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Neuro-development of high-risk newborns- An experience from rural tertiary care center of Western India

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ABSTRACT

Introduction: Neurodevelopment of an infant is affected by various factors like birth weight, perinatal events, environmental factors, psychosocial, socioeconomic condition, genetic, racial and nutritional factors, and hypoxic ischemic Encephalopathy following perinatal Asphyxia. Timely and appropriate intervention can modify many of these disabilities.
Aim: To assess the neurodevelopmental outcome of high-risk neonates discharged from NICU.
Materials and Methods: 80 Babies, discharged from NICU were followed up to the one year, and their Neurodevelopment assessment was done at 6 and 12 months of age by using DASII. Babies were diagnosed as delayed development if development quotient of < 70% was found. Associated risk factors like birth weight, gestational age at birth, perinatal events and course during NICU stay were analyzed.
Result: Mean DMoQ and DMeQ and overall DQ at 6 month were 81%, 82%, 81.5% and at 12 months of age 85%, 86%and 85.5% respectively. Out of 80 patients, 16(20%) babies had development delay at 6th months and 10(12.5%) at 12 months. 16(20%) babies with delayed development at 6 months had DMoQ 46.2+14.7, DMeQ 42.7 +13.8 and Mean DQ of 44.5 +14.3. 10(12.5%) babies with delayed development at 12 months had DMoQ 65.5+15.5, DMeQ 61.6+16.5 and mean DQ of 63.5 +14.1. 9 out of 10 babies having delayed development at 12 months had birth asphyxia at birth.
Conclusion: We concluded that Incidence of neurodevelopment delay among high-risk infant is significantly high in babies with birth asphyxia, HIE and seizure. An appropriate follow-up program is helpful in early detection of development delay.

1. Introduction

Neurodevelopment is clinically evident by acquisition of cognitive skills, emotional and social interaction, and sound physical and mental health.[1] Development denotes maturation of functions or acquisition of new skills and is intimately related to maturation and myelination of central nervous system.Neuro-developmental assessment helps in diagnosis of various disorders including developmental disabilities, learning disabilities, autistic spectrum disorders, attention disorders, etc. Changes in neuromotor function during the first year of life are related to the maturation of the central nervous system. Thus, it is important to detect abnormalities in neurodevelopment as early as possible. There are various factors affecting neurodevelopment of an infant including birth weight, perinatal events, environmental factors, psychosocial, socioeconomic, genetic, racial and nutritional factors. Hypoxic ischemic Encephalopathy (HIE) following

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perinatal asphyxia, hypoglycemia, hypothyroidism, bilirubin encephalopathy, SGA and prematurity are an important cause of later neurodevelopmental impairment in infants.[2–6] Outcome of the children with severe HIE is consistently poor. Behavioral monitoring is required for all children with HIE and neurodevelopmental assessment is also needed for children with moderate Neonatal Encephalopathy.[7]

Very often, problems are identified very late and only few rehabilitation measures can be taken and may not bring out the desired result. Timely and appropriate intervention can modify many of these disabilities.[2] The neurodevelopment disability can be identified by certain perinatal risk factors. A structured plan of follow-up can be designed in order to assess their developmental status at the earliest by using simple developmental assessment tools like the Development Assessment Scales for Indian Infants (DASII), Denver Developmental Screening Test (DDST) or Trivandrum Developmental Screening Chart (TDSC) even by general pediatrician. Now, focus of pediatric care is shifting from merely survival to intact survival of the infants. Early identification of developmental delay and intervention can give better neurological outcome and a better quality of life has become the need of the hour. A very influential factor (and consequently a very significant educational means) is the use of intervention movement programs. A developmentally adequate movement program can enhance motor development, thus preventing the long-term negative consequences that an unfavorable influence of several genetic or the aforementioned environmental factors may have.[3]

In India, there is growing interest and awareness about the above-mentioned facts. It is realized that team effort is required for early identification and proper management of patient with delayed developmental. If early intervention is done to modify social and psychosocial environment of the infant, it would make a huge difference in neurodevelopmental outcome. Approximately 10-20% of all live born babies need Intensive Care for various reasons including birth asphyxia, meconium aspiration syndrome, preterm with low birth weight, neonatal sepsis and many others.[8] These babies are at high-risk of adverse neurodevelopment. There are very few studies reported from this part of country on neurodevelopmental outcome of high-risk newborn. Therefore, current study was conducted to assess the neurodevelopmental outcome of high-risk newborn discharged from NICU of Dhiraj hospital at one year of age.

