Section: Paediatrics

Original Research Article

ASSESSMENT OF NEURODEVELOPMENTAL OUTCOME OF PRETERM VERY LOW BIRTH WEIGHT BABIES AT THE CORRECTED AGE OF 1 YEAR

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Abstract

Background: Very low birth weight (VLBW) babies born preterm are likelier to experience negative neurodevelopmental outcomes. To recommend patients for early intervention, it is crucial to identify early determinants connected to the outcome. **Aim:** To assess the neurodevelopmental outcome of preterm VLBW babies registered at DEIC, ICH&RC, Madurai, by examination and followup at serial intervals till the corrected age of one year. **Materials and Methods:** The study included preterm neonates who were followed up at the corrected ages of 3, 6, 9 and 12 months and had birth weights between 1000 and 1499 g. The Hammersmith method is used for neurological examination during follow-up, and the Denver development screening test is used for developmental assessment. **Result:** The VLBW infants serially assessed for neurodevelopmental outcome using DDST and HINE revealed that neurodevelopmental outcome at the corrected age of 1 year was influenced largely by neonatal complications such as RDS (60%) and sepsis (54%). Jaundice was also found in 62% of infants. The final neurodevelopmental status of the preterm VLBW infants at the corrected age of 1 year showed a significant delay as per DDST (35%) and HINE (34%)—birth asphyxia, mechanical ventilation, neonatal convulsions, and faulty feeding directly correlated with the significant delay. **Conclusion:** Birth asphyxia, mechanical ventilation, newborn convulsions, and improper feeding were identified as risk factors for poor neurodevelopmental outcomes in children born preterm. Long-term monitoring and evaluation of these babies is critical and might impact the outcome through quality survival.

INTRODUCTION

A preterm birth occurs before 37 weeks of pregnancy. This is further broken down into four categories: extreme preterm (EPT <28 weeks), very preterm (VPT 28 to 32 weeks), moderate preterm (MPT 32-34 weeks) and late preterm (LPT 34 to 37 weeks).[1] A significant contributor to newborn and toddler death and morbidity is preterm delivery. Premature births are thought to account for 11.1% of all births globally. Infants born at the end of their lives have a higher chance of survival and thanks to modern neonatal intensive care procedures.[2] Comparing MPTs and LPTs to EPTs and VPTs, the probability of unfavourable consequences are greater. A range of diseases, including cerebral palsy, visual and auditory deficiencies, motor and cognitive function impairments, and behavioural issues, can result from prematurity and causes the neonatal morbidity.[3] To direct the clinical care of infants born prematurely, inform parents, and aid in the development, targeting, and evaluation of therapies, early identification of characteristics that affect long-term outcomes is essential.[4]

The very low birth weight infant (VLBWI) death rate was significantly reduced throughout the 1980s and 1990s due to substantial advancements in obstetric and neonatal intensive care, stabilising at 15% in the early 2000s.[5] During the same period, epidemiological trends that were more significant than the parallel decline in rates of long-term neuro psychomotor disability in this population included an increase in the prevalence of preterm births and notable improvements in the survival rates of infants

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with low birth weight and low gestational age.[6] Particularly in the 1990s, there was no change in the prevalence of neuromotor and cognitive handicaps. It was also confirmed that children with lower gestational ages and birth weights tended to have worse outcomes.[7]

Very preterm newborns survival, rising quickly in the 1980s and 1990s, has plateaued in the new millennium as chronic neonatal morbidity and neurodevelopmental disabilities are becoming better recognised in these at-risk infants.[8] Children, adolescents, and young adults who were former preterm babies are a growing patient group, and their quality of life and neurodevelopmental outcomes are significant research issues. The risk factors for considerable developmental delay and neurodevelopmental impairment (NDI) in extremely low birth weight survivors have been described. They are related to an unfavourable neurodevelopmental outcome and rising neonatal morbidity.[9] There is a substantial corpus of research on risk factor models for the neurodevelopmental outcomes of VPT children. However, few, if any, have been created in normal clinical practice or adopted for use in research studies or policy reviews. Of all VLBW newborns, 5–10% have substantial motor impairments (e.g., cerebral palsy), and 25–50% have cognitive, behavioural, or attention issues. Given the lifelong nature of the sequelae, these deficiencies and impairments can profoundly affect people, families, and public health care resources.[10]

The above mentioned factors explain the increased significance of monitoring preterm newborns hospitalised in neonatal intensive care units for both short- and long-term developmental outcomes.

