



Neurodevelopmental Outcome of High Risk Newborns

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Abstract

Background: Developmental challenge in children is an emerging problem across the globe, which is largely associated with improved neonatal survival. Improved newborn care is leading to salvage of many critically ill newborns, but many of them survive with brain damage, leading to ultimate developmental disability. Sick neonates, particularly preterm babies, very low birth weight (VLBW) and extremely low birth weight (ELBW) babies (birth weights less than 1500 and 1000 g respectively) with perinatal hypoxia and hypoxic-ischaemic encephalopathy, sepsis, severe jaundice etc. are most vulnerable to poor neurodevelopmental outcome.

Methods: Present study entitled "Neurodevelopmental outcome in high risk newborns" was undertaken with the objectives to study the incidence of neurodevelopmental abnormalities in high risk

newborns and risk factors associated with adverse Neurodevelopmental outcome. The study was conducted in Department of Pediatrics, Sardar Patel Medical College and P.B.M. Hospital Bikaner between April 2018 to September 2019.

Results: Prevalence of neurodevelopmental abnormalities was 42.3% at 3 months and the prevalence declined to 24.2% at 9 month and 22.5% at 12 month follow-up.

Conclusion: The prevalence of neurodevelopmental abnormalities was lesser at 12 months evaluation in comparison to prevalence at 3 months, signifying that neurodevelopmental abnormalities due to various risk factors are partially reversible. Maximum improvement in mean DQ was observed in babies with hyperbilirubinemia, prematurity, hypoglycaemia and hypocalcaemia. This finding underscores the importance of early detection of neurodevelopmental

abnormalities and initiation of early intervention measures to reduce the prevalence of neurodevelopmental abnormalities in high risk newborns.

Keywords: Neurodevelopmental, follow-up, children.

Introduction

Developmental challenge in children is an emerging problem across the globe, which is largely associated with improved neonatal survival¹. Improved newborn care is leading to salvage of many critically ill newborns, but many of them survive with brain damage, leading to ultimate developmental disability. Sick neonates, particularly preterm babies, very low birth weight (VLBW) and extremely low birth weight (ELBW) babies (birth weights less than 1500 and 1000 g respectively) with perinatal hypoxia and hypoxic-ischaemic encephalopathy, sepsis, severe jaundice etc. are most vulnerable to poor neurodevelopmental outcome². Insult to the developing brain may lead to gross and fine structural changes resulting in smaller brain size, reduced white and grey matter, ventriculomegaly, decreased callosal projections and altered fibre tract organization, which eventually affects neural function³. Hence, a close neurodevelopmental follow-up of these high-risk newborns is essential for early detection of any brain damage, to prevent or restrict a poor neurodevelopmental outcome through early intervention.

Though perinatal and newborn care is improving in rural India, a section of the rural population is still deprived of all the available facilities, due to socio-economic, cultural and topographical reasons. There is very scanty data from these areas, regarding neurodevelopmental outcome of high risk newborns and the magnitude of the problem of evolving developmental challenges.

Recognition of precipitating factors and adequate preventive measures, detection of early markers of developmental delay and early intervention measures can go a long way in preventing childhood disability. This calls in for a neurodevelopmental follow-up of high risk babies by a specialized team, using proper scientific methodology.

Material and Methods

Study Place: This study was conducted in Department of Paediatrics S.P. Medical College, P.B.M. Associated Group of Hospital, Bikaner Rajasthan.

Study Design: Hospital Based Prospective Observational Study.

Study Duration: 18 months (April 2018 to September 2019).

Study Population: Newborn admitted in NICU with high risk factors

1. Neonatal Septicemia
2. HIE Grade II
3. Prematurity
4. Low Birth Weight
5. Hypoglycemia
6. Hyperbilirubinemia
7. Hypocalcemia
8. Neonatal Seizures
9. Hospital Stay >3 days
10. Mechanical Ventilation >2 days

Sample Size: The following sample formula was used

$$n = Z^2 P(1-P)/d^2$$

where

n= sample size

Z= Z statistic for a level of confidence (95%)

P=Expected prevalence of proportion (in proportion of one; if 20%, P= 0.2), and

d= Precision (In proportion of one; if 5%, d= 0.05) allowable maximum error is 20% of prevalence.