2. Materials and Methods

This was a prospective observational study carried out at Dhiraj Hospital from April 2017 to July 2017 after approval from Sumandeep Vidyapeeth institutional ethics committee. Sample size was calculated using following formula.

$$N=Z^2p(1-p)/d^2$$

where N is the sample size, z is the confidence level, p is the sensitivity and d is the precision. Based on previous studies conducted for Neurodevelopmental outcome, it was found that, incidence of development delay was 22.5%, so with a relative precision of 2.9% and confidence level of 95%, the minimum sample size required for present study was estimated to be 80.

All moderate to high risk neonates which require NICU admission for at least 24 hrs, with following characteristics were included in the study: (i) All newborns with BW ≥ 1500 gm or gestation ≥ 32 weeks having any of following co-morbid conditions like Neonatal Meningitis, Received mechanical ventilation for >48 hours, moderate to severe birth asphyxia, Hypoxic ischemic encephalopathy stage 2 or higher, Symptomatic hypoglycaemia, Hypothyroidism, Symptomatic polycythemia, baby of HIV positive mother, Hyperbilirubinemia requiring intensive phototherapy or exchange transfusion, cholestasis, Abnormal neurological examination at discharge, seizures, chronic lung disease, IVH grade III, and periventricular leukomalacia (ii) All newborns with birth weight <1500 gm or gestation age < 32 weeks with or without afore-mentioned significant morbidities requiring NICU care. The newborn with congenital malformations, musculoskeletal deformity, short NICU stays for antibiotics or phototherapy and those who lost to follow-up were excluded. Patients were enrolled after obtaining written informed consent from their parents. During enrolment and on each follow up visit, detailed history and neurological examination was done to detect neurological deficits and tone abnormalities.

Neurodevelopment assessment was done at 6 and 12 months of corrected age using DASII. This test was administered by physiotherapist trained in DASII and rendering regular services in the department. Both mental and motor development indices were calculated according to standard protocol for DASII. The respective ages were used to calculate motor and mental development quotients respectively by comparing them with their chronological age (CA) 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. The motor and mental indices were standardized scores that were distributed in the same manner as IQ scores with a population mean of standard deviation of 16. The test needed a special kit to perform and cooperation of the child. Abnormal neurodevelopmental outcome was diagnosed if any of either MoQ or MeQ was < 70%.

Collected Data were entered in Microsoft Excel and analyzed using Epi info 7.1. data was analyzed in terms of percentages, mean and standard deviation.

3. Results

Total 110 cases were enrolled, 30 babies lost to follow up (12 babies at 6 month and another 18 babies at 12 months). Therefore, 80 babies were followed up till one year of the corrected gestational age.

There were 53(66.3%) boys and 27 (33.7%) girls. Majority of mothers 52(64.9%) were from the rural areas. Most of patients 37, (46.3%) were from the lower socio-economic class.

Table 1: Basic demographic profile of participants

Gender	Frequency	Percent
Female	27	33.8
Male	53	66.3
Locality		
Rural	52	64.9
Urban	28	35.1
Socio-Economic class		
1 (Upper)	0	0
2 (Upper Middle)	0	0
3 (Lower Middle)	18	22.5
4 (Upper Lower)	25	31.3
5 (Lower)	37	46.3

Total 39 babies (48.8%) were born pre term. No any infant was < 28 weeks or > 42 weeks of gestation age. The mean gestational age was 33.3 ± 2.4 weeks. 52(65.0%) newborn were low birth weight, 14(17.6%) were very low birth weight and only one (1.3%) was extremely low birth weight. The mean birth weight was 2114.46 ± 750 gm. Detail of gestational age and birth weight are presented in table. Six newborn (7.5%) were small for date and 74 (92.5%) were appropriate for gestational age.Table 1

