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Original Research Article

Assessment of developmental outcome of neonatal seizures at NICU of tertiary care centre hospital

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ABSTRACT

Background: Seizures are relatively common among first month of life. New-born with neonatal seizures are at risk of developmental delay. The objective of this study was to assess the developmental outcome of neonatal seizures and to study the factors associated with delayed developmental outcome in neonatal seizures.
Methods: A prospective observational Study was conducted in 71 term and preterm neonates with documented seizure admitted in Medical college hospital, Jabalpur. A predesigned pretested questionnaire was used. The face to face interview technique was used for collection of data by mother, followed by clinical examination of newborn and investigations were done. DDST II was used for developmental assessment of neonates.
Results: Neonates with delayed developmental outcome are 42.62%. Delayed developmental outcome is significantly associated with male sex, low birth weight, prematurity and multiple frequencies of seizures.
Conclusions: The delayed developmental outcome was high among neonatal seizures.

Keywords: Development delay, Neonate, Seizure

INTRODUCTION

Neonatal seizure is paroxysmal behaviors caused by hypersynchronous discharge of a group of neurons.[1] Neonatal seizures are the most common overt manifestation of neurological dysfunction in the newborn. It may be the first and the only manifestation of neurological dysfunction after a variety of insults. Neonatal seizures are clinically significant because very few are idiopathic.

The prevalence is approximately 1.5% and overall incidence approximately 0.7 - 2.7 per 1000 live births.[2] The incidence in pre-term infants is very high (57-132 per 1000 live births).[2] Most (80%) neonatal seizures occur in the first 1-2 days to the first week of life. Continuous EEG monitoring of infants after one clinical seizure showed that 79% of subsequent EEG seizures were clinically silent. Such phenomenon seems to be more common in preterm infants. According to Volpe neonatal seizures were classified in 5 types: subtle seizures, tonic seizure, clonic seizure, myoclonic seizure, non-paroxysmal repetitive behavior.[3] The immature brain seems more prone to seizures; these are more common in the neonatal period than during any other time throughout life.[1] This may reflect the earlier development of excitatory synapses, predominating over inhibitory influences at early stages of maturation. Developmental delay (DD) occurs when a child does not reach developmental milestones at the expected age. Five key domains of development abound for children under five years of age namely;[4]

- Gross motor skills
- Fine motor skills
- Communication skills
- Cognition skills and
- Social/personal activities.

These are expected changes in skill developments that a child must pass through at predictable periods and in a predictable manner

A child may be affected in one or more of these domains during growth and development which underscores the importance of proper developmental screening.

The Denver developmental screening test (DDST) 4 is a widely used assessment for examining the developmental progress of children from birth until the age of 6 year.[4]

There are very few study has been conducted to determine the developmental outcome of newborns with neonatal seizures in India therefore we attempt to find out the developmental outcome of neonatal seizures and factors associated with delayed developmental outcome in neonatal seizures.

METHODS

The prospective observational study was conducted in 71 term and preterm neonates admitted at tertiary care centre, Department of Paediatrics, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India. Ethical clearance was taken from ethical committee of university and medical college. Before conducting study all the procedure were fully explained to mother and written consent were taken. All consecutive term and preterm neonates with documented seizure who were discharge from NICU with proper consent and counselling of parents were included in study during November 2014 - October 2015. The following neonates were excluded from study;

- Babies of mother on anti-epileptics
- Neonates with documented seizure due to congenital malformation e.g. congenital hydrocephalus, anencephaly, mylomeningocele
- Refusal by mother to participate in the study
- Neonatal death

A predesigned proforma was used for data collection. The face to face interview was taken from mother, followed by clinical examination of new-born and investigations.

Basic information and examination details were collected at the time of admission. At the time of discharge neurological examination, head circumference, history of Antiepileptic drugs and EEG were recorded. 3 follow up (at 1 month, at 3 month, and at 6 month) were done. At the follow up visit recording of complain of seizures, neurological examination, head circumference and history of anti-epileptic drug, development assessment, assessment of tone Amiel Tyson method, EEG, and BERA findings were recorded.

Neurodevelopment assessment was done by the Denver developmental screening test II. The neurodevelopment examination was performed at the time of admission and discharge then on follow up to assess the progress of encephalopathy. Neurodevelopment assessment was done by the Denver developmental screening test II (more commonly known as Denver II test). Denver II is worldwide popular simple model to assess child development in four domains - gross motor, fine motor-adaptive, language and personal social. It consists of 125 items, divided into 4 above mentioned categories. The items were arranged in chronological order according to the ages at which most children pass them. The test was administered in 10-20 minutes and consists of masking the parents question and having child performs various tasks-each task on DDST II was graded as pass, fail or refuses to cooperate.

