

# Neonatal Seizure: A Clinical Riddle for the Physician

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## Abstract

**Aim:** Neonatal seizures are less likely to be idiopathic. Proper diagnosis of etiology can help in prompt management. The study was done to diagnose the preventable causes early and develop strategies for the prevention of neonatal seizures.

**Materials and Methods:** This prospective observational study was done among neonates who developed seizures before or during the stay in the Neonatal Intensive Care Unit (NICU), irrespective of gestational age and birth weight from June 2018 to May 2019.

**Results:** In the study, 4.95% of the total admitted babies were with seizure out of which 66.2% were term. Most of the seizures were detected within 24 hours of birth (53.6%) in neonates of primigravida (62%) and who are delivered normally (74.7%). Present study showed subtle seizures- 45.1%, multifocal clonic seizures - 39.4%, focal clonic seizures - 8.5% and tonic seizure - 7% of cases (n =71). Birth asphyxia (49.5%) being the most common cause followed by sepsis (29.5%) and metabolic abnormalities (25.4%). Most of the patients required only phenobarbitone (80.28%), a few patients required more than one anticonvulsant.

**Conclusion:** Neonatal seizures have an impact on cognitive, behavioural or epileptic complications later in life. The commonest cause of neonatal seizures is perinatal asphyxia.

**Keywords:** Neonatal Seizure, Etiology, Type, Ultrasound Findings.

## Introduction

Seizures during the neonatal period are relatively common. Most recent available global data shows it to be 1.1 to 8.5 per 1000 live births, with greater frequency in premature and low birth weight babies as compared to term babies. By definition neonatal seizures is a paroxysmal alteration in motor activity, behaviour or autonomic function that results from the abnormal electrical activity of the brain, during the neonatal period. The National Neonatal Perinatal Database (NNPD; 2002-03), which collected data from 18 tertiary care units across India, had reported an incidence of 10.3 per 1000 live-births. Neonatal seizures are usually classified in the following types: subtle, multifocal, focal, clonic, tonic, and myoclonic seizures. Subtle seizures are so termed be-

cause the clinical manifestations are mild and are often missed. In the new-born, seizures are always due to an underlying cerebral or biochemical abnormality. Perinatal asphyxia is the common cause of neonatal seizures. Perinatal asphyxia is the clinical condition that occurs due to impaired gaseous exchange during the 1<sup>st</sup> or 2<sup>nd</sup> stage of labour leading to foetal hypoxemia and hypercarbia. Rare causes include pyridoxine dependency and inborn errors of metabolism (IEM). The seizure may also occur due to meningitis and meningoenephalitis secondary to intrauterine infections (TORCH group, syphilis). Intracranial Haemorrhages (ICH) like subarachnoid, intraparenchymal or subdural haemorrhage contribute to neonatal seizures in term neonates and intraventricular haemorrhage

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(IVH) in preterm neonates. Most seizures due to intracranial haemorrhage occur between the 2<sup>nd</sup> and 7<sup>th</sup> day of life. Seizures occurring in the term 'well-baby' on day 2 to day 3 of life is often due to subarachnoid haemorrhage. Neonatal seizure increases the susceptibility of the developing brain to subsequent seizure-induced injury. Neonatal seizure has an adverse effect on neurodevelopment and may predispose to cognitive, behavioural or epileptic complications later in life. A neonatal seizure is dissimilar from those in a child or adult because generalized tonic convulsions do not occur during the first month of life as the arborisation of axons and dendritic processes, as well as myelination, are incomplete in the neonatal brain.

### Materials And Methods

This prospective observational study was conducted in Midnapore Medical College Hospital, West Bengal from June 2018 to May 2019. All the neonates who developed seizures before or after admission in the Neonatal Intensive Care Unit (NICU), irrespective of gestational age and birth weight are included in the study. Institutional Ethical clearance and informed consent were obtained from parents and caregivers on behalf of the neonates before including them in the study. Non-probability purposive sampling method was used and the sample size was 71. Haemodynamically unstable or very sick neonates and neonates with major congenital anomaly were excluded. A detailed history was obtained for all eligible babies and was thoroughly examined and monitored closely. Diagnosis of convulsion and classification of the type of convulsion were done by clinical expertise. Blood samples were drawn for analysis of sugar, calcium, electrolytes, complete blood counts, sepsis screening and culture. Lumbar puncture was done in selected and suspected cases of meningitis and CSF was analysed for biochemical and cytological parameters, and culture was done. Cranial ultrasound was done in all cases soon after stabilization. Data were entered and analysed in SPSS version 12. Descriptive statistics

for all variables done and the tests of significances for associations were assessed using the chi-square test. The purpose of the study is to find out the preventable causes of neonatal seizures and to develop strategies for early detection and prevention of metabolic causes like hypoglycaemia and hypocalcaemia as well as proper and adequate ante-natal and intra-natal care to prevent neonatal seizures from screening. Because every episode of neonatal seizures results in some neurological loss.

