

**ORIGINAL RESEARCH**

# Clinico-Etiological Parameters and short-Term Outcome of Seizures in Term Neonates: Experience of a Tertiary Care Center

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**ABSTRACT**

**Background:** Neonatal seizures constitute a common neurological emergency and they are often the first sign of neurological dysfunction. Neonatal seizure is associated with a high risk of mortality as well as neurological impairment/epilepsy disorders in later life. Common causes include hypoxic-ischemic encephalopathy, intracranial hemorrhage, meningitis, hypoglycemia, hypocalcemia, other metabolic disturbances etc. **Methods:** We conducted this observational study in NICU of NMCH, Patna over 2-year duration from June 2019 to May 2021 including term neonates of less than 1 month age with seizure and who stayed for >24 hours. Parameters studied were demographic profile, etiology, type of seizure, time of onset of seizure & short-term outcome. **Result:** Of the 104 neonates studied, male: female ratio was 1.27:1. Mean GA was 39.2 ±1.4 weeks and mean admission weight was 3.06±0.63 Kg. Perinatal asphyxia was the commonest risk factor (47.1%) followed by septicemia-meningitis (30.8%) and metabolic disturbances (hypoglycemia, hyponatremia, hypocalcemia) in 31.7%. Subtle seizure was the commonest seizure type (29.5%) followed by focal clonic seizures (26.6%) whereas tonic seizures were the least common (10.1%). 74.8% of the events were reported before 72 hours of age and the rest 25.2% were reported after 72 hours of age. In neonates with seizure, mortality was 29.8%, mean duration of hospital stay was 9.7±2.8 days. There was a significant increase in duration of hospital stay and delay in commencement of oral feeds, but there was no significant increase in mortality, need of ventilator support or inotrope support in such neonates as compared to term neonates without seizures. **Conclusion:** HIE and sepsis-meningitis was accountable for approximately 75% of total neonatal seizure cases. Subtle seizures were the commonest clinical type of seizure which was closely followed by focal clonic seizure. Most of the neonates developed seizure within 72 hours of life. Occurrence of seizure in term neonate seems to significantly increase duration of hospital stay and delay the commencement of oral feeds without increasing mortality.

**Key words:** Hypoxic ischemic encephalopathy, Neonatal seizure, term neonates, seizure type.

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**INTRODUCTION**

Neonatal seizure (NS) is classically defined as an event of paroxysmal alteration in neurological function i.e. motor, behavior and/or autonomic function<sup>1</sup> in infants less than 4 weeks of age. This is a common neurological problem. Infact seizures occur more frequently in neonatal period than at any other time of life. The reported incidence in India is about 10.3/1000 live births<sup>2</sup>. However, as its clinical recognition is difficult, the true incidence of neonatal seizures is difficult to determine. Though they are

often the first sign of neurological dysfunction, their clinical expression at this age is quite variable, poorly organized, often subtle and not discernible from other clinical conditions, especially in a sick neonate.

Seizures in newborn are different from those in older children in terms of etiology, type, onset as well as later outcome.<sup>3</sup> Common causes of neonatal seizures include hypoxic-ischemic encephalopathy, intracranial hemorrhage, meningitis, hypoglycemia, hypocalcemia, other metabolic disturbances, congenital malformation etc. Neonatal seizure carries

a high risk of mortality as well as neurological impairment/epilepsy disorders in later life.<sup>4</sup> With advances in neonatology, mortality from NS has decreased considerably from 40% to about 20% over the years, but occurrence of long-term neurological or development problems hasn't changed much and still remains around 30%.<sup>5</sup> This can be partly explained by any delay in diagnosis as well as subsequent improper and inadequate management.

Based on this background and considering the burden of neonatal seizures at our tertiary care level teaching hospital, we intended to conduct this study for better understanding of the factors associated with it and its short-term outcome. As the etiology and complications is quite different in term and preterm neonates, we decided to include only term neonates in the present study.