Aim

The study aims to evaluate the neurodevelopmental progress of VLBW babies born preterm and registered at DEIC, ICH & RC, Madurai, till the corrected age of one year and to underline the importance of maintaining a careful eye on these newborns for a long time due to the increased risk of neurodevelopmental disorders.

MATERIALS AND METHODS

This longitudinal observational study was conducted at DEIC, ICH &RC, Madurai, for 18 months (January 2020 to June 2021). The study included all preterm neonates registered at DEIC, Madurai, with birth weights between 1000 and 1499g, and informed consent was obtained from all patients.

The study selected 112 infants, and these infants are followed up at DEIC, ICH & RC, Madurai, at the corrected ages of 3, 6, 9 and 12 months. The Hammersmith method is used for neurological examination during follow-up, and the Denver development screening test is used for developmental assessment. Neonates with major congenital anomalies were excluded.

HINE is a straightforward scoring system for evaluating children between the ages of 2 and 24 months that takes into account several neurological examination components, such as cranial nerves, posture, tone, movements, and reflexes. Several tests assess each component, with a maximum overall score of 78. The cut-off scores for 3, 6, 9, and 12 months are 50, 52, 59, and 60, respectively. Together with the above mentioned factors, asymmetries in the motor domain and behavioural factors are also checked without scoring.

Neonates are monitored and assessed by serial neurodevelopmental assessments at the District Early Intervention Centre (DEIC), ICHRC, Madurai from the day of discharge up to the corrected age of one year. All newborns weighing 1000 and 1499 grams born between January 2020 and June 2021 were included in the study and monitored until June 2021.

Chi-Square Test was used for statistical analysis. The proportion with a Confidence Interval of 95 percent and a p-value of .05 is significant. The study outcome is statistically analysed using Epi info v7 software and SSPS 17.

RESULTS

The study included 112 infants collected within the period above. However, 27 instances were lost in follow-up. Hence only 85 newborns were included in the analysis in this longitudinal study. Among the study subjects, 48 were male, and the remaining 37 were female [Table 1].

Table 1: Neonatal outcome of VLBW infants

Neonatal outcome		Frequency	Percentage
Birth asphyxia	No	60	70.6 %
	Yes	25	29.4 %
Mechanical Ventilation	No	53	62.4 %
	Yes	32	37.6 %
Neonatal Sepsis	No	39	45.9 %
	Yes	46	54.1 %
RDS and H/O surfactant administration	No	34	40 %
	Yes	51	60%
Neonatal convulsions	No	57	67.1 %
	Yes	28	32.9 %
Neonatal jaundice	No	32	37.6%
	Yes	53	62.4%

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According to our study results, Birth asphyxia was observed in only 29.4% of infants and had the lowest prevalence. Jaundice affected 62.4% of infants, with the highest prevalence. Other neonatal outcomes observed were convulsions (32.9%), RDS and H/O surfactant administration (60%), sepsis (54.1 %), and 37.6 % of infants requiring Mechanical ventilation. The follow-up study revealed that 63.5 % were breastfed [Figure 1].

Table 2: Results of neurodevelopmental examination at the corrected ages of 3, 6, 9 and 12 months

Follow-up		DDST		HINE	
		Frequency	Percentage	Frequency	Percentage
Month 3	Normal	6	7.1%	23	27.1%
	Suspect	79	92.9%	62	72.9%
Month 6	Normal	25	29.4%	38	44.7%
	Suspect	60	70.6%	47	55.3%
Month 9	Normal	50	58.8%	33	38.8%
	Suspect	35	41.2%	52	61.2%
Month 12	Normal	55	64.7%	29	34.1%
	Suspect	30	35.3%	56	65.9%

DDST and HINE scores at month 3 showed that only 7.1 and 27.1% of babies were normal, followed by only 29.4 and 44.7 % being normal at month 6. As the normalcy rate increased, at months 9 and 12, it was observed that 58.8 and 38.8% of babies. 64.7 and 34.1 were declared normal through DDST and HINE, respectively [Table 2].

Consequently, the final interpretation of the neurodevelopmental outcome of the VLBW babies at the corrected age of 1 year by HINE and DDST showed that respective normalcy rates were 66 and 65% [Figure 2].