### Results

This study aimed to determine etiology, clinical profile and biochemical abnormalities to help in early recognition, treatment and better prognosis/outcome in neonatal seizures. The total number of new-born babies admitted during the study period was 1432 out of which 71 (4.95%) babies were with seizure. In this present study, there were 47 (66.2%) term, 24 (33.8%) preterm neonates, 38 (53.5%) male and 33 (46.5%) female neonates (Table 1).

**Table 1: Distribution of Cases According to the Maturity and Sex (n=71)**

	Number	Percentage
Term	47	66.2%
Preterm	24	33.8%
Male	38	53.5%
Female	33	46.5%

Seizures have been detected in neonates < 24 hours of life consisting of 38 (53.6%) cases, 24 - 72 hours 7%, > 72 hours to 7 days 32.4%, and > 7 days 7% of cases. In

**Table 2: Distribution of Cases According to the Religion and Socio Economic Status (n=71)**

	Religion			Socio economic status (modified B.G Prasad scale)			
	Hindu	Muslim	Christian	Upper-middle class	Middle class	Lower-middle class	Lower class
Number of cases	36	27	8	7	31	17	16
Percentage	50.7%	38.0%	11.3%	9.9%	44.0%	23.6%	22.5%

**Table 3: Distribution of Cases According to the Place of Birth, Birth Order and Mode of Delivery.**

	Place of birth		Gravida		Mode of delivery		
	Home delivery	Institutional delivery	Primi gravida	Multi gravida	Normal vaginal delivery	Instrumental delivery	Caesarean section
Number of cases	3	68	44	27	53	4	14
Percentage	4.2%	95.8%	62%	38%	74.7%	5.6%	19.7%

Table 4: Distribution of Cases According to the Age of Onset and Type of Seizure (n=71)

	Hours of life				Type of seizure				
	<24 hours	24-72 hours	72 hours to <7 days	>7 days	Subtle	Multi focal clonic	Focal clonic	Tonic	Myoclonic
Number of cases	38	5	23	5	32	28	6	5	0
Percentage	53.6%	7%	32.4%	7%	45.1%	39.4%	8.5%	7%	0%

Table 5: Etiological Distribution of Cases (n=71)

Cause	Associated causes	Number of cases	Percentage	Total
Birth asphyxia	Isolated birth asphyxia	30	42.5%	35(49.5%)
	Sepsis	3	4.25%	
	Hypoglycaemia	2	2.8%	
Sepsis	Meningitis	11	15.5%	21(29.5%)
	Associated birth asphyxia/hypoglycaemia/hypocalcaemia	10	14%	
Metabolic abnormalities	Isolated hypoglycaemia	7	9.9%	18(25.4%)
	Hypoglycaemia with sepsis	3	4.3%	
	Hypoglycaemia with birth asphyxia	2	2.8%	
	Other metabolic causes	6	8.4%	

the present study, subtle seizures constituting 45.1% of neonates, multifocal clonic seizures - 39.4%, focal clonic seizures - 8.5% and tonic type - 7%. None of the babies had myoclonic seizures.

Birth asphyxia was the most common cause of seizures observed in our study and it consisted of 49.5% of neonates in total. Isolated cases of birth asphyxia were seen in 30 (42.5%) cases, associated with sepsis and hypoglycaemia in 3 (4.2%) and 2 (2.8%) cases respectively. Sepsis accounting for 21 (29.5%) cases and 10 (14.0%) cases were associated with birth asphyxia, hypoglycaemia and hypocalcaemia. There were total of 18 (25.4%) cases of metabolic abnormalities including hypoglycaemia and hypocalcaemia. Hypoglycaemia was the most common cause consisting of 21.1% of the cases. Isolated hypoglycaemia accounting for 7 (9.9%) cases 3 (4.2%) cases associated with sepsis and 2 (2.8%) cases with birth asphyxia.

Out of 71 neonates in 57 (80.28%) neonates the seizure was controlled with phenobarbotone only, in 9 (12.67%) neonates with phenobarbitone and phenytoin both, in 3 (4.25%) neonates levetiracetam was required along with previous two drugs to control seizures and in 2 (2.81%) neonates seizure was not controlled by these medications and required midazolam infusion along with ventilator support.

