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Original Research Article

Neurodevelopmental outcome of very low birth weight and extremely low birth weight newborn at 12 months of corrected age associated with prenatal risk factors

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ABSTRACT

Background: Various neuro-developmental impairment (NDI) among very low birth weight babies (VLBW) and extremely low birth weight (ELBW) babies are common in Indian scenario. This study was designed to assess the impact between prenatal risk factors and neuro-developmental outcomes of premature infants.
Methods: This descriptive study was conducted on 143 VLBW and ELBW babies admitted in SNCU of North Bengal Medical College, Darjeeling, West Bengal and discharged babies were followed up.
Results: Total 143 neonates were studied among male 82 (57.3%) and female 61 (42.7%) and AGA: SGA ratio was 1.97. Birth weight ranged from 500 to 1500grams with mean was 1199.6±244.14 and the median was 1240 gm. The mean gestational age (Mean± SD) was 29.65±2.032 weeks with range 24-32 weeks and the median was 30 weeks. 28 (19.6%) had PIH, 39 (27.3%) had multiple gestation, 18 (12.6%) had perinatal infection and 25 (17.5%) had birth asphyxia. CRIB II score ranged from 3-18 with mean was 8.021±3.883 and median was 7. 73.4% (105/143) were discharged alive. Significant positive correlations were found among birth weight, gestational age, perinatal infection ($p<0.001$). Adverse neonatal outcome was associated with CRIB II score ≥10. Total CRIB II score with parameters of NDI like developmental delay, cerebral palsy, visual abnormality, absent ABR showed good correlation ($p<0.001$). Fisher Exact test revealed significant association between total score and Cerebral palsy ($p=0.0005$), visual abnormality ($p=0.0005$), absent ABR ($p=0.0002$).
Conclusions: Perinatal risk factors influence future NDI in very low and extremely low birth weight babies. They should be identified and treated promptly to achieve good outcome.

Keywords: CRIB II score, Neuro-developmental outcome, Perinatal risk factors, Premature baby

INTRODUCTION

Low birth weight is a significant public health issue worldwide and is associated with of both short- and long-term consequences. It is assumed that 15% to 20% of all births globally are LBW, representing more than 20 million births in a year and 95.6% of them from developing countries.

Survival of LBW babies is improved as the perinatology is advanced but it is difficult to answer questions regarding quality of life for the infant who survived and more so for an NICU individual. High risk refers to the likelihood of neurodevelopmental insufficiency which is a group of interrelated chronic nonprogressive disorders of the central nervous system (CNS) caused by injury to or malformation of the developing brain. They form a

spectrum ranging from cognitive impairment, motor impairment and intellectual disability to sensory impairment to the more subtle disorders of CNS function. These more subtle disorders of higher cortical function include language disorders, learning disability, minor neuromotor dysfunction, visual-perceptual problems, executive dysfunction, attention deficits, and behavioral problems. Intellectual disability has replaced by the more stigmatic term mental retardation.

Neurodevelopmental impairment (NDI) is a spectrum of disorder and refers to cerebral palsy (CP), intellectual disability, severe hearing impairment, and severe visual impairment, and at times it may include seizure disorder, severe learning disability, or hydrocephalus. Preterm infants and sick full-term infants treated at neonatal intensive care unit have an increased risk of neurodevelopmental disabilities compared with the general population. Several perinatal and demographic risk factors with different capacities to predict neurodevelopmental disabilities have been identified. Abnormalities on neonatal neurologic examination and neuroimaging studies are better predictors of outcome than preceding obstetric conditions, electronic foetal heart rate abnormalities, metabolic acidosis, or Apgar scores at birth.[1] As birth weight and gestational age decrease, rates of complications of prematurity and neurodevelopmental disability increase.[2] Neither risk nor statistical association implies causation, but studies of risk factors can provide important insights into aetiology of neurodevelopmental disability.[1-4] Strong evidence links cerebral palsy in preterm infants to ischemic and/or cytokine-mediated brain injury with perhaps also a role for insufficient levels of developmentally regulated neuro protective substances (example- thyroxin, hydrocortisone).[3] A comprehensive developmentally based family-oriented follow-up clinic helps to ensure early diagnosis of neurodevelopmental disability shape early intervention strategies to meet the infant's and family's evolving needs and provide parents with continuity and on-going support during a difficult period of uncertainty and adjustment.