As per literature review in Indian study, the prevalence of NDD in high risk newborn is taken as 35%.

$$n = Z^2 P(1-P)/d^2$$

$$n = 1.96^2 * 0.35 * .651 / .07^2$$

$$n = 178$$

Total 200 cases were screened out of which 22 lost to follow up. So finally 178 consecutively born newborn neonates having defined high risk factors were included and followed up for 12 months.

Inclusion Criteria

- Neonates admitted in NICU with neurodevelopment risk and followed for 12 months.
- Given consent for the study.

Exclusion Criteria

- Patients who did not give consent for the study
- Patients who did not come back at follow up

Method

One hundred and ninety six newborns admitted in NICU of Department of Pediatrics, S.P. Medical College with neonatal factors were included in the study. Data about birth history, gestational age, antenatal history, maternal history, risk factors, treatment given and condition at discharge were collected in a predesigned proforma.

At the admission guardians were counselled. These infants were examined at 3 months, 6 months, 9 months and 12 months age and their neurodevelopmental assessment was done by Development Assessment Scales for Indian Infants (DASII) method and a composite DQ (motor and mental DQ) was calculated. This scale consists of 67 items for assessment of motor development and 163 items for assessment of mental development. Motor scale was assessed control of gross and fine motor muscle groups. Mental scale was assessed cognitive, personal and social skills development. Both mental development index and

psychomotor development index were calculated by DASII. The age placement of the item at the total score rank of the scale was noted as the child's developmental age. This converted the child's total scores to his motor age (MoA) and mental age (MeA). The respective ages were used to calculate patient's motor and mental development quotients respectively by comparing them with patient's chronological age and multiplying it by 100. (DMoQ = MoA/CA x 100 and DMeQ = MeA/CA x 100). The composite DQ was derived as an average of DMoQ and DMeQ for clinical interpretation.

Observations

Table 1: Sex wise distribution of neonates

Gender	No. of Cases	%
Female	71	39.9
Males	107	60.1
Total	178	100

Table 1 shows the distribution of 178 studied neonates according to sex. Out of 178 neonates, 71(39.9%) were females while 107(60.1%) were males.

Table 2: Distribution of cases according to gestational age of neonates

Gestational Age (weeks)	No. of Cases	%
<37	77	43.3
≥37	101	56.7
Total	178	100

Table 2 shows the distribution of 178 studied cases according to gestational age. Out of 178 cases, 77(43.3%) had <37 weeks gestational age while 101(56.7%) were ≥37 weeks gestational age.

Table 3: Distribution of cases according to birth weight (kg)

Birth Weight (kg)	No. of Cases	%
<2.5	93	52.2
>=2.50	85	47.8
Total	178	100

Table 3 shows the distribution of cases according to birth weight. Out of total 178 cases, 93(52.2%) babies were <2.5kg and 85(47.8%) babies had their birth weight >=2.50 kg.

Table 4: Distribution of cases according to risk factors

Risk Factors	No. of Cases	%
Seizures	36	20.2
Septicemia	28	15.7
Hyperbilirubinemia	30	16.9
HIE-II	40	22.5
Preterm	77	43.3
Low Birth Weight	93	52.2
Hypoglycemia	9	5.1
Hypocalcemia	19	10.7
Hospital Stay >3 days	140	78.7
Mechanical Ventilation >2 days	7	3.9

Table 5 shows distribution of cases according to risk factors. Seizures were present in 36(20.2%) cases, hyperbilirubinemia was present in 30(16.9%) cases, HIE-II was present in 40(22.5%) of cases, LBW was present in 93(52.2%) of cases, Septicemia was present in 28(15.7%) cases, 77(43.3%) cases were preterm, 9(5.1%) cases had hypoglycemia while 19(10.7%) patients had hypocalcemia, 140(78.7%) patients stayed at hospital for >3days while 7(3.9%) patients in our study group needed mechanical ventilation for >2 days. some newborns had more than

one risk factor. Multiple risk factors were simultaneously present in many neonates.