Table 2: Distribution according to Gestational age & birth weight

Gestational age (Weeks)	Frequency	Percent
<28	0	0
28- 32	12	15.0
33-36	27	33.8
37-42	41	51.3
>42	0	0
Birth weight (kg)		
<1	1	1.3
1.0-1.49	13	16.3
1.50-1.99	22	27.5
2.0- 2.49	16	20.0
2.50-3.5	28	35.0
Total	80	100.0

Prematurity was the commonest indication for NICU admission 33(43.8%), followed by birth asphyxia 24(30.0%), neonatal hyperbilirubinemia 23(27.5%) and neonatal seizure 13(16.3%). Total 11(13.8%) developed septicemia. Hypoglycemia and meconium aspiration syndrome were found in one newborn (1.3%) each. Of these 80 infants, 26 infants (32.5%) had > one morbidity. Table 2

Table 3: Morbidity pattern of study participants

Morbidity	Frequency	Percentage
Prematurity	35	43.8
Birth asphyxia	24	30.0
Without HIE	15	18.75
With HIE stage 2	9	11.25
With HIE stage 3	0	0.0
Neonatal Hyperbillirubinemia	23	27.5
Seizure	13	16.3
Sepsis	11	13.8
Hypernatremic dehydration	2	2.6
Meconium Aspiration Syndrome (MAS)	1	1.3
Hypoglycemia	1	1.3

Note: HIE-Hypoxic ischemic encephalopathy, MAS-Meconium aspiration syndrome. ROP-Retinopathy of prematurity.

Ventilatory support was required in 28 (35%) newborn. 41 (51.3%) babies required vasopressor support for shock management. Table 3

At 6th month, 64 babies had normal development. Motor DQ in these babies was 85.9 + 7.3, mental DQ was 87.2 +14.8 and mean DQ was 86.6 +15.1. 16 babies (20%) were developmentally delayed. Motor DQ in these babies was 46.2+14.7, mental DQ was 42.7 +13.8 and Mean DQ was 44.5 +14.3. Table 4

At end of 12 months, 70 infant had normal development. Motor DQ in these babies was 90.6+12.4, mental DQ was 92.1+14.1 and mean DQ was 91.4 +13.1. Developmental delay was found in 10(12.5%) infants. Motor DQ in these babies was 65.5+15.5, mental DQ 61.6+16.5 and mean DQ was 63.5 +14.1.

Motor DQ at 12 month improved by 19.3%(41.7% from baseline of 6 months development) and Mental DQ improved by 18.9% point (44.3% from baseline of 6 months development). There was Improvement in mean DQ by 19%(42.7%).

There was no difference in terms of neurological outcome in relation to gender, socioeconomic class and birth weight. Maturity at birth seems to be associated with developmental delay which was significantly more in term children 9(22.0%, p = 0.01).Table 5

Prematurity, Neonatal sepsis, Neonatal hyper-bilirubinemia, Meconium aspiration syndrome, hypoglycemia and use of Vasopressor were not found to be significantly associated (p value > 0.05) with developmental delay. All these babies had normal development at 12 month.

Birth asphyxia (p value 0.001) and neonatal seizure (p value 0.001) and were found as significant contributing

Table 4: Comparison of Developmental Quotient (DQ) in subject with normal and delay development

	Development(n)	Motor DQ (SD)	Mental DQ (SD)	Mean DQ (SD)
Development at 6 months	Delay (16)	46.20(+14.67)	42.70(+13.81)	44.5(+14.3)
	Normal (64)	85.93(+14.80)	87.19(+16.7)	86.6(+15.1)
Development at 12 months	Delay (10)	65.47(+15.55)	61.59(+16.51)	63.5(+14.1)
	Normal (70)	90.65(+12.41)	92.08(+14.11)	91.4(+13.1)

Table 5: Developmental outcome at 12 months of age in relation to demographic profile