Several prenatal risk factors like gestational birth weight, age, sex, multiple gestation, perinatal infection, birth asphyxia, and clinical risk index for babies score –II (CRIBS II) have adverse neuro-developmental outcomes of very premature infants.[5] CRIB II scoring system which has five variables: (i) Birth weight (ii) Gestational age (iii) gender (iv) Base deficit and (iv) Temperature on admission, is a risk index for new born weighing less than 1500 grams. The range of score for weight compared with gestational age in male is 0-15 and in female is 0-14 and for base excess 0-7 and for temperature the score is 0-5. At the end the scores are totalled. Favourable prognosis with lower scores and attained the best results with score of one.

The present study was done to assess the impact of several perinatal risk factors and their impact on neurodevelopmental outcome in very low and extremely low birth weight babies.

METHODS

A descriptive study with prospective design was conducted among 143 VLBW and ELBW babies admitted at SNCU and PICU at North Bengal Medical College and Hospital, Darjeeling, West Bengal and discharged babies were followed up. The study was conducted from June 2016 to August 2017.

Inclusion criteria

All preterm new born of both sexes admitted in SNCU and PICU 23 to 32 weeks of gestational age and birth weight <1500 grams.

Exclusion criteria

All preterm new born less than 23 weeks of gestation, birth weight <500 grams, gross congenital malformation, genetic disorder, delivery room death and inborn error of metabolism.

Study tools

The study was conducted by using Measuring tape, Torch, Cubes, Percussion hammer, DDST chart, DASII, Proforma, Statistical package for social sciences (SPSS) V 20, EpiCalc 2000 v 1.2 statistical software and Analyze-it in MS excel.

Data collection

Gestational age in week calculated from the first day of last menstrual Period (LMP). Newborn data: Gestational age by obstetrical ultrasonography and Expanded New Ballard Score where LMP is unknown. Gender and Birth weight by digital weighing scale. Blood analysis including base excess and temperature (Celsius) on admission.

Developmental and neurological score using DDST chart and standard neurological examination by Amiel-Tison method. Ophthalmological and BERA examination report. Developmental assessment and neurological examination on follow up of discharged babies at 1st, 3rd, 6th, 9th, 12th months.

The final CRIB II score (ranged from 0 to 27) was obtained by the arithmetic sum of the individual scores: (i) birth weight (ii) gestational age (iii) base deficit (iv) temperature on admission and (v) sex. The scores were further classified into four levels as follows; Level 1: 0 to 5, Level 2: 6 to 10, Level 3:11 to 15, Level 4 above 15.[6]

Very low birth weight (VLBW)

Less than 1,500 gm (up to and including 1,499 gm)

Extremely LBW (ELBW)

Less than 1,000 gm (up to and including 999 gm).

Small for gestational age (SGA)

Birth weight more than 2SD below the mean or less than the 10th percentile of a population specific weight versus gestational age plot.

Statistical analysis

Independent t test, Pearson's chi-square test and Fisher Exact test were used to analyze the data. All tests were tailed with $p<0.05$ as significant and performed by SPSS v 20 Chicago.

Ethical approval

The study was approved by of North Bengal Medical College and Hospital, Darjeeling, West Bengal ethics committee.

RESULTS

Total 143 babies were studied among which 82 (57.3%) were males and 61(42.7%) were females.

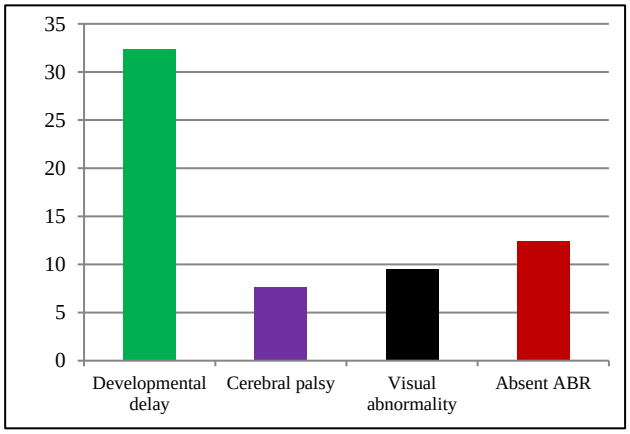

Figure 1: Frequency distribution of babies with neurodevelopmental outcome.