Interpretation of DDST II was made as follow

- Normal - if a child passes, fail or refuse an item of the test which the age line falls on between 25th and 75th percentile
- Delayed - when a child fails or refuse a task within the age line cut through > 75th percentile.

Data thus obtained was coded and entered into Microsoft excel worksheet. This was analysed using SPSS version 20 and Epi Info version 7.1.5.2. To find out the association of DDST with the study variables, chi-square test and Fisher exact test was applied. The statistical significance was evaluated at 5% level of significance.

RESULTS

Table 1: Distribution of newborn according to general profile.

Variable	Frequency (n = 71)	%
Age at admission		
24 ≤hours	15	21.13%
25 to 72 hours	30	42.25%
>72 hours	26	36.62%
Gender		
Male	40	56.34 %
Female	31	43.66%
Birth weight		
<1500 gm	12	16.90%
1500 to 2500 gm	39	54.9%
>2500 gm	20	28.1%
Maturity status		
Preterm	18	25.35 %
Term	53	74.65 %

Study enrolled 71 cases during study period of these, 61 were followed up for completed 6 months and 10 were lost during follow up. As table 1 shows that about 79% newborn ages at admission were >24 hours while only 21.13% newborns age at admission were 24 ≤ hours. The mean age of admission was 4.12 days. Out of 71 newborn 56.34% were male and 43.66% were female. According

to maturity status about one fourth of study subjects were found to be preterm.

Table 2 shows that the developmental outcome among 57.38% newborn was found to be normal and among 42.62% delayed. Male had 60% increase in risk of having delayed developmental outcome to those of female but this difference was not found to be statistically significant.

Table 2: Cross tabulation between gender and DDST (n = 61).

Gender	DDST		Total (%)
	Normal (%)	Delayed (%)	
Male	16 (48.48)	17 (51.52)	33 (100)
Female	19 (67.86)	9 (32.14)	28 (100)
Total	**35 (57.38)**	**26 (42.62)**	**61 (100)**

$\chi 2$ (1, N = 61) = 2.32; p = 0 .127; RR (male:female) = 1.60 (CI 0.85 - 3.01).

Table 3 shows that low birth weight subjects had 8.8 times the risk of having delayed developmental outcome compared to those of normal birth weight and this difference was found to be statistically significant (p < 0.001).

Table 3: Cross tabulation between birth-weight and DDST (n = 61).

Birth weight (grams)	DDST		Total (%)
	Normal (%)	Delayed (%)	
<2500	20 (44.44)	25 (55.56)	45 (100)
≥2500	15 (93.75)	1(6.25)	16 (100)
Total	**35 (57.38)**	**26 (42.62)**	**61 (100)**

P value <0.001; RR = 8.88 (CI 1.36 - 60.36).

Table 4: Cross-tabulation between maturity and DDST.

Maturity status of newborn	DDST		
	Normal (%)	Delayed (%)	Total (%)
Term	34 (66.66)	17 (33.33)	51 (100)
Preterm	1 (10)	9 (90)	10 (100)
Total	**35 (57.37)**	**26 (42.62)**	**61 (100)**

p = 0.001; RR = 2.70; (CI 1.73- 4.19).

Table 4 shows that preterm subjects had 2.70 times the risk of having delayed developmental outcome compared to those of term newborn and this difference was found to be statistically significant (p = 0.001).

Table 5 shows that Subtle seizure were most common type 81% (n = 50) of seizure in our study and it has better prognosis than other type of seizure. Thirty four newborns were normal and 16 developed sequelae, while babies with tonic (n = 4) and Clonic (n = 2) seizure all had developmental delay. Five newborns had both (subtle and clonic) type of seizure in them 4 had delayed developmental and one was normal in development.

Table 5: Cross tabulation between type of seizure and DDST (n = 61).

Types of seizures	DDST		Total (%)
	Normal (%)	Delayed (%)	
Subtle	34 (68.00)	16 (32.00)	50 (100)
Tonic	0 (0.00)	4 (100.00)	4 (100.00)
Clonic	0 (0.00)	2 (100.00)	2 (100.00)
Subtle and clonic	1 (20.00)	4 (80.00)	5 (100.00)
Total	**35 (57.37)**	**26 (42.62)**	**61 (100.00)**

P value < 0.05

Table 6 shows that occurrence of single seizure invariably associated with normal DDST score while multiple frequency of seizures were associated with delayed developmental outcome.