Table 5: Prevalence of neurodevelopmental abnormalities at 3, 6, 9 and 12 months of age

Follow Up (month)	Total No. of cases evaluated	Abnormal Cases (DQ ≤70)		Normal Cases (DQ >70)	
		No.	%	No.	%
3	178	75	42.1	103	57.9
6	178	75	42.1	103	57.9
9	178	43	24.2	135	75.8
12	178	40	22.5	138	77.5

Prevalence of cases with abnormal neurodevelopmental outcome (DQ ≤70) was 42.1% at 3 and 6 months, 24.2% at 9 months and 22.5% at 12 months follow up.

Table 6: Pattern of neurodevelopmental abnormality

Follow Up (month)	Total No.	Motor DQ ≤70		Mental DQ ≤70	
		No.	%	No.	%
3	178	75	42.1	75	42.1
6	178	75	42.1	75	42.1
9	178	43	24.2	43	24.4
12	178	40	22.5	40	22.5

At 3 months out of total 178 cases, 42.1% cases were abnormal and no change was found at 6 months, while at 9 months out of total 178 cases, 43(24.2%) cases remain abnormal and at 12 month follow up only 40(22.5%) cases remained abnormal. All cases in our study had impairment in both motor as well as mental domain.

Table 7: Percentage Improvement in Neurodevelopmental outcome in neonates with different risk factors

Risk Factors	No. of abnormal Cases at 3 month	No. of abnormal Cases at 12 month	Improvement in neurodevelopmental abnormality (%)
Hyperbilirubinaemia	5	2	60.0
HIE-II	26	21	19.2
Preterm	38	18	52.6
Low Birth Weight	39	24	38.5
Hypoglycemia	4	2	50.0
Hypocalcemia	4	2	50.0
Seizure	22	15	31.8
Hospital Stay (>3 days)	62	36	41.9
Mechanical Ventilation (>2 days)	7	6	14.3

Many neonates with adverse neurodevelopmental outcome ($DQ \leq 70$) at 3 months follow-up showed improvement and were found to have $DQ > 70$ at 12 month follow-up. The highest percentage of improvement was observed in babies with hyperbilirubinemia 60% followed by prematurity (52.6%), hypoglycaemia and hypocalcemia (50%), hospital stay (>3 days), septicemia (33.3%), seizure (31.8%), HIE-II (19.2%) least improvement was seen in babies who were mechanically ventilated. (>2 days, 14.3%)

Table 8: Improvement in mean DQ from 3 months to 12 months follow-up in babies with neurodevelopmental abnormalities

Risk Factors	Mean DQ <70 at 3 months		Mean DQ <70 at 12 months		t	p
	Mean	SD	Mean	SD		
	Septicemia	62.50	3.45	65.21		
Hyperbilirubinaemia	63.34	4.72	65.00	0.00	0.499	0.705
HIE-II	62.54	3.32	65.72	0.85	4.163	<0.001
Preterm	62.22	3.23	65.83	1.03	4.791	<0.001
Low Birth Weight	62.22	3.21	65.77	0.98	5.241	<0.001
Hypoglycemia	60.00	0.00	65.84	1.18	6.988	0.090
Hypocalcemia	63.33	4.71	65.00	0.00	0.499	0.705
Seizure	63.56	3.44	65.67	0.85	2.147	0.050
Hospital Stay (>3 days)	63.15	3.38	65.74	0.93	4.377	<0.001
Mechanical Ventilation (>2 days)	63.14	3.38	65.73	0.96	4.312	<0.001

Mean DQ of neonates with neurodevelopmental abnormalities was compared at 3 and 12 month follow-up.

