group 2 (5%) babies had CP, both where spastic one baby had diplegia and other baby had quadriplegia whereas there was no case of C.P among controls.

Figure 10: Cerebral palsy rate in cases group at 2 year of corrected age

Table 11: Comparison of weight, height, & head circumference at corrected age 2 years on basis of AGA & SGA in cases (ELBW)

variables	AGA(N=25)	SGA(N=14)	p-value
Weight (Kg)	10.13±1.7	9.9±1.1	0.628
Height(cm)	81.7±5	81.9±2.9	0.593
Head circumference(cm)	46.55±1.64	45.35±1.4	0.616

Values are expressed in Mean ± SD; P value < 0.05 is significant

Table -11 Shows growth parameters in which cases (ELBW) were divided into two group on the basis of AGA & SGA. Among these in AGA group mean (standard deviation) weight was 10.13±1.7, mean (standard deviation) height was 81.66±4.9 and mean (standard deviation) head circumference 46.02±1.6 while in SGA group mean (standard deviation) weight was 9.88±1.1, mean (standard deviation) height 80.88±2.9 & head circumference was 45.75±1. 3.92. These result statistically not significant, P-value were more than 0.05.

Figure 11a: Comparison of weight at 2 year of corrected age in AGA & SGA in case group

Figure 11b: Comparison of height at 2 year of corrected age in AGA & SGA in case group

Figure 11c: Comparison of Head circumference at 2 year of corrected age in AGA & SGA in case group

Table 12: Development profile-III in AGA & SGA babies in case group

DEVELOPMENT PROFILE-III	AGA (N=25)	SGA (N=40)	P-Value
Domains Physical	84.44±8.8	84.64±6.0	0.939
Domains Adaptive behavior	81.48±6.7	80.21±7	0.583
Domains Social-emotional	86.06±9.3	85.07±8.1	0.748
Domains Cognitive	76.76±10	73.21±7.1	0.258
Domains community	81.44±9.1	81.14±11	0.929
General development score	73.12±8.3	71.36±7.8	0.521

Values are expressed as Mean ± SD; P value < 0.05 is significant

Table-12, showed distribution of development profile-3 in AGA & SGA of cases. In AGA group mean (standard deviation) domains physical scale was 84.44±8.8, mean domains adaptive behavior was 81.48±6.7, mean domains social-emotional was 86.04±9.3, mean domains cognitive scale was 76.76±10, mean domains communication scale was 81.44±9.1, mean General development score (GDS) 73.12±8.3 & while in SGA group mean (standard deviation) domains Physical scale was 84.64±6, mean domains adaptive behavior was 80.21±7, mean(S.D) domains social-emotional was 85.07±8.1, mean(S.D) domains cognitive scale was 73.21±7.1, mean (S.D) domains communication scale was 81.14±11, & mean general development score (GDS) 71.36±7.8 these result, statistically not significant, P-value were more than 0.05.

Figure 12: Compression of Development profile-III at 2 year of corrected age in AGA & SGA of case group.

Table 14: Comparison of DP III of males & females at corrected age 2yrs in case group.

DP-III	Male (N=22)	Female (n=17)	P-value
Domains physical	86.0±8.4	82.7±6.7	0.210
Domains adaptive behavior	81.6±5.6	80.2±8.1	0.529
Domains social emotional	85.6±8.8	85.7±9.2	0.965
Domains cognitive	75.5±7.2	75.4±11.6	0.965
Domains communication	80.9±9.3	82.0±10.5	0.738
GDS	72.8±7.0	72.0±9.5	0.746

Table-14, showed distribution of development profile-3 of male & female at corrected age 2yrs in case group. In male group mean (standard deviation) domains physical scale was 86.0±8.4, mean domains adaptive behavior was 81.6±5.6, mean domains social-emotional was 85.6±8.8, mean domains cognitive scale was 75.5±7.2, mean domains communication scale was 80.9±9.3, mean General development score (GDS) 72.8±7.0 & while in female group mean (standard deviation) domains Physical scale was 82.7±6.7, mean domains adaptive behavior was 80.2±8.1, mean(S.D) domains social-emotional was 85.7±9.2, mean(S.D) domains cognitive scale was 75.4±11.6, mean (S.D) domains communication scale was 82.0±10.5, & mean general development score (GDS) 72.0±9.5 these result, statistically not significant, P-value were more than 0.05.

Figure 14: Comparison of DP-III of male & female at corrected age 2 yrs in case group.

Table 16: Comparison of Gross development score (GDS) in cases & controls.

