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RESEARCH ARTICLE

NEURO DEVELOPMENTAL AND GROWTH PATTERNS AMONG PRETERM VERY LOW BIRTH WEIGHT (VLBW) & EXTREMELY LOW BIRTH WEIGHT (ELBW) BABIES AT ONE YEAR CORRECTED GESTATIONAL AGE, A FOLLOW UP STUDY

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ABSTRACT

Background: Advances in the neonatal management has led to increase in survival of most very low birth weight and extremely low birth babies resulting in surge in number of infants with aberrations in growth and department. Early detection of such aberrations leads to marked improvement in ultimate outcome of such children. **Methods**: A hospital based case control follow up study was under taken in the department of pediatrics Government medical college Srinagar.72 out of 78 preterm low birth weight and extremely low birth weight who survived to discharge were registered as cases and 64 term babies admitted as suspected sepsis were registered as controls after ruling out sepsis between January 2014 to June 2014 .Gestational age was estimated by recommended methods and serial computation of Z-scores was done from anthropometric measurements at different intervals during first year of life. Neurodevlopmental assessment was done at one year corrected age using Denver Developmental screening test. Hearing assessment was done by transient evoked otoacoustic emissions and auditory brainstem responses. Screening for Retinopathy of prematurity was done per set protocol. Data was analyzed by standard statistical methods. **Results:** Among VLBW and ELBW infants, there was a significant decline in Z-scores of all three anthropometric parameters from birth to discharge. Thereafter they showed increasing trend throughout infancy. However, all anthropometric Z-scores of these infants continued to be significantly lower than NBW infants ($P<0.05$).Six infants among cases and none among controls had developmental delay at one year corrected age.18 cases had evidence of retinopathy of prematurity more so in extremely low birth babies .Three infants among cases had significant hearing impairment. **Conclusion:** Very low birth and extremely low birth babies remain smaller, lighter and have significantly lower neurodevelopmental indices at one year corrected age as compared to normal birth weight counterparts despite advances in neonatal care, a challenge for neonatal care providers.

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INTRODUCTION

The in-utero early sensory experiences of the fetus are essential for normal brain development during the perinatal period. The premature infant (considered as extra-uterinefetus) is deprived of in-utero sensory experiences, ratherexposed to unusual sensory stimuli in the Neonatal Intensive Care Units (NICU) that pose risk to the developing brain in terms of adverse neurodevelopment aloutcomes (Ramachandran, 2013). Improving outcomes beyond survival for high-risk newborns in resource-limited countries is an emerging challenge.

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As the survival rate of high risk newborns improve with advancing perinatal care services, the total number of infants with unique follow-up needs increase. Numerous studies have shown that despite reduction in neonatal mortality, the incidence of chronic morbidities and adverse outcomes have not declined much. This highlights the paramount importance of monitoring the growth and neurodevelopmental outcome of NICU graduates through a multidisciplinary approach (Das *et al.,* 2017). The period between 20-32 weeks after conception is one of rapid brain growth and development. Illness, undernutrition and infection during this time may compromise neurodevelopment. The clinical consequences can include serious neuromotor problems principally cerebral palsy, visual and hearing impairments, learning difficulties, psychological, behavioural and social problems (Nair *et al.,* 2018).

In infants with physical, social, adaptive and cognitive developmental delay or having a diagnosed condition with high probability of resulting in developmental delay, early stimulation services need to be initiated. Compensatory mechanisms exist for all cerebral function and this plasticity of brain is encouraged by early stimulation (Das *et al.,* 2017). The motor abilities acquired during the first year of life are appropriate milestones to indicate prognosis for global development, since the first 12 months after birth are considered one of the most critical periods in child development.

It is during this phase that children, and particularly children such as Preterms and low birth weight infants who are at increased risk of developing deficiencies, should be monitored in appropriate follow-up programs that assess their development longitudinally in order to detect signs of abnormalities, with a view to referring them for intervention programs aimed at minimizing the effects of these abnormalities (Silva *et al.,* 2011). We did this study to evaluate growth and neuro developmental outcome in very low birth weight and extremely low birth weight babies at one year corrected age.

METHODS

This hospital based case control follow up study was under taken in the department of pediatrics Government medical college Srinagar after proper consent from parents of babies and ethical clearance from ethical committee of government medical college Srinagar. A total of 78 preterm VLBW & ELBW neonates who survived to discharge out of 113 preterm VLBW & ELBW neonates admitted over six month period in our Nicu between January 2014 to June 2014 were enrolled as cases. Out of 78,two died while 4 were lost to follow up .64 out of 84 term babies who were admitted as cases suspected sepsis and discharged after ruling out sepsis were enrolled as controls.20 term babies were lost to follow up. Gestational age was determined on the basis of last menstrual period, first trimester ultrasonography and new ballard score.