### **Aim & Objectives**

**Aim:** To study the clinico-aetiological parameters & short-term outcome of neonatal seizure in term neonates.

### **Objectives**

1. To study clinical profile and risk factors for seizures in term neonates.
2. To characterize the type of seizures in them.
3. To study time of onset of seizures and short term outcome of seizures in these neonates

## **MATERIALS AND METHODS**

**Study Setting:** N.I.C.U of deptt of Pediatrics N.M.C.H Patna, Bihar, India

**Study duration:** 2 years, from June 2019 to May 2021.

**Study design:** Hospital based prospective observational study.

**Inclusion criteria:** We included consecutively admitted term babies of less than 1 month age with neonatal seizure at our NICU who stayed for >24 hours.

**Exclusion criteria:** babies born preterm, seizures occurring after 1 month of age, neonatal tetanus cases and neonates with obvious congenital malformation were excluded from the present study. Neonates who stayed less than 24 hours in our NICU or who left against medical advice or who needed referral to some other hospital due to their medical/surgical condition were excluded from the final analysis.

**Study technique:** After obtaining written informed consent from the guardians, we enrolled potential neonates in this study. All enrolments underwent thorough physical and neurological examination and

focused history taking from guardians. Information was collected in detail and data pertaining to baseline characteristics, admission diagnosis and lab investigation reports was recorded in a structured proforma. HIE staging was done using Sarnat and Sarnat classification. Blood sample was sent for detection of sepsis, metabolic disturbances including hypoglycemia (defined as serum glucose <45mg/dl), hypocalcemia (defined as total serum Calcium <7mg/dl), hypomagnesemia (defined as serum magnesium levels < 1.5 mg/dl), hypernatremia (defined as serum sodium >150 meq/dl), hyponatremia (defined as serum sodium <130 meq/dl), hypokalemia (defined as serum potassium <3.5 meq/dl), hyperkalemia (defined as serum potassium >5.5 meq/dl), hyperphosphatemia (defined as serum phosphorus >8 mg/dl) etc. X-ray chest, USG cranium, thyroid profile was done whenever required. Lumber puncture was done for CSF analysis in all cases with suspected meningitis. Blood culture and septic screen was done in all cases with suspected sepsis.

**Statistical analysis:** All data so obtained was first entered in Microsoft excel sheet and then analyzed by SPSS version 20 software. Results were presented as mean, standard deviation, percentage as appropriate. Dichotomous events were compared by Chi-Square test and continuous variables were compared by Student t-test. P value less than 0.05 was considered significant

## **RESULT**

Occurrence of NS was 18.6 per 100 term neonates admitted to our NICU. Out of the 104 neonates finally studied, 47 (45.2%) were female and 59 (56.7 %) were male. Mean GA was 39.2 weeks, SD 1.4 weeks and mean admission weight was 3.06 Kg, S.D 0.63 Kg. Out of them 78 (75%) were referred to us from peripheral institutions (outborn), while 26 (25%) neonates were born in our institution (inborn).

Of the 104 neonates studied, hypoxic ischemic encephalopathy (HIE) was the commonest cause for neonatal seizure (n=49, 47.1% of neonates). Among these, HIE stage -2 was seen in 33.6 % (n =35) and HIE stage-3 was seen in 13.5% (n=14). Second to HIE was septicemia- meningitis (n=32, 30.8%). Other causes include- hypocalcemia (n=14, 13.5%), hypoglycemia (n=12, 11.5%), hyponatremia (n=7, 6.7%), hyperbilirubinemia kernicterus (n=4, 3.8%) and unknown etiology (n=3, 2.9%).

**Table 1: Risk factors for neonatal seizures**

<b>Etiology of seizures</b>	<b>Number of patients</b>	<b>Percentage</b>
HIE 2	35	33.6
HIE 3	14	13.5
Septicemia and meningitis	32	30.8
Hypocalcemia	14	13.5
Hypoglycemia	12	11.5

Hyponatremia	7	6.7
Hyperbilirubinemia- kernicterus	4	3.8
Unknown	3	2.9

(17 neonates had more than 1 risk