GDS	CASE(N=39)	CONTROL(N=39)	P-value
≤ 85	36(92.3%)	33 (84.6%)	
≥ 85	3(7.7%)	6 (15.4%)	

Table-16, Comparison of Gross development score (GDS) in two groups, on the basis of GDS Score, less than 85 and more than 85. In cases, 36 babies was less than 85 & 3 babies was more than 85 while in controls 33 babies was less than 85 & 6 babies was more than 85, however the difference was statistically not significant.

Figure 16: Comparison of Gross development score (GDS) in cases & controls

Table 17: GMFCS in cases & controls at corrected age of 2 yrs

	Case (N=39)	Control (N=39)	P-value
GMFCS	1.05±0.22	1.00±0	0.15

Table17, GMFCS in cases & controls at corrected age 2 yrs. The mean (S.D) GMFCS in cases was 1.05±0.22 & the mean (S,D) GMFCS in controls was 1.00±0 which was statistically not significant, P-value were more than 0.05.

Figure 17: GMFCS in cases & controls at corrected age of 2 yrs

DISCUSSION

In this prospective study we have enrolled 39 babies who were extremely low birth weight (ELBW) of which 56% (N=22) were male babies and 44% (N=17) were female babies with mean GA was 29.8±2 weeks and mean birth weight was 867.3±71.5 grams. 64% (N=25) of babies belong to AGA group (14 male and 11 female) and 36% (N=14) babies belonged to SGA group (8 male and 6 female).

Study by, Hack et al(21) enrolled ELBW babies with a GA less than 26 weeks and birth weight less than 800 grams, while Bracewell et al (14), enrolled babies who were born at 25 completed week of gestation or less, whereas NICHD trial (15)enrolled ELBW babies with mean gestation of 26 wks and mean birth weight 796 gms in the cohort. Lemon JA et al (16)had enrolled ELBW infants whose birth weight was 501-750 gram, and gestation generally between 23 and 25 weeks.

According to the report of high risk follow up group from Hong Kong,(17) they enrolled ELBW babies with their mean gestational age 26.2 (1.8) weeks and mean birth weight 789 (125) gms in their cohort.

Hence the gestation of our babies were higher as compared to other studies reported from west and Hongkong. The birth weight however were comparable which signifies that our babies were more growth retarded as compared to babies of western origin who were ELBW.

In our study the neonatal morbidities amongst survivors and followed up till 2 years where 17% babies were ventilated, 19% had sepsis, 5% had NEC, 22% Apnea, 14% hypoglycemia, 36% babies had NNJ & 14% had polycythemia, though in our original cohort of ELBW babies (N=149) 88% had respiratory distress, of which 68% received ventilation.

Shanker et al (13) reported morbidities in ELBW babies over seven year (1994-2000) period showed, 65% had Respiratory distress, 52% had sepsis, 13% had NEC & 36% had hypoglycemia. This shows a significant number of ELBW babies were sick at birth as expected which would have affected their long term growth and neurodevelopment. Relatively less morbidities in survivors in our cohort shows that more sick babies died during neonatal period.

In our study mean duration of hospital stay was 48 ± 19.9 days, whereas study by, K.K. Roy et al showed mean duration of hospital stay in ELBW babies was 36 days. This may be due to more sickness in our original cohort babies. Mean discharged weight was 1481.62 ± 312 grm and PCA was 35.03 ± 9.8 weeks. This shows poor growth at discharge which is probably due to inadequate postnatal nutrition. In ELBW babies along with breast-feed they also require additional supplementation/ fortification (13).

our result shows that height (81.3 ± 4.2) and head circumference (45.9 ± 1.6) in ELBW babies at 2 years of corrected age was found to be lesser than the control group and which was statistically significant though we did not find any difference in weight (10.04 ± 1.4 Vs. 10.75 ± 1.1) at 2 years. Studies from developing and developed country showed significant growth retardation in the form of decreased height, weight and head circumference. Study by Bracewell et al, (14) enrolled babies with gestational age <26 weeks, these babies had significantly impaired growth (height, weight and head circumference) at 30 months. Saigal et al (18) study at adulthood, body size of both sexes of ELBW participants was significantly smaller in both height and weight compared with their peers.

This is similar to our studies weight pattern in our control group probably signifies that even in term babies weaning is inadequate leading to poor weight gain during 1st 2 years of life.