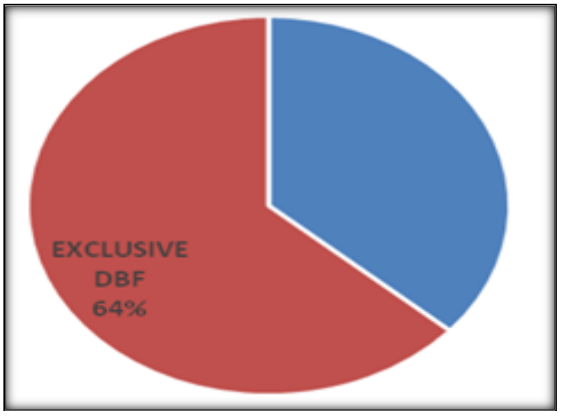

Figure 1: Percentage of VLBW babies who are exclusively breastfed during follow up

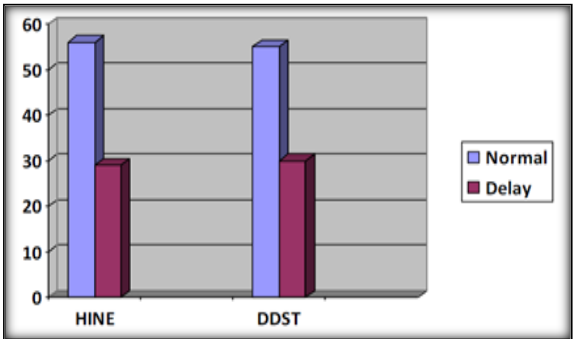

Figure 2: Final neurodevelopmental outcome of the VLBW babies at the corrected age of 1 year by HINE and DDST

The final neurodevelopmental outcome of the VLBW infants at the corrected age of 1 year shows a significant delay in 34% of infants by HINE and in 35% of infants by DDST.

Table 3: Correlation between neonatal outcomes and neurodevelopmental scores, DDST at one year

Neonatal Outcome		Count		Total (100%)	P-value
		Normal	Suspect		
Mechanical Ventilation	No	44 (83%)	9 (17%)	53	<0.0001
	Yes	11 (34.4%)	21 (65.6%)	32	
	Total	55 (64.7%)	30 (35.3%)	85	
Sepsis	No	29 (74.4%)	10 (25.6%)	39	0.086
	Yes	26 (56.5%)	20 (43.5%)	46	
	Total	55(64.7%)	30(35.3%)	85	
Convulsion	No	46(80.7%)	11(19.3%)	57	<0.0001
	Yes	9(32.1%)	19(67.9%)	28	
	Total	55(64.7%)	30(35.3%)	85	
Direct breastfeeding	No	12(38.7%)	19(61.3%)	31	<0.0001
	Yes	43(79.6%)	11(20.4%)	54	
	Total	55(64.7%)	30(35.3%)	85	
Birth Asphyxia	No	44 (73.3%)	16(26.7%)	60	0.01
	Yes	11(44.0%)	14(56.0%)	25	
	Total	55(64.7%)	30(35.3%)	85	

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Correlation between the birth asphyxia and neurodevelopmental outcome of the VLBW babies at one year showed that out of 25 neonates with birth asphyxia, fourteen infants had a neurodevelopmental delay at the end of 1 year, which is statistically significant with a p-value of 0.01 and 0.006 for DDST and HINE, respectively (Tables 3 and 4). Also, the correlation between mechanical ventilation at the neonatal period and neurodevelopmental outcome at one year showed that out of 32 neonates with a history of mechanical ventilation at the neonatal period, twenty-one infants had a neurodevelopmental delay at the end of 1 year, which is statistically significant with a p-value of 0.0001 [Tables 3 and 4].

Table 4: Correlation between neonatal outcomes and neurodevelopmental scores, HINE at one year

Neonatal Outcome		Count		Total (100%)	P value
		Delay	Normal		
Mechanical Ventilation	No	8(15.1%)	45(84.9%)	53	<0.0001
	Yes	21(65.6%)	11(34.4%)	32	
	Total	29(34.1%)	56(65.9%)	85	
Sepsis	No	9(23.1%)	30(76.9%)	39	0.048
	Yes	20(43.5%)	26(56.5%)	46	
	Total	29(34.1%)	56(65.9%)	85	
Convulsion	No	11(19.3%)	46(80.7%)	57	<0.0001
	Yes	18(64.3%)	10(35.7%)	28	
	Total	29(34.1%)	56(65.9%)	85	
Direct breastfeeding	No	18 (58.1%)	13 (41.9%)	31	<0.0001
	Yes	11(20.4%)	43(79.6%)	54	
	Total	29(34.1%)	56(65.9%)	85	
Birth Asphyxia	No	15(25.0%)	45(75.0%)	60	0.006
	Yes	14(56.0%)	11(44%)	25	
	Total	29(34.1%)	56(65.9%)	85	