Small for dates, dysmorphic, neonates with hypoxic ischemic encephalopathy and those with gross malformations were meticulously excluded. All VLBW babies were started on enteral feeds as early as possible and parentral nutrition was initiated on first day of life when indicated. All ELBW and most VLBW babies received parenteral nutrition with incremental enteral feeds. Anthropometric measurements were recorded by standard techniques and serial computation of Z scores for all anthropometric variables was done at birth*,* discharge*,* 40 weeks post menstrual age and at 1,3,6,9 and 12 months of corrected age by using Fenton's reference before 40 weeks and by new WHO growth standards beyond 40 weeks. Neuro developmental assessment was done at one year corrected gestational age by using Denver Developmental screening test. Devlopmental quotient was calculated by assessing developmental milestones in all four domains .Cases of cerebral palsy were diagnosed on basis of clinical assessment. Hearing assessment was done by TEOAE and ABR/BERA at term and six months corrected age in department of ENT government medical college srinagar. Screening for retinopathy of prematurity was done as per fixed protocol in ophthalmology section of our hospital. All the data was analyzed with standard statistical methods.

RESULTS AND ANALYSIS

Growth Parameters:-Among VLBW and ELBW infants, there was a significant decline I all three anthropometric parameters from birth to discharge. Thereafter, there was an increase in all Z-scores during infancy. After 40 wks PMA, the difference of each anthropometric Z-score from respective birth Z- scores was insignificant. However, all anthropometric Z-scores of these infants continued to be significantly lower than NBW infants, throughout infancy (P<0.05). This is shown in following tables (table1-6).

Table 1. Showing Z Scores for weight in cases at various time intervals

Time Interval	Mean	SD	Diff. from Birth	P-value
Birth	-1.42	1.782	-	-
Discharge	-2.53	1.431	-1.11	<0.001*
40 Weeks	-2.17	1.536	-0.75	0.008*
1 Month	-1.84	1.295	-0.42	0.107
3 Months	-1.72	0.954	-0.3	0.439
6 Months	-1.49	1.163	-0.07	0.892
9 Months	-1.40	1.056	0.02	0.943
12 Months	-1.26	0.856	0.16	0.438

Table 2. Showing Z Scores for length in Cases at various time intervals

Time Interval	Mean	SD	Diff. from Birth	P-value
Birth	-1.27	1.329	-	-
Discharge	-2.29	1.658	-1.02	<0.001*
40 Weeks	-1.93	0.986	-0.66	0.014*
1 Month	-1.61	1.452	-0.34	0.214
3 Months	-1.38	1.115	-0.11	0.769
6 Months	-0.85	1.241	0.42	0.098
9 Months	-1.04	0.878	0.23	0.356
12 Months	-1.12	0.915	0.15	0.545

Table 3. Showing Z Scores for head circumference in Cases at various time intervals

Time Interval	Mean	SD	Diff. from Birth	P-value
Birth	-0.91	1.235	-	-
Discharge	-1.78	1.458	-0.87	0.003*
40 Weeks	-1.49	1.019	-0.58	0.031*
1 Month	-1.32	0.857	-0.41	0.127
3 Months	-1.23	0.973	-0.32	0.346
6 Months	-1.15	1.119	-0.24	0.534
9 Months	-1.04	0.885	-0.13	0.608
12 Months	-0.98	1.213	-0.07	0.855

Table 4a. Comparison between Cases and Controls based on Z Scores for weight

Time Interval	Cases		Controls		P-value
	Mean	SD	Mean	SD	
Birth	-1.42	1.782	-0.43	1.556	0.002
1 Month	-1.84	1.295	-0.52	1.216	<0.001
6 Month	-1.49	1.163	-0.39	0.963	<0.001
12 month	-1.26	0.856	-0.31	1.115	0.004

Table4b. Comparison between Cases and Controls based on Z Scores for length

Time Interval	Cases		Controls		P-value
	Mean	SD	Mean	SD	
Birth	-1.27	1.329	-0.19	0.869	<0.001
1 Month	-1.61	1.452	-0.26	0.923	<0.001
6 Month	-0.85	1.241	-0.18	0.785	<0.001
12 month	-1.12	0.915	-0.13	0.692	<0.001

Table4c. Comparison between Cases and Controlsbased on Z Scores for head circumference

Time Interval	Cases		Controls		P-value
	Mean	SD	Mean	SD	
Birth	-0.91	1.235	-0.13	0.658	<0.001
1 Month	-1.32	0.857	-0.15	0.783	<0.001
6 Month	-1.15	1.119	-0.12	0.712	<0.001
12 month	-0.98	1.213	-0.09	0.841	<0.001

Table 5a: Comparison between VLBW &ELBW infants and NBW infants based on Z Scores for weight

	Birth	12 Months
Cases	-1.42	-1.26
Controls	-0.43	-0.31

Table 6. Comparison based on development quotient among Cases and Controls

Development Quotient	Cases (n=72)		Controls (n=64)		P-value
<70	6	8.3	0	0	
70-85	36	50.0	15	20.8	<0.001*
86-100	30	41.7	49	68.1	
Mean S±D	78.8	4.56	±91.4	3.12	±

Developmental quotient: Preterm VLBW and ELBW infants lag in their development as compared to normal birth weight infants at 1 year corrected age. 6 infants with DQ<70 were developmentally delayed while as 30 infants with DQ 70 – 85 were at high risk for developmental delay.