In this study, ultrasonography (USG) of the cranium was conducted on all admitted cases with seizures. 39 (54.9%) neonates had no abnormal finding. 32 (45%) cases had abnormal findings as follows - hypoxic-ischemic changes in 22 (30.95%) cases, intracranial haemorrhage in 2 (2.8%), ventriculomegaly in 5 (7.2%) and hydrocephalus in 3 (4.2%) cases.

In the present study, 46 (64%) neonates recovered with no abnormalities or sequelae, 13 (18.3%) cases discharged with sequelae, 2 (2.8%) were discharged against medical advice and 10 (14%) died in spite of adequate treatment measures.

## Discussion

Neonatal seizure is very often a riddle to diagnose and to manage promptly for a physician. The occurrence of seizures may be the first indication of neurological disorder and the time of onset of seizures has a correlation with the etiology and prognosis. This study aimed to determine etiology, clinical profile and biochemical abnormalities to help in early recognition, treatment and better prognosis/outcome in neonatal seizures. The total number of new-borns admitted in the NICU during the study period was 1432 with an incidence rate of 4.95% of neonatal seizures. Similar findings were observed in the study conducted by Aziz A *et al.* where the incidence rate was 3.9%. Seizures have been found to have a higher incidence

Table 6: Cranial Ultrasonographic Finding of Cases (n=71)

USG findings	Number of cases	Percentage
No abnormality	39	54.9%
Hypoxic ischemic changes	22	30.9%
Intracranial haemorrhage	2	2.8%
Ventriculomegaly	5	7.2%
Hydrocephalus	3	4.2%

in neonates < 24 hours of life consisting of 53.6% cases, followed by age group > 72 hours to 7 days 32.4%, 24 - 72 hours 7% and > 7 days of life 7% as shown in table 4. In our study, we observed that seizure risk is more in term neonates than preterm and male neonates were predominant with male to female ratio of 1.15:1 as seen in table 1. Suryavanshi AR *et al* reported 76.25% terms and 23.75% preterm in their study and preponderance of male infants among the seizure population was also reported in study by Omene JA *et al*. There were 50.7% neonates belong to Hindu, 38.0% to Muslim and 11.3% to Christian community whereas 9.9% neonates were belong to upper-middle-class family, 44.0% to the middle-class family, 23.6% lower middle class and 22.5% belong to lower class family. (Table 2). None of the neonates was belonged to the upper class according to the modified BG Prasad scale 2019. There were 95.8% new-borns who had institutional deliveries and 4.2% being delivered at home. 74.7% neonates were born normally, 5.6% by instrumental delivery and 19.7% born by caesarean section. Most of the new-borns were born to 62% primigravida and 38% multi-gravida mothers. Similar findings reported by Suryavanshi AR *et al*<sup>8</sup> where 48 (60%) cases born to primigravida mothers and 32 (40%) to multigravida respectively. Seizures have been found to have in neonates < 24 hours of life consisting of 38 (53.6%) cases. In the present study, subtle seizures constituting 45.1% of neonates, multifocal clonic seizures - 39.4%, focal clonic seizures - 8.5% and tonic type - 7%. None of the babies had myoclonic seizures. Taksande A *et al* observed that subtle seizures were the commonest type of fits occurring in 50% of neonates. Birth asphyxia was the most common cause of seizures observed in our study and it consisted of 49.5% of total neonates. Isolated cases of birth asphyxia were seen in 30 (42.5%) cases, associated with sepsis and hypoglycaemia in 3 (4.25%) and 2 (2.8%) cases respectively. The association between birth asphyxia and type of seizure was not significant (p-value = 0.090). There was a total of 18 (25.4%) cases of metabolic abnormalities including hypoglycaemia and hypocalcaemia. Hypoglycaemia was the most common cause consisting of 17% of the cases. Isolated hypoglycaemia accounting for 7 (9.9%) cases, 3 (4.3%) cases associated with sepsis and 2 (2.8%) cases with birth asphyxia. This finding was not significant (p > 0.05). In this study, 54.9% neonates had no abnormal findings and 45% cases had abnormal findings - 2.8% neonates had intracranial haemorrhage, 7.2% had ventriculomegaly, 4.2% had hydrocephalus and 30.95% had hypoxic-ischemic changes on cranial ultrasound examination. In the present study, 18.3%

of cases discharged with sequelae, and 14% died in spite of adequate treatment measures. The decreased mortality in our study may be due to the exclusions of all severely ill or hemodynamically unstable neonates.

## Conclusion

Neonatal seizures typically signal the underlying significant neurological injury. Neonatal seizures are unique and distinctive in comparison to seizures in adults as well as other paediatric patients. The recognition of the etiology for the neonatal seizures are often helpful with respect to prognosis and treatment - this is the riddle for the treating physician.

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