In case group at 2 year of corrected age weight, height and head circumference was plotted on WHO chart which showed weight in 20.5% babies had less than 3rd centile, in 59% they were between 3rd-15th

centile, in 7.7% they were between 15th-50th centile & 13% babies were at greater than 50th centile. Length was 25.6% babies had less than 3rd centile, 56.4% were lies at between 3rd-15th centile, 2.56% were lies at 15th-50th centile & 15.38 % babies were lies at greater than 50th centile and head circumference was 35.89% babies had less than 3rd centile, 43.58% were lies at between 3rd-15th centile, 10.25% were lies at 15th-50th centile & 10.25 % babies were lies at greater than 50th centile. Whereas study by, Susan et al used growth charts developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (published May 30, 2000), growth outcome at 18 to 22 months of corrected age in ELBW babies showed weight, length and head circumference were less than 10th centile. study from AIIMS by Pradeep et al (19) showed, Nearly one-third infants were undernourished, a half were stunted and one-fourth had microcephaly at 18 months corrected age.

Dusick et al (20) previously reported on growth outcomes at 18 to 22 months corrected age in a cohort of ELBW infants, 46% of the infants were below the 10th percentile for weight and 43% were below the 10th percentile for length and head circumference.

This shows that ELBW babies uniformly have poor growth pattern due to initial poor growth during postnatal period and subsequent inadequate catch up during infancy.

Neurological development: Neurological assessment of the babies was done by clinical neurological examination and developmental profile-3. Cerebral palsy is a major handicap, which is dreaded by physician caring for high-risk infants. In our study we have conducted neurological assessment of ELBW babies at corrected age of 2 years and we found that incidence of cerebral palsy was 5% (N=2/39) in ELBW babies. We have very scanty report of neurological outcome in ELBW babies from India most reports are of VLBW babies.

A study from Pune by Chaudhari et al, (5) reported the rate of CP among low birth weight babies was 4% at 2 years corrected age however they had very less number of ELBW babies in their cohort. study from AIIMS by Pradeep et al (19) reported 4.5% babies had CP at 18 month of corrected age and 9.7% babies had developmental delayed. A study from our hospital by Kanya et al, (3) on long term neurodevelopmental

and behavioral outcome on very low birth weight babies showed 3% of babies had cerebral palsy at corrected age of 2 years and there were 20 ELBW babies in that cohort amongst ELBW babies one baby (6.6%) had CP.

Report of high risk follow up group from Hong Kong, showed that the rates of cerebral palsy and intellectual impairment were 12% and 16% in ELBW babies (17) and the mean gestational age was 26.2 (1.8) wks and mean birth weight was 789 (125) gms in that cohort.

Wilson – Costello et al. reported improved survival in ELBW babies during 1990-1998 period as compared to during 1982-1989 period (from 49% to 67%) however the CP rate also increased along with improved survival rate (16 to 25%) and neurodevelopmental abnormality increased from 26% to 36%. However subsequently (during 2000-2002) there was an improving trend in the outcomes of ELBW due to improvement in neonatal care and recorded rate of cerebral palsy declined from 13% to 5% and adverse neurodevelopmental outcome from 35% to 23%. There is a declining trend in CP rate amongst VLBW babies as reported by European database study (21) and the rate fell from 60.6 per 1000 live born VLBW infants in 1980 to 39.5 in 1996.

In our ELBW babies, the CP rate was lower as compared to western literature probably due to higher gestation in our babies and nearly 36% of our ELBW babies were SGA. It may also be explained due to lesser survival amongst extremes of gestation in our study.

We have performed Developmental profile- III tests on all babies, in which physical domains, includes items measuring gross and fine motor skills, coordination, strength, stamina, and flexibility. Adaptive behavior scale, this scale measures an individual's age-appropriate independent functioning, which includes the ability to use current technology. Social-Emotional scale, measures skills related to interpersonal behaviors and the demonstration of social and emotional competence. Cognitive scale, which measures perception, concept development, number relations, reasoning, memory, classification, time concepts, and related mental acuity tasks and Communication scale score reflects ability to understand spoken and written language as well as use both verbal and nonverbal skills to communicate.

Our study showed significant difference in domains physical (84.5 ± 7.8 Vs. 90 ± 3.5 , $p=0.000$) and domains adaptive (81 ± 6.7 Vs. 85.3 ± 5.4 , $p=0.003$). However there is paucity in literature regarding developmental assessment in ELBW by applying DP-III test. Most of the studies from developed and developing country used Bayley scale to assess the neurological outcome in these babies, which showed abnormal mental developmental index and psychomotor developmental index.