The above tables show the correlation between neonatal sepsis and neurodevelopmental outcome at one year. Out of 46 neonates with neonatal sepsis, 20 infants had neurodevelopmental delay assessed at the end of 1 year by DDST and HINE, which is not statistically significant with a p-value of 0.086 and 0.048. Tables 3 and 4 also show the correlation between neonatal convulsions and neurodevelopmental outcomes at one year. Out of 28 neonates with neonatal convulsions, 19 infants had a neurodevelopmental delay at the end of 1 year by DDST, which is statistically significant with a p-value of 0.001 and 18 had developmental delay assessed by HINE with a statistically significant p-value of 0.001.

The correlation between exclusive breastfeeding and neurodevelopmental outcome at one year showed that out of 31 neonates who were not exclusively breastfed. Nineteen infants had neurodevelopmental delay done by DDST at the end of 1 year, which is statistically significant with a p-value of 0.001. Eighteen had developmental delay assessed by HINE with a statistically significant p-value of 0.001.

DISCUSSION

In this longitudinal study, 112 VLBW neonates were discharged from NICU and registered at DEIC, ICH &RC, Madurai for follow-up. Since 27 subjects were lost in follow-up, the study was conducted with 85 infants. The VLBW infants were serially assessed for neurodevelopmental outcomes at corrected at the ages of 3, 6, and 9 months up to 1 year of age. The assessment was done by using DDST and HINE tests. The study aimed to evaluate the neurodevelopmental outcome at the corrected age of 1 year. This, in turn, was influenced by many factors in the case of preterm VLBW babies. These factors include neonatal complications such as birth asphyxia, respiratory distress syndrome, mechanical ventilation, sepsis, convulsions, and jaundice. Apart from these, the correlation between exclusive breastfeeding and the neurodevelopmental outcome was also studied.

Of the babies followed up, 48 were male, and 37 were female. A similar increase in the prevalence of male babies was reported earlier by Mandal et al.[11] Associated neonatal complication analysis revealed that jaundice was observed to affect 62.4% of infants with the highest prevalence, and birth asphyxia had the least prevalence. Mandal et al. also reported dominance in jaundice among preterm neonates.[11] RDS and H/O surfactant administration (60%) and sepsis (54.1 %) also occurred at higher rates. A likely dominance in the need for RDS and H/O surfactant administration was reported earlier by Ward and Beachy.[12] Among neonatal infectious diseases, sepsis was found to occur in a significant number of preterm-born babies across the world.[13]

In our study, the developmental assessment at the corrected age of 3 months by DDST showed that only 6 out of 85 infants were normal, and 79 out of 85 (93%) had significant developmental delays. Neurological examination by HINE revealed a delay in 62 out of 85 infants (73%). Assessment at the corrected age of 6 months showed 60 out of 85 (71%) had significant delay by DDST, and 38 out of 85 (45%) infants had suboptimal scores by HINE, thus having significant neurodevelopmental delay. A decrease in the frequency of babies with developmental delay based on HINE score at month six was reported in a likely study.[11]

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The developmental assessment at the corrected age of 9 months by DDST showed that 50 out of 85 infants were normal and 35 out of 85 (41%) had significant developmental delays. Neurological examination by HINE revealed a delay in 33 out of 85 infants (39%). The final neurodevelopmental status of the preterm VLBW infants at the corrected age of 1 year showed a significant delay in 30 out of 85 infants (35%) by DDST, and by HINE, 29 out of 85 (34%) had a significant developmental delay. This follows the results published by Kharlukhi et al.[14] Comparing these factors and the neurodevelopmental outcome at the corrected age of 1 year, birth asphyxia, mechanical ventilation, neonatal convulsions, and faulty feeding directly correlated with the significant delay. In contrast, neonatal sepsis and jaundice did not correlate statistically with the neurodevelopmental outcome of the VLBW preterm infants. It was confirmed that late-onset sepsis, despite its low prevalence, is a substantial risk factor for the development of a severe sequelae, particularly in children with a low gestational age.[15]

