

**PREDICTIVE VALUE OF ETIOLOGY AND TYPE OF SEIZURES FOR DEVELOPMENTAL OUTCOME IN NEONATES WITH SEIZURES AT 6 MONTH OF AGE**Akhil Singh<sup>1</sup>, Jyotsna Shrivastava<sup>2</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: OBJECTIVE:** To study the predictive value of etiology and type of seizures for developmental outcome in full term neonates with seizures at 6 month of age. **DESIGN:** Prospective Observational study. **SETTING:** Tertiary care centre, Gandhi Medical College, Bhopal **PARTICIPANTS:** full term hospitalized neonates with documented seizures. Newborns admitted for complaints other than seizure, hypoxic-ischemic encephalopathy (HIE) stage I, preterms and neonates born to mother on anti-epileptic therapy were excluded from the study. **RESULTS:** Out of total 54 registered neonates 7 expired and 5 lost to follow up. HIE being the most common cause and subtle seizure being the most common type of seizures. Among remaining 42 cases, 29 cases had normal and 13 cases had abnormal developmental outcome after 6 month of follow up. When classified this case on the basis of etiology and type of seizures and co-related them with developmental outcome, results were not statistically significant with p value of 0.1152 and 0.522 respectively. **CONCLUSION:** Etiology and types of seizure when co related with developmental outcome did not show statistical significance in our study.

**KEYWORDS:** Etiology, outcome, seizures, DDST.

**INTRODUCTION:** Neonatal seizure is a paroxysmal behaviour caused by hyper synchronous discharge of a group of neurons.<sup>[1]</sup> 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 0.95–3.5 per 1000 live births.<sup>[2,3]</sup> The incidence in pre-term infants is very high (57–132 per 1000 live births).<sup>[4]</sup> Most (80%) neonatal seizures occur in the first 1–2 days to the first week of life.

The present study was aimed to find out co-relation between etiology and type of seizures with the developmental outcome of newborns at 6 month of age.

**MATERIAL AND METHODOLOGY:** This was prospective observational study at NICU of Gandhi Medical College, Bhopal from April 2012 to March 2013 after taking ethical committee approval and parental consent, on full term neonates with documented seizure episode during neonatal period. Sample size was computed in accordance to DePaulo method of sample size calculation for qualitative research.<sup>[5]</sup> Babies of mother on anti-epileptics, pre-term neonates, full term neonates with undocumented seizures and HIE I cases were excluded from the study.

In present study, gestational age of the newborn was calculated by the New Ballard Scoring system.<sup>[6]</sup> Seizures were—“reported or observed repeated involuntary muscle contractions, abnormal

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tonic extensions or jerky movements of any part of the limb, face or mouth that was not stimulus sensitive or repetitive abnormal chewing, ocular fixation or cycled fluttering, pedaling movements, lip smacking".<sup>[7]</sup> Neonatal hypocalcaemia was—"total serum calcium concentration <7mg/dl and hypomagnesium at serum magnesium levels lower than 1.6 mg/dl"<sup>[8]</sup>. Blood sugar less than 45mg/dl was considered as hypoglycaemia and WBC  $\geq 32/\text{mm}^3$  in CSF was considered as meningitis.<sup>[9,10]</sup>

Detailed clinical examination was done for all the cases which included anthropometry, physical and general and systemic examination. The special emphasis was given to neurological examination which includes level of consciousness, muscle tone, activity, tendon reflexes, neonatal reflexes, size and reaction of pupil, presence of jitteriness and seizures. Routine investigations was done in all cases which include complete blood count, CRP, serum electrolytes, serum calcium, serum bilirubin, blood sugar and cranial ultrasound to find out the etiology of seizure. Various neonatal seizures were classified as subtle, focal tonic, focal clonic and myoclonic.<sup>[11]</sup> Neonates having ocular fixation or cycled fluttering, chewing, lip smacking, cycling, paddling, autonomic disturbance and apnea were classified as subtle seizures. Neonates showing rhythmic jerky movements were classified as clonic seizures. Tonic seizures were classified when neonates showed sustained flexion and extension of extremities and myoclonic seizures were classified when neonates showed lightning fast jerky movements of upper or lower limbs.

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 105 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 is administered in 10-20 minutes and consists of asking the parents question and having child perform various tasks. Each task on DDST II were graded as pass (P), fail (F) or refuse to co-operate (R).

Follow up was done at 4<sup>th</sup> week, 12<sup>th</sup> week and 6<sup>th</sup> month of age and recorded on same development chart. - Statistical analysis was done using Fisher exact test to find the significance of various EEG patterns in predicting outcome.

**RESULTS:** We had enrolled 54 full term babies who had seizures with in neonatal period and co-related various parameters of seizures with their developmental outcome. Of these 54 cases, 29(53.7%) were male and 25(46.3%) were female. 38% were full term low birth weight (1500-2500 grams) and 16(29.6%) of them had weight >2500grams. 7 cases expired during the course of treatment and 5 cases we lost to follow up. Remaining were 42 cases where follow up was done up to 6 month of age.

Among 42 cases, most common cause of seizure came out to be hypoxic ischemic encephalopathy (HIE). In 32(76.1%) cases of HIE, 12(37.5%) had abnormal neurodevelopmental outcome (p value=0.1572). In 3(7.14%) cases of meningitis 1(33.3%) had abnormal neurodevelopment (p value = 0.333). 7 cases had metabolic disorder (n1=5 hypocalcemia, n2=2 hypoglycemia) had normal development at 6 month of postnatal age. But overall statistical analysis was not significant (p = 0.1152).