Table 7. Comparison of incidence of Nero motor disability among Cases and Controls

Category		No of infants	Cerebral Palsy		P-value
			No.	%age	
Cases	ELBW	15	2	13.3	
	VLBW	57	4	7.0	
	Total	72	6	8.3	0.029*
Controls		64	0	0.0	

Table 8. ROP in studied infants

Category	No. of infants	ROP	
		No.	%age
ELBW	15	5	33.3
VLBW	57	13	22.8
Total	72	18	25.0

Table 9. Detection of hearing impairment by TEOAE and ABR in enrolled infants

Hearing Impairment		Cases (N=72)		Controls (n=64)				
		No.	%age	No.	%age			
Teoae	Positive	9	12.5	4	6.3	Teoae	TP=2	FP=11
	Negative	63	87.5	60	93.8		FN=1	TN=122
ABR	Positive	4	5.6	0	0	ABR	TP=3	FP=1
	Negative	68	94.4	64	100		FN=0	TN=132

TP=True positive, FP=False positive, FN=False negative, TN=True negative

Table 10. Confirmation of hearing impairment by ABR in screened positive cases at 6 months corrected age

Hearing	Cases		Controls	
Positive	No.	%age	No.	%age
Positive	3	4.2	0	0.0
Negative	7	9.7	4	6.3

Table 11. Accuracy of TEOAE in diagnosis of infants with hearing impairment

Variable	Value	95 Confidence Interval
Sensitivity	100	(89.2, 100)
Specificity	99.3	(92.2, 99.9)
PPV	75	(19.4, 99.4)
NPV	100	(94.7, 100)

Table 11. Accuracy of ABR in diagnosis of infants with hearing impairment

Variable	Value	95% Confidence Interval
Sensitivity	100%	(89.2%, 100%)
Specificity	99.30%	(95.8%, 99.9%)
PPV	75%	(19.4%, 99.4%)
NPV	100%	(97.3%, 100%)

Neuromotor disability: Out of 72 enrolled cases, 6 infants (VLBW = 4, ELBW =2) with DQ<70 were diagnosed as cases of cerebral palsy. The data in table 7 reflects incidence of cerebral palsy more in ELBW infants than VLBW infants.

Retinopathy of prematurity: Among 72 enrolled cases, 18 cases were that of retinopathy of prematurity with prevalence more in ELBW infants than VLBW infants as show in table below.

DISCUSSION

Advances in neonatal care allow survival of very low birth infants, who are prone to a range of longterm complications in comparison to their term normal birth weight counterparts.[5] Most of low birth neonates (VLBW&ELBW) in our study were smaller and had lower Z-scores for weight, length and head circumference compared to normal birth weight counterparts possibly due to associated adverse intrauterine factors consistent with findings as reported by Modi et al[6],Gutbrod et al[7]and Finnstrom et al. (1998). All of cases in our study experienced fall in their Z score for weight, length and head circumference similar to observations of Modi *et al.* (2013).This was possibly because of associated morbidities and inappropriate nutritional management in our NICU.Our cases had a decline in Z score of 1.11,0.98 and 0.87 for weight, length and head circumference similar to findings of Modi et al[6]and Monique Rijken[9].

After early growth retardation, these infants experienced a steady improvement in all anthropometric parameters from hospital discharge to 1year similar to observations of Finnstrom et al. (1998) and Monique Rijken[9] but despite catch up,our cases remained shorter and lighter than their normal birth weight counterparts consistent with findings of of Modi *et al.* (2013) and Finnstrom et al. (1998). Very low birth and extremely low birth infants have been observed to have poor long term neuro developmental outcome (MoniqueRijken, 1996-1997; Marita, 2001). Poor head growth has been linked poor neurological outcome as in our study and was similar to results of Modiet al. (2013). Mean developmental quotient in our study was 78-80 similar to Procianoy *et al.* (2009). Retinopathy of prematurity was present in 33.33% and 22.8% of extremely low birth and very low birth babies respectively. The higher prevalence of Retinopathy of prematurity in extremely low birth babies than low birth weight babies was similar to findings of Hungi *et al.* (2012) although overall prevalence was higher than our study (41.5% vs 25%) but most

Indian studies show prevalence in range between 20% to 46% as reported by varughese *et al.* (2001) consistent with our study. Hearing evaluation was done with transient evoked otoacoustic emissions in 72 cases and 64 controls and failed test was obtained in 9 and 4 babies respectively but all four of among controls passed Auditory brain stem responses while as four among nine cases who failed on intial screen also failed on Auditory brain stem responses. Among four hearing impaired infants, one passed repeat Auditory brain stem responses and only 3 infants among cases (4.12%) were labeled as hearing impaired, consistent with Nair *et al.* (2018)

Conclusion

Very low birth and extremely low birth babies remain smaller, lighter and have significantly lower neurodevelopmental indices at one year corrected age as compared to normal birth weight counterparts .It remains debatable whether low birth infants catch up to normal weight counterparts or continue to grow along their birth centiles. A larger cohort with longterm follow up is required to address this domain as well as possibility of missing subtle neurodeficits at younger age.

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