Similarly, broncho pulmonary dysplasia, a complex respiratory condition that preterm infants, especially those with low birth weight, are susceptible to, was discovered to be more common in our sample. Similar larger cohorts of subjects are included in studies by international networks, and hence is a significant risk factor for the development of major sequelae, confirming what is already reported in the literature, particularly in child development. In this regard, we want to emphasise that a strategy we frequently employ in our NICU that is mostly consistent with previous research is avoiding respiratory issues by using prenatal steroid medication and early surfactant administration.[16] Jaundice was not associated with the neurodevelopmental outcome of VLBW preterm children. However, it has been established that hyperbilirubinemia is more common, more severe, and has a longer course in preterm infants than in term neonates.[17]

CONCLUSION

Although there has been an improvement in the survival rate of VLBW newborns over the past ten years, the neurodevelopmental morbidities they are associated with present significant challenges. To identify neurodevelopmental disorders early and increase the assessment for intervention, long-term evaluation and follow-up of these newborns are crucial. This might potentially affect the result in the form of quality survival.

REFERENCES

1. Hollier LM. Preventing preterm birth: what works, what doesn't. Obstet Gynecol Surv 2005; 60:124–31.
2. Bronstein JM. Preterm Birth in the United States. Cham: Springer International Publishing. https://doi. org/10.1007/978-3-319-32715-0; 2016.
3. Soleimani F, Zaheri F, Abdi F. Long-term neurodevelopmental outcomes after preterm birth. Iran Red Crescent Med J 2014; 16: e17965.
4. Thébaud B, Goss KN, Laughon M, Whitsett JA, Abman SH, Steinhorn RH, et al. Bronchopulmonary dysplasia. Nat Rev Dis Primers 2019; 5:78.
5. Saugstad OD, Aune D. Optimal oxygenation of extremely low birth weight infants: a meta-analysis and systematic review of the oxygen saturation target studies. Neonatology 2014; 105:55–63.
6. Franco RC, Franção P, Junior PR, Menezes V, Leite BD, Junior RN, et al. Estratégias de intervenção sensório-motora para crianças prematuras no cuidado intensivo neonatal: uma revisão sistemática. Braz. J. Dev. 2020; 6:49877-97.
7. Vollmer B, Stålnacke J. Young adult motor, sensory, and cognitive outcomes and longitudinal development after very and extremely preterm birth. Neuropediatrics 2019; 50:219–27.
8. Rogers EE, Hintz SR. Early neurodevelopmental outcomes of extremely preterm infants. Semin Perinatol 2016; 40:497–509.
9. Agarwal PK, Shi L, Rajadurai VS, Zheng Q, Yang PH, Khoo PC, et al. Factors affecting neurodevelopmental outcome at 2 years in very preterm infants below 1250 grams: a prospective study. J Perinatol 2018; 38:1093–100.
10. Kats D, Payne L, Parlier M, Piven J. Prevalence of selected clinical problems in older adults with autism and intellectual disability. J Neurodev Disord 2013; 5:27.
11. Mandal S, Tani T, Datta S, Mallick A, Biswas S, Ghosh S. Prospective observational follow-up study of high-risk infants discharged from SNCU and NICU of a tertiary centre in Kolkata. J Curr Med Res Opin 2022; 5:1399–417.
12. Ward RM, Beachy JC. Neonatal complications following preterm birth. BJOG 2003; 110:8–16.
13. Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal infectious diseases: evaluation of neonatal sepsis. Pediatr Clin North Am 2013; 60:367–89.
14. Jacquilyne K, Udayakumar N, Saji J, Fatima Shirly A, Sanmathi S, Siri Ishwarya P. Effectiveness of bedside clinical screening tools in predicting short-term neurodevelopmental delay among very-low-birth-weight preterms: A prospective observational study. Cureus 2021; 13: e20355.
15. Orcesi S, Olivieri I, Longo S, Perotti G, La Piana R, Tinelli C, et al. Neurodevelopmental outcome of preterm very low birth weight infants born from 2005 to 2007. Eur J Paediatr Neurol 2012; 16:716–23.
16. De Nisi G, Berti M, Malossi R, Pederzini F, Pedrotti A, Valente A. Comparison of neonatal intensive care: Trento area versus Vermont Oxford Network. Ital J Pediatr 2009; 35:5.
17. Watchko JF, Maisels MJ. Jaundice in low birthweight infants: pathobiology and outcome. Arch Dis Child Fetal Neonatal Ed 2003; 88: F455-8.

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