Risk factors		Development		Total	X^2	P
		Normal	Abnormal			
Gender	Male	46(86.7%)	7(13.2%)	53(100.0%)	0.07	0.1
	Female	24(88.8%)	3(11.1%)	27(100.0%)		
SE class	Lower middle	16(88.9%)	2(11.1%)	18(100.0%)	0.4	0.8
	Upper lower	21(84.0%)	4(16.0%)	25(100.0%)		
	Lower	33(89.2%)	4(10.8%)	37(100.0%)		
Weight according to GA	AGA	65(87.8%)	9(12.2%)	74(100.0%)	0.10	0.7
	SGA	5(83.3%)	1(16.7%)	6(100.0%)		
Birth weight	LBW	48(92.3%)	4(7.7%)	52(100.0%)	3.1	0.07
	Normal	22(78.6%)	6(21.4%)	28(100.0%)		
Gestational age	Preterm	38(97.4%)	1(2.6%)	39(100.0%)	6.8	**0.01**
	Term	32(78.0%)	9(22.0%)	41(100.0%)		
Total		70(80.0%)	10(20.0%)	80(100.0%)		

(Note: SE class- socioeconomic class, AGA= appropriate for gestational age, SGA- small for gestational age, LBW- low birth weight)

Table 6: Developmental outcome in relation to morbidity

Morbidity	Development						P value
	Normal			Abnormal			
	No (%)	DQ % at 12 month		No (%)	DQ % at12 month		
		Mo DQ	Me DQ		Mo DQ	Me DQ	
Prematurity	38(97.4)	90.0	91.3	1(2.6)	44.0	49.0	0.56
Vasopressor given	33(80.5%)	87.2	88.9	8(19.5%)	57.4	54.1	0.08
Ventilation	22(78.6%)	88.5	90.6	6(21.4%)	54.3	50.5	0.07
NHB	21(91.3%)	91.7	92.1	2(8.7%)	44.0	35.0	0.67
Birth asphyxia	15(62.5%)	82.6	83.4	9(37.5%)	58.4	53.7	**0.001**
Sepsis	9(81.8%)	89.8	89.6	2(18.2%)	69.0	58.5	0.69
Seizure	3(23.1%)	81.0	81.3	10(76.9%)	56.1	51.2	**0.001**
MAS	1(100.0%)	92.0	94.0	0(0.0%)	NA	NA	1.00
Hypoglycemia	1(100)	89.0	91.0	0(0.0%)	NA	NA	1.00

(Note: NHB- neonatal hyperbilirubinemia, MAS- meconium aspiration syndrome)

factors for developmental delay. Total 24 newborn admitted with birth asphyxia. Of them, 14 (58.3%) and 9 (37.5%) had development delay at 6 month and 12 month respectively. At 12 month, severe development delay (DQ<50%) and moderate development delay (DQ= 50 to 70%) were found 4 and 5 babies respectively. Nine newborn (11.2%) developed HIE following birth asphyxia. All of them had development delay at 12 month. Thirteen newborn had seizure during NICU stay. Of them, most common reason for seizure was Birth asphyxia with HIE 9(69.2%) followed by sepsis 2(15.4%), hypoglycemia 1(7.6%) and Neonatal hyperbilirubinemia 1(7.6%). 3 (23.1%) babies had normal development at 12 month of age.Table 6

Gender, maturity at birth, birth weight and birth weight according to gestational age did not show significant difference in development at 6 month or 12 month of corrected gestational age. But there was significant difference in development in babies without birth asphyxia and babies with birth asphyxia at 6 months (p = 0.02) and at 12 months (p=0.03). Similarly there was significant difference in development in babies with seizure and without seizure at six months of age (p=0.03) and at 12 months of age (p=0.03).Table 7

Birth asphyxia with HIE 9(100%), neonatal seizure 10(76.9%), term birth 9(22%) and neonatal hyperbilirubinemia 2(8.3%) were found as significant contributing factors for developmental delay.