Figure 1 shows risk of developmental delay was more for total score >5 as compared to total score ≤5 and the risk was significant.

Non-survivors represented was 38 (26.6%) while survivors represented was 105 (73.4%). Clinical and demographical distribution of the study sample revealed low birth weight and appropriate for gestational age outnumbered than extreme low birth weight and small for gestational age (Table 1). Most common neurodevelopmental impairment was developmental delay (32.4%) followed by absent ABR (12.4%) then visual abnormality (9.5%) with least cerebral palsy (7.6%) (Figure 1).

CRIB II score was calculated and classified into 4 levels with mean total score (Mean± SD) was 8.021±3.883 and the median was 7 with range 3-18 and higher the CRIB II score poorer were the neurodevelopmental outcome (Table 2, 5 and Figure 2, 3, 4, 5).

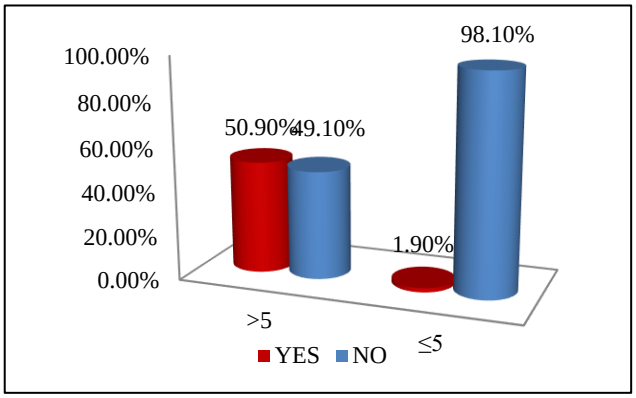

Figure 2: Total score versus developmental delay: percentage of cases in each group.

Figure 2 shows Fisher Exact test has significant association between total score and Cerebral palsy (p=0.0005). Chi-square (x^2) test was not applicable as one of the cell frequencies was zero.

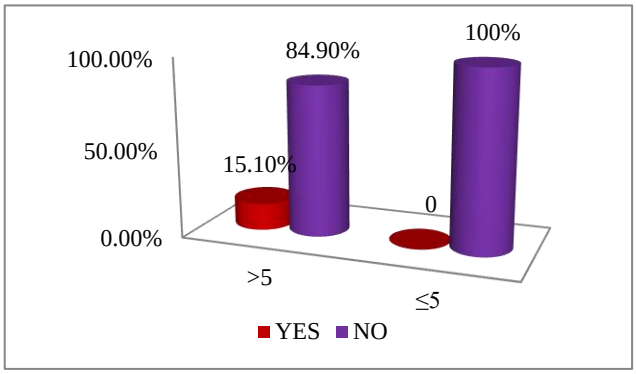

Figure 3: Total score versus cerebral palsy: percentage of cases in each group.

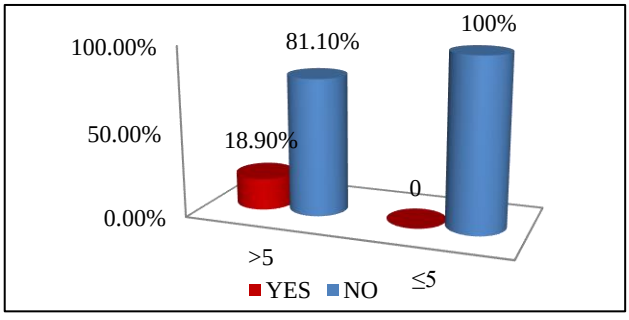

Figure 4: Total score versus visual abnormality: percentage of cases in each group.

Figure 4 shows Fisher Exact test has significant association between total score and visual abnormality (p=0.0005). Chi square (x^2) test was not applicable as one of the cell frequencies was zero.