Doyle et al (22) studied in preterms at 2 year of age and used Bayley II for neurodevelopment assessment which showed Moderate or severe cerebral palsy, developmental quotient < -2 SD relative to controls and rate of disability was 28%.

Mikkola et al (23) studies in ELBW babies (GA was 22-26 wks) babies, neuroassessment at 5 years showed Moderate or severe cerebral palsy, severe visual impairment, deafness with hearing aids, epilepsy, shunted hydrocephalus, intelligence quotient < 50 and rate of disability was 25%.

Studies from our country by Chaudhari et al (5) and Kanya et al (3) used DASII scale, which also showed abnormal motor and mental development. Study by Kanya et al (3) showed developmental assessment the mean mental and motor quotients of our VLBW babies were lower than the Pune study group babies (less than 70 vs 90). ELBW children have moderate to severe deficits in academic achievement, attention problems, and internalizing behavioral problems, which are adverse outcomes that were strongly correlated to their immaturity at birth. All behavioral problems, attention problems were most pronounced in these babies. Attention-deficit hyperactivity disorder, mainly the inattentive type is prevalent among ELBW children. Early identification and intervention for these problems might improve child functioning and ameliorate parent and child distress. Hence our studies were consistent with other reports of poor developmental status in a high proportion of ELBW babies. (20)

We did not find any difference in neurodevelopmental and growth outcome amongst SGA and AGA babies. However Pune study reported that preterm AGA babies show earlier catch up than preterm SGA babies (24) and at 6 years preterm SGA had lowest IQ scores (25)

Though the NICHD trial did not report the outcomes separately in SGA babies, Gutbord et al. (26) reported

long term developmental outcomes in VLBW SGA babies at 20months. They found SGA babies had poor head growth, early developmental delay and later language problem.

However, we did not find such difference which probably can be explained due to shorter duration of study. It may be again explained due to the fact that ELBW babies suffer so much postnatal growth retardation that at long run there is no difference between SGA and AGA.

SUMMARY

In the presence study, we assessed the growth, and neurological outcome in extremely low birth baby attained 2yrs±3 months of corrected age. The study population consisted of 39 children of ELBW baby born during 2009 -10 at PGIMER & same number of normal birth weight children at 2yr±3 months of corrected age who satisfied the inclusion and exclusion criteria. These children were enrolled from neonatal follow up clinic who were already undergoing longterm follow up.

For growth outcome, we used weight, height & head circumference measurement of child, for neurological and developmental outcome used clinical neurological examination and DP-III.

Base line demographic characteristics of our ELBW babies (Cases) where as follows.

- 1) Mean (S.D) gestational age of ELBW babies was 29.87 ± 2.3 week
- 2) Mean (S.D) birth weight 867 ± 71.1 grams, Mean (S.D) length 35 ± 2.1 cm & head circumference was 25.76 ± 1.9 cm.
- 3) Mean hospital stay in the ELBW babies was 48.6 ± 19.9 days.
- 4) Mean birth weight and gestational age of control group where 2684 ± 166.2 g and 39.03 ± 0.9 weeks.

At 2year of corrected age we found

1. Weight was similar in both in case group & control group. (10.04 ± 1.4 Vs 10.75 ± 1.1)
2. Height and head circumference were smaller in cases than control group. (81.4 ± 4.3 Vs 84.4 ± 3.3 and 45.9 ± 1.6 Vs 46.8 ± 1.5)
3. 5% Babies had cerebral palsy in case group (N=2/39) and none in control group
4. Gross development score(GDS) in Development profile-III in both study group (cases & controls) was similar (72.49 ± 8.08 Vs 73.54 ± 9.3 , $p=0.596$)
5. Significant difference in domains physical (84.5 ± 7.8 Vs 90 ± 3.5 , $p=0.000$) and domains adaptive

(81 ± 6.7 Vs. 85.3 ± 5.4 , $p= 0.003$) in cases as compared to controls

6. There was no difference between SGA and AGA among cases in growth and neurological development

7. There was no difference between male and female in case group in any parameter

Conclusion:

There is very scanty data from our country on longterm follow up of ELBW babies. Our data shows that our ELBW cohort remained small in height and had smaller head circumference though weight was similar as compared to normal control babies. There was no difference between SGA and AGA babies amongst ELBW babies. Cerebral palsy rate is lower as compared to western data. Developmental profile-III shows only in 2 parameters Domains physical & Adaptive behavior which were delayed in the ELBW group as compared to control group. .

We need to have much larger study group size and longer follow up period in our country to reach more logical conclusion.

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