Table 7: Motor and Mental Development Quotient in relation to important demographic and morbidity parameters

Parameters	Development quotient at 6 Month				Development quotient at 12 Month			
	MO DQ Mean(SD)	ME DQ Mean(SD)	Mean DQ Mean(SD)	P value	MO DQ Mean(SD)	ME DQ Mean(SD)	Mean DQ Mean(SD)	P value
Male	80.3(16.9)	81.3(17.8)	80.8(17.3)	0.3	84.6(14.9)	85.2(16.0)	84.9(15.4)	0.4
Female	82.3(13.2)	82.3(16.7)	82.3(15.0)		86.7(10.0)	86.3(13.5)	86.5(11.7)	
Pre term	85.9(10.2)	87.0(9.0)	86.5(9.6)	0.1	89.1(8.9)	90.3(8.1)	89.7(8.5)	0.2
Term	76.3(18.4)	76.5(21.5)	76.4(20.0)		81.7(15.9)	81.1(18.6)	81.4(17.2)	
LBW	82.6(15.9)	84.1(15.7)	83.3(15.8)	0.09	86.5(13.5)	87.6(13.9)	87.1(13.7)	0.1
Normal weight	78.0(15.2)	77.0(19.5)	77.5(17.3)		83.1(13.2)	81.8(16.7)	82.5(14.9)	
AGA	81.4(14.5)	82.0(16.0)	81.7(15.2)	0.09	85.7(12.6)	86.0(14.1)	85.9(13.3)	0.9
SGA	75.3(28.2)	77.0(31.2)	76.2(29.7)		80.2(22.3)	80.5(26.1)	80.3(24.2)	
No Birth asphyxia	87.2(10.9)	88.5(12.0)	87.9(11.5)	**0.02**	90.4(9.1)	91.3(9.9)	90.9(9.5)	**0.03**
Birth asphyxia	66.2(15.4)	65.5(17.4)	65.9(16.4)		73.3(14.3)	72.3(16.9)	72.8(15.6)	
Without seizure	86.2(7.1)	87.7(7.9)	86.9(7.5)	**0.03**	89.9(6.2)	90.9(6.0)	90.4(6.1)	**0.03**
Seizure	53.4(18.9)	50.5(19.7)	52.0(19.3)		61.9(16.2)	58.2(18.1)	60.0(17.1)	

(Note: MO DQ- Motor development quotient, ME DQ- Mental development quotient, SD-Standard deviation, LBW- Low birth weight, AGA- Appropriate for gestational age, SGA- Small for gestational age.)

4. Discussion

First year of life is very important in regard to development, especially high-risk infants. With improved newborn care many critically sick newborns survive but with residual brain damage. Therefore, achieving normal development in a child, who had bad perinatal and neonatal course is a challenge and is an emerging problem. With improved newborn care many critically ill newborns survive but with brain damage. That lead to developmental delay and disability.

There were 53(66.3%) boys and 27 (33.7%) girls in the study. Similar results were reported in study by N. Chattopadhyay et al.[9]This difference might be due to gender bias prevalent in society, which is more concerned about the wellbeing and survival of male offspring.

About half of total babies 39 (48.8%) in current study were pre-term. The mean gestational age was 33.3 ± 2.4 weeks. Out of 80 babies, nearly two third newborn 52(65.0%) had low birth weight. Among low birth weight babies, 14 babies (17.6%) had very low birth weight (less than 1500 gm) and only one (1.3%) of baby had extremely low birth weight (less than 1000 gm). The mean birth weight was 2114.46 ± 750 gm. Six newborn (7.5%) were small for date and 74 (92.5%) were appropriate for gestational age. In a study by S. Das et al. proportion of LBW and preterm was 43.7% and 26.4% respectively, whereas that of SGA babies was (25.8%).[10]

In current study, prematurity was the commonest reason of NICU admission 33 (43.8%), followed by birth asphyxia 24(30.0%), neonatal hyperbilirubinemia 23 (27.5%) neonatal seizure 13(16.3%) and septicemia 11(13.8%). Hypoglycemia and meconium aspiration syndrome were found in 1(1.3%) newborn each. 26(32.5%) newborn had more than one indication of NICU care. Similar indications for NICU admission were reported in the study conducted by K. Godbole et al. i.e. Prematurity (47.6%), hyperbilirubinemia (26.1%) and Birth asphyxia (21.4%).[11] Study by S. Das et al. reported commonest indication for NICU admission as HIE 37(23.1%), neonatal hyperbilirubinemia(5.8%), sepsis with meningitis 5(3.2%) and prematurity 4(2.5%). 100(64.52%) babies had more than one risk factors.[10] Similarly in study by K. Godbole et al. 54.54% had more than one risk factors.[11]