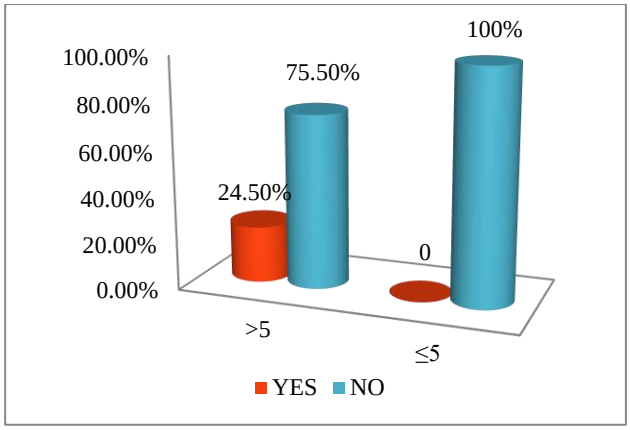

Figure 5: Total score versus absent ABR: percentage of cases in each group.

Figure 5 shows Fisher Exact test has significant association between total score and absent ABR (p=0.0002). Chi-square (x^2) test was not applicable as one of the cell frequencies was zero.

Neurodevelopmental impairment among AGA and SGA babies in the form of developmental delay, visual abnormality, absent ABR was statistically significant (p<0.05) but cerebral palsy did not show significant correlation (p=0.23) (Table 3).

Incidence of developmental delay, cerebral palsy, visual abnormality and absent ABR in case of female child is 27.3%, 15.6%, 15.6% and 15.6% and in male child is about 26.2%, 3.3%, 6.6% and 11.5% respectively (Table 4).

Pregnancy and birth related precipitating factors like intrauterine growth condition, PIH, multiple gestation, infection and birth asphyxia did not show statistically significant correlation among gender (Table 6).

Table 1: Clinical and demographic profile of the study sample.

Characteristic	Result n=143	
	No. of cases	Percentage
Birth weight (gms)		
500-1000	34	23.8
1000-1500	109	76.2
Gestation		
24-≤28 weeks	37	25.9
>28-≤32 weeks	106	74.1
Intrauterine growth category		
Appropriate for gestational age (AGA)	95	66.4
Small for gestational age (SGA)	48	33.6
Sex		
Male	82	57.3
Female	61	42.7
Pregnancy induced hypertension	28	19.6
Multiple gestation	39	27.3
Infection or sepsis	18	12.6
Birth asphyxia	25	17.5

Table 2: CRIB II score classification and outcome.

CRIB II score level	Distribution of samples according to total score		Outcomes				P value
			Discharged (n=105)		Expired (n=38)		
	N	%	N	%	N	%	
Level I (0-5)	52	36.4	52	49.5	0	0	<0.001
Level II (6-10)	56	39.2	53	50.5	3	7.9	
Level III (11-15)	27	18.9	0	0	27	71.1	
Level IV (>15)	8	5.5	0	0	8	21.1	

Table 2 shows CRIB II score classification. It also shows as the total score increases neonatal outcome is poor (p value <0.001).

Table 3: Distribution of neurodevelopmental outcome among AGA and SGA discharged babies.

Neurodevelopmental outcome (discharged babies)		Intrauterine growth condition (n=105)				P value
		AGA (N=81)		SGA (N=24)		
		N	%	N	%	
Developmental delay	Yes	16	19.8	12	50	0.004
	No	65	80.2	12	50	
Cerebral palsy	Yes	5	6.2	3	12.5	0.23
	No	76	93.8	21	87.5	
Visual abnormality	Yes	4	4.9	6	25	0.005
	No	77	95.1	18	75	
Absent ABR	Yes	7	8.6	6	16.7	0.037
	No	74	91.4	18	83.3	

Table 3 shows neurodevelopmental outcome. Developmental delay, visual abnormality, absent ABR showed statistically significant correlation (p<0.05) but cerebral palsy does not show significant correlation with a p value 0.23.

Table 4: Neurodevelopmental delay comparison between surviving children based on gender.

Growth and neurodevelopmental delay		Gender (n=105)				P value
		Female (n=44)		M (n=61)		
		N	%	N	%	
Developmental delay	N	32	72.7	45	73.8	0.458
	Y	12	27.3	16	26.2	
Cerebral palsy	N	38	86.4	59	96.7	0.05
	Y	4	15.6	2	3.3	
Visual abnormality	N	38	86.4	57	93.4	0.188
	Y	6	15.6	4	6.6	
Absent ABR	N	38	86.4	54	88.8	0.488
	Y	6	15.6	7	11.5	

Table 4 showing growth and neurodevelopmental delay comparison between surviving children based on gender. Almost all the comparisons are statistically insignificant.