Table 6: Cross tabulation between frequency of seizures and DDST (n = 61).

Frequency of seizures	DDST		Total (%)
	Normal (%)	Abnormal (%)	
Single	33 (100)	0 (0)	33 (100)
Multiple	2 (7.14)	26 (92.86)	28 (100)
Total	**35 (57.38)**	**26 (42.62)**	**61 (100)**

P value < 0.001.

DISCUSSION

Iype and colleagues have followed up a large cohort of newborns with neonatal seizures over 2-8 months to assess neurodevelopmental outcome they found 68% of the babies followed up were normal; 32% had an abnormal neurological outcome.[5] In our study delayed developmental outcome was seen 42%.

There was male preponderance for abnormal DDST found. This is consistent with finding of Mwanik M et al in who studied neonatal seizures in a rural Kenyan district hospital.[6] However, Digra SK and Gupta A conducted a study in all neonates less than 28 days of life, in SGMS Hospital, Government Medical College, Jammu over a period of 6 month, who were also reported male preponderance in their results.[7] Fernandes et al found that male sex was a risk factor for delays in motor development.[8] Male sex was also associated with an increased risk of delayed language and social-emotional development. While sex is not a factor that is directly modifiable, research into the mechanism by which female sex confers protective against developmental impairment could provide insight into potential preventive strategies.

In this study, out of total 61 newborn 6 are <1.5 gm, in them all are abnormal DDST, 39 are low birth weight that is 1.5-2.5 out of them 19 having abnormal DDST rest are normal, 16 newborn having weight >2.5 kg and in them only one newborn having abnormal DDST. The risk for neurodevelopmental deficit increases with decreasing birth weight resulting in relatively high risk of cerebral palsy, developmental delay and subnormal academic achievement.[9] Pisani F et al development a scoring system for early prognostic assessment after neonatal seizures. They concluded that birth weight on one of the best outcome predictor on multiple logistic regressions.[10]

Very low birth weight (VLBW) infants are at higher risk of poor growth and neurodevelopmental outcomes, due to associated adverse perinatal risk factors and postnatal morbidities. Several studies have reported high incidence of growth failure and poor neurological outcome during infancy and childhood.[1,2,4] There have been a few studies from India, reporting growth and neurodevelopment of low birth weight infants.[6,7,10] However, there is paucity of data on these outcomes of VLBW infants. Recently, Mukhopadhyay et al have reported neurodevelopmental outcome of VLBW infants from northern India.[11]

The developing brain of premature babies is extremely vulnerable to injury so, prematurity was found to be associated with poor developmental outcome this is may be as prematurity may result in neurological impairment such as periventricular leucomalacia (Iida, Takashima and Takeuchi) and intra-ventricular haemorrhage (levene, fawer, and lamont) and physical impairment (Rosenblith and Sims- Knight) which may lead to developmental delay.[12-14]

All the newborn with single episode of seizures had normal developmental outcome. Total 28 newborn having multiple episode of seizure during their neonatal life, out of which 26 newborns had developmental delay and 2 had normal DDST.

In present study, on analyzing co-relation between types of seizures and neurodevelopmental outcome at 6 month of age, subtle seizures came out to be most common type of seizures in 84.8% (n = 60) out of which 67% (n = 40) had normal outcome while remaining 33.3% (n = 20) had abnormal outcome, while tonic and clonic seizure having poor developmental outcome. Brunquell PJ et al had done a study to predict outcome bases on clinical seizures types in newborn.[11] They were able to establish significant relationship between type of seizures and outcome. They followed 77 cases over a period of 7 years and finally concluded that subtle and generalized tonic seizures had a significantly higher prevalence of epilepsy, mental retardation and cerebral palsy. Subtle seizures were in addition more likely to be associated with abnormalities on neurological examination at follow up.[11] Similar comparison for those with focal and multifocal clonic, focal tonic and multifocal myoclonic seizures revealed no significant differences in their study. Shankar JM et al in (AIIMS NICU protocol) mentioned that myoclonic seizures carry the worst prognosis in terms of neurodevelopmental outcome and seizures recurrence.[15] Focal clonic seizures have the best prognosis.[15] Again we realized that larger sample size is required to comment on accurate co-relation between type of seizures and neurodevelopmental outcome.

In our study we found that 42.62% subjects is associated with delayed developmental outcome which is quite high and developmental delay is significantly associated with male sex, low birth weight, prematurity and multiple frequency of seizures. Prevention of low birth weight might helpful in control of delayed developmental outcome for which further studies required.

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