Statistically significant improvement in mean DQ was observed in babies affected with septicemia, HIE-II, prematurity, low birth weight, prolonged hospital stay and mechanical ventilation.

In neonates having risk factors such as hyperbilirubinemia, hypoglycemia, hypocalcaemia and seizures a significant improvement in mean DQ was not observed from 3 to 12 month follow-up.

Discussion

The present prospective, hospital based, observational study was done in Department of Paediatrics S.P. Medical College, Bikaner, Rajasthan between April 2018 to September 2019 (18 months). The study enrolled 200 consecutively born neonates having defined high risk factors fulfilling the inclusion and exclusion criteria and these were followed up for 12 months. These cases were evaluated for their

neurodevelopmental outcome by Developmental Assessment Scales for Indian Infants (DASII) method. Out of 200 patients initially enrolled 22 were lost to follow-up, so finally 178 were assessed at 3, 6, 9 and 12 months of age for their neurodevelopmental outcome.

In present study prevalence of abnormal neurodevelopmental outcome (DQ<70) was 42.1% at 3 months of age and at 6 month, 24.2% at 9 months and 22.5% at 12 months age. On contrary Korres et al* (2005) 0.2% had risk factors. Whereas Nair et al (2014) found prevalence of developmental delay using the DASII 13.3%.

The prevalence of neurodevelopmentally abnormal neonates declined from 42.1% at 3 month to 22.5% at 12 month age indicating neuronal recovery at adverse event. Chattopadhyay and Mitra* (2015) reported that developmental delay was present in 31.6% of study population. Zaramella et al* (2008) observed that 75.5% of the patients had a normal Mental Development Index (MDI), while 24.5% showed a delayed performance (8.8% mildly and 15.7% severely).

All cases in our study had impairment in both motor as well as mental domain. out of total 75 (DQ \leq 70) abnormal cases, 33 and 42 were female and males respectively, at 3 and 6 months, at 9 month out of total 43 abnormal cases, 17 and 26 were female and male respectively while at 12 months, out of total 40 abnormal cases, 15 and 25 cases were female and male respectively. (P value >0.05).

Neurodevelopmentally abnormal cases according to gestational age (weeks), maximum 49.4% were <37 weeks at 3 and 6 months, 27.3% and 23.4% respectively at 9 and 12 months follow-up. 36.6% at 3 and 6 months and 21.8% at 9 and 12 months follow-up for term babies. The difference was statistically insignificant

whereas Resegue* (2008) showed significant relationships between developmental abnormality and prematurity.

When assessed according to birth weight 41.9% low birth weight babies were neurodevelopmentally abnormal at 3 and 6 month and only 28% and 25.8% babies were found abnormal at 9 month and 12 month follow-up respectively. While the proportion of abnormal babies with birth weight \geq 2.5 kg was 42.4% at 3 and 6 month, 20% at 9 month and 18.8% at 12 month follow-up. Whereas Mwaniki et al* (2010) incidence was 39.5 [95% confidence interval (CI) 26.4-56.7] per 1000 live-births and incidence increased with birth weight. Nair et al* (2014) It was observed that a significant odds ratio for DASII mental deviation quotient (DQ) was seen for low birth weight (1.49).

At 3 and 6 month 29 and 46 cases (N=75) belonged to rural and urban area respectively, at 9 month 14 and 29 cases (N=43) and while at 12 months follow-up out of total 40 abnormal cases, 13 and 27 cases belonged to rural and urban area respectively in abnormal group and the difference was statistically insignificant (p>0.05).

Conclusion

The prevalence of neurodevelopmental abnormalities was lesser at 12 months evaluation in comparison to prevalence at 3 months, signifying that neurodevelopmental abnormalities due to various risk factors are partially reversible. Maximum improvement in mean DQ was observed in babies with hyperbilirubinemia, prematurity, hypoglycaemia and hypocalcaemia. This finding underscores the importance of early detection of neurodevelopmental abnormalities and initiation of early intervention measures to reduce the prevalence of neurodevelopmental abnormalities in high risk newborns.

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