Table 5: Relation of CRIB II score and neurodevelopmental outcome.

Total CRIB II score					P value
	Mean	SD	Minimum	Maximum	
Developmental delay					
Yes	8.21	1.197	5	10	<0.001
No	5.25	1.434	3	9	
Cerebral palsy					
Yes	9.00	1.069	7	10	<0.001
No	5.8	1.745	3	9	
Visual abnormality					
Yes	8.8	0.919	7	10	<0.001
No	5.76	1.745	3	10	
Absent ABR					
Yes	8.308	1.251	6	10	<0.001
No	5.725	1.758	3	10	

Table 5 showing correlations of Total CRIB II score with parameters of neuro-developmental delay like developmental delay, cerebral palsy, visual abnormality, absent ABR. All showing good correlations which is statistically significant (p<0.001).

Table 6: Comparison of contribution of different precipitating factors with gender.

Precipitating causes		Gender				P value
		Females (n=61)		Males (n=82)		
		N	%	N	%	
Intrauterine growth Condition	AGA	41	67.2	54	65.9	0.812
	SGA	20	32.8	28	34.1	
PIH	N	50	82	65	79.3	0.587
	Y	11	18	17	20.7	
Multiple gestation	N	47	77	57	69.5	0.610
	Y	14	23	25	30.5	
Infection	N	58	95.0	79	96.3	0.613
	Y	3	4.9	3	3.6	
Birth asphyxia	N	50	81.9	68	82.9	0.640
	Y	11	18.1	14	17.1	

Table 6 showing comparison of contribution of different precipitating factors with gender. None of them proved to be statistically significant with p>0.05.

DISCUSSIONS

Premature births are out-numbered by males with higher susceptibility of mortality.[7] This finding is consistent with my study where male to female cases were 1.3:1 respectively with higher mortality in males. A simple and useful method of risk-adjustment is important to ensure accurate assessment for quality care of newborn.[8] My study revealed positive associations between the birth weight, the gestational age, base excess, temperature and the mortality: the lower the gestational age and birth weight the higher the mortality that was considered to be statistically significant ($p<0.001$).

Non-survivors had a mean CRIB II score higher than survivors. Optimize value of CRIB II score at which maximum sensitivity of 97.5% and specificity of 50% is 9.5 for predicting mortality of VLBW babies. Similar result was obtained by Ezz-Eldin et al, Jafrashteh et al, Jasik et al and Heidarzadeh et al in their studies.[9-12] Perinatal risk factors like birth weight, gestational age, perinatal infection is associated poor neurological outcome ($p<0.001$). CRIB II score is a good parameter and score ≥10 associated with neurodevelopmental impairment. Total CRIB II score with parameters of neurodevelopmental impairment like developmental delay, cerebral palsy, visual abnormality, absent ABR shows good correlation ($p<0.001$). Fisher Exact test shows significant association between total score and cerebral palsy ($p=0.0005$), visual abnormality ($p=0.0005$), absent ABR ($p=0.0002$). Neurodevelopmental impairment comparison between surviving children based on gender did not show statistically significant difference Higher birth weight and advanced gestational age are protected against adverse neuro-developmental outcomes in both groups.

This study shows major neurological abnormalities are 32.4% Developmental delay (isolated delay but no CP), 12.4% Deafness, 7.6% Cerebral palsy (CP), 9.5% Blindness and/ or ROP and more with higher CRIB II score that is comparable with study done by Ho et al (13) to estimate the prevalence and pattern of neuro-developmental handicap at 2 years of age in VLBW admitted to a level 3 Malaysian nursery in 1993. We observed 70.2% was normal functionally whereas 23.3% had mild, 1.3% moderate, 2.5% severe and 2.5% multiple severe functionally handicap respectively. Some western literature (Procianoy et al, Gutbrod et al, Gabriel et al) and a few eastern literature (Modi et al, Pradip et al, Mukhopadhyay et al) show the incidence of neuro-developmental abnormality is lower in comparison to our study.[14-19] Though the incidence of hearing and visual abnormality is higher in my study, developmental delay and cerebral palsy are quite comparable that might be due to high rate of post-natal morbidity in VLBW babies and sample size is quite small in comparison to those studies.