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SL. NO.	ETIOLOGY	N	OUTCOME		p value
			Normal	Abnormal	
1	HIE	32	62.5 %(20)	37.5 %(12)	0.1572
2	Meningitis	3	66.7 %(2)	33.3 %(1)	0.333
3	ICH	0	0 %(0)	0 %(0)	1
4	Congenital Malformation	0	0 %(0)	0 %(0)	1
5	Hypocalcemia	5	100 %(5)	0 %(0)	0.0253
6	Hypoglycemia	2	100 %(2)	0%(0)	0.157
<b>TOTAL</b>		<b>42*</b>	<b>69.1%(29)</b>	<b>30.9%(13)</b>	
<b>*7 expired and 5 lost to follow up p value 0.1152</b>					

**Table 1: Etiology and its co-relation with developmental outcome**

Out of 42 cases, 31 (73.8%) had subtle seizure of which 70.9% (n=22) had normal outcome while 29.3% (n=9) had abnormal outcome (p value=0.195). 4 (9.5%) cases had focal tonic seizure of which only 1 (25%) had abnormal outcome (p value=0.3173) while out of 6 clonic seizures 2 (33.3%) had abnormal outcome (p value =0.4140). There was only one case of myoclonic seizure in this study, he had abnormal outcome at 6 month of age (p value=0.3173). Co-relation of types of seizure with developmental outcome also did not come out to be statistically significant (p value=0.522)

SL. NO.	TYPE OF SEIZURES	N	OUTCOME		p value
			Normal	Abnormal	
1	Subtle	31	70.9%(22)	29.3 %(9)	0.0195
2	Focal Tonic	4	75 %(3)	25 %(1)	0.3173
3	Focal Clonic	6	66.7 %(4)	33.3 %(2)	0.4140
4	Myoclonic	1	0 %(0)	100 %(1)	0.3173
<b>TOTAL</b>		<b>42*</b>	<b>69.1%(29)</b>	<b>30.9%(13)</b>	
<b>*7 expired and 5 lost to follow up p value 0.522</b>					

**Table 2: Seizure type and its co-relation with developmental outcome**

**DISCUSSION:** The most prominent feature of neurologic dysfunction in the neonatal period is the occurrence of seizures. Seizures in neonates are relatively common with variable clinical manifestations. They are powerful predictor of long term cognitive and developmental impairment. Also despite the important therapeutic and diagnostic advances that have entered in the practice of neonatal intensive care in recent years, perinatal asphyxia continues to be an important cause of neonatal mortality and morbidity. Hence it is necessary to evaluate this aspect in details.

Hasan Tekgul in 2006, done a study to delineate the etiology profile and neurodevelopmental outcome of neonatal seizures in term newborn infants. They found strong co-relation between seizure etiology and outcome.<sup>12</sup> Most common etiology was Hypoxic ischemic encephalopathy and was responsible for majority of infants with poor long term outcome which was in contrast to present study findings where this co-relation came out to be insignificant (p = 0.1152).

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Kenton R. Holden et al in 1982, co-related prenatal and perinatal events with outcome in cases of neonatal seizures and had reported similar results as of present study. They followed up to the age of 7 years and concluded that seizure are a major indicator off perinatal asphyxia and a predictor of subsequent neurological deficit, most infants who survived did well.<sup>[13]</sup>

M. Jeeva Shankar et al in 2010 (AIIMS NICU Protocol) mentioned that “hypocalcemia carry a good prognosis for long term neurodevelopmental outcome while seizures related to hypoglycemia, cerebral malformation and meningitis have a risk for adverse outcome”.<sup>[11]</sup> Results on hypocalcemia were similar to presnt study where all 5 cases of hypocalcemia had normal neurodevelopmental outcome. Although all cases of hypoglycemia (n=2) also had normal neurodevelopmental outcome at 6 month of age but this can be attributed to small sample size. Further studies of large number of neonates are required to confirm these observations and have accurate co-relation.

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 73.8% (n=31) of cases of which 70.9% (n=22) had normal outcome while remaining 29.3% (n=9) had abnormal outcome. Although on statistical analysis this co-relation did not come out to be significant in our study (p = 0.522).

In 2002, Philip J. Brunquell et al done a study to predict outcome based on clinical seizures types in newborn. 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.<sup>[14]</sup> Similar comparison for those with focal and multifocal clonic, focal tonic and multifocal myoclonic seizures revealed no significant differences in their study.

M. Jeeva Shankar et al in 2010 (AIIMS NICU Protocol) mentioned that “Myoclonic seizures carry the worst prognosis in terms of neuro-developmental outcome and seizure recurrence. Focal clonic seizures have the best prognosis.”.<sup>[11]</sup>

**CONCLUSION:** Neonatal seizures are of major concern in newborns and predicting outcome in later ages still remains a challenging task for health care professionals. Etiology and types of seizure when co related with developmental outcome did not show statistical significance in our study. There is absolute need for further studies with larger sample size to establish any co relation. Accurate co-relation if established would be of great assistance to clinician for planning further management and hence minimizing future disabilities.

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