Number of patients with development delay at 12 months decreased to 10 from 16 cases at 6 months of age. Improvement in both components of development quotients was observed. Improvement in Motor, Mental and total mean DQ at 12 month was 41.7%, 44.3% and 42.7% respectively. Similar improvement in DQ was observed in study by S. Baburaj et al. number of children with delayed development reduced from 6(12.7%) at 4 months of follow up to 4(8.5%) and 2(4.2%) at 8 and 12 months of follow up.[12]Higher prevalence of delayed development (57.4%) was reported in study conducted by K. Godbole et al. The difference in number of patients was primarily due to higher cut off (motor or mental DQ < 85) they have considered in defining development delay.[11] Gender was not a significant factor influencing outcome of high-risk newborn.[9,11]

In current study, socio economic status (p value 0.8) and weight for age (p value 0.7) did not show significant difference in developmental outcome which is similar to findings of other studies.[7,10,13]Similarly no significant association was found in Low birth Weight babies and developmental delay, finding similar to study by S. Baburaj et al and S. Das et al.[10,12]

In current study 1/39 preterm and 9/41 term babies had delayed development at 12 months of age (p 0.01). Among preterm babies 1(2.6%) child had developmental delay, which was significantly lower than term children 9(22.0%, p 0.01). Incidence of preterm was lower (26.4%) in the study of S. Das. Development delay was more common

in term newborn as compared to preterm newborn but not statistically significant (Term: 29, 25.9% v/s Preterm: 6,14.6%, p 0.19).[8] S. Baburaj at al. also reported higher incidence of developmental delay among term babies (11.1% v/s 6.9%).[10]

This high incidence of developmental delay cannot be explained exclusively by maturity only. Usually full-term babies are admitted in NICU only when they have associated risk factors. In current study 16 and 10 patients at 6 months and 12 months of age respectively had developmental delay. Almost all of these patients had significant history of birth asphyxia along with other associated morbidities except one patient which had bilirubin encephalopathy. Out 24 asphyxiated newborn, 15(62.5%) and 9 (37.5%) had development delay at 6 month and 12 month respectively. S. Baburaj et al. reported that half of newborn with birth asphyxia (2 out 4) had development delay at 12 months of age which was higher than current study.[12]

Thirteen newborns developed seizure during NICU stay. Most common reason for seizure was birth asphyxia with HIE 9(69.2%), sepsis 2(15.4%), hypoglycemia 1(7.6%) and neonatal hyperbilirubinemia 1(7.6%). 10 babies (76.9%) had development delay at 12 month. Of these 10 infants with developmental delay, 9 had HIE following birth asphyxia. Similar findings were reported in other studies.[9,14]

Mean motor and mental DQ in term newborns was found lower than preterm babies. It is mainly seen due to co-morbid factors, mainly birth asphyxia & HIE. Similar finding was observed in study by S. Baburaj et al.[12]

In current study, mean DQ was higher in LBW but not significant as compared to normal weight babies. This observation is contradictory to study by S. Baburaj et al. who reported that Mean DQ in normal weight babies was slightly higher but statistically not significant.[12]

5. Conclusion

Delayed neurodevelopment among high-risk infant is significantly associated with birth asphyxia in Term baby, with HIE and seizure. Most neurodevelopment delay go undetected in the early years of life if not assessed periodically. Improved perinatal care, early detection, and early intervention will reduce incidence of developmental delay. High risk infants have to be assessed periodically in follow up clinics, irrespective of their birth weight or gestational age. A proper and appropriate follow-up program and early initiation of supportive therapy will be helpful in case of development delay.

6. Limitation

The limitation of the study is the small sample size. Detailed subgroup analysis would have given more insight into the various etiological and other risk factors. Comparison of high-risk group with control group population would have given clearer picture.

7. Conflict of Interest

No conflict of interest.

8. Source of Funding

None.

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