Limitations of the study

This study was done in small sample size (n=143) with one year follow up period so we might miss some delayed neuro-developmental sequelae.

CONCLUSION

Each VLBW and ELBW babies are unique, so they need close and longer follow up due to high risk for development of neurodevelopmental impairment. Neurodevelopmental impairment comparison between surviving children based on gender did not show statistically significant difference.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Nelson KB. The epidemiology of cerebral palsy in term infants. Ment Retard Dev Disabil Res. 2002;8:146-50.
2. Behrman RE, Butler AS, editors. Preterm birth: causes, consequences, and prevention. National Academies Press. Washington, DC. 2007.
3. Allen MC. Preterm outcomes research: A critical component of neonatal intensive care unit. Ment Retard Dev Disabil Res. 2002;8:221.
4. O' Shea TM. cerebral palsy in very preterm infants; new epidemiological insight. Ment Retard DevDisabil Res Rev. 2002;8:135.
5. Parry G. CRIB II: an update of the Clinical Risk Index for Babies Score. Lancet. 2003;361(9371):1789-91.
6. Brito AS, Matsuo T, Gonzalez MR, de Carvalho AB, Ferrari LS. CRIB score, birth weight and gestational age in neonatal mortality risk evaluation. Rev Saude Publica. 2003;37(5):597-602.
7. Zeitlin J, Saurel-Cubizolles MJ, De Mouzon J, Rivera L, Ancel PY, Blondel B, et al. Fetal sex and preterm birth: are males at greater risk? Hum Reprod. 2002;17:2762-8.
8. Parry G, Tucker J, and Tarnow-Mordi W. CRIB II: an update of the clinical risk index for babies score. Lancet. 2003;361(9371):1789-91.
9. Ezz-Eldin ZM, Hamid TAA, Youssef MRL, Nabil HE-D. Clinical Risk Index for Babies (CRIB II) Scoring System in Prediction of Mortality in Premature Babies. Journal of Clinical and Diagnostic Research. 2015;9(6):SC08-11.
10. Jafrasteh A. Clinical Risk Index for Neonates II score for the prediction of mortality risk in premature neonates with very low birth weight. World Family Medicine. 2017;15(8):183-7.
11. SindičićDessardo N, Jašić M, Dessardo S, ManestarRukavina K. CRIB II score versus gestational age and birth weight in preterm infant

mortality prediction: who will win the bet? Signavitae: journal for intesive care and emergency medicine. 2016;11(1):172-81.
12. Heidarzadeh M, Ghorbani F, Dastgiri S. Prediction Value of CRIB-II in Outcome of Preterm and Low Birth Weight Infants: A Prospective Cohort Study. International Journal of Pediatrics. 2016;4(4):1583-9.
13. Ho JJ, Amar HSS, Mohan AJ, Hon TH. Neurodevelopmental outcome of birth weight very low babies admitted to a Malaysian nursery. Journal of Paediatrics and Child Health. 1999;35(2):175-80.
14. Procianoy RS, Koch MS, Silveira RC. Neurodevelopmental outcome of appropriate and small for gestational age very low birth weight infants. J Child Neurol. 2009;24:788-94.
15. Gutbrod T, Wolke D, Soehne B, Ohrt B, Riegel K. Effects of gestation and birth weight on the growth and development of very low birthweight small for gestational age infants: a matched group comparison. Arch Dis Child Fetal Neonatal Ed. 2000;82F208:F208-14.
16. Phatak P. Developmental patterns and profiles of preterm babies with adequate weight during first two years of life. Psychol Stud. 1989;34:181-6.
17. Modi M, Saluja S, Kler N, Batra A, Kaur A, Garg P et al. Growth and Neurodevelopmental Outcome of VLBW Infants at 1 Year Corrected Age. Indian Pediatrics. 2013;50:573-77.
18. Sharma PK, Sankar MJ, Sapra S, Saxena R, Karthikeyan CV, Deorari A et al. Growth and Neurosensory outcomes of preterm very low birth weight infants at 18 months of corrected age. Indian journal of Pediatr. 2011;78(12):1445-90.
19. Mukhopadhyay K, Malhi P, Mahajan R, Narang A. Neurodevelopmental and Behavioral Outcome of Very Low Birth Weight Babies at Corrected Age of 2 Years. Indian J Pediatr. 2010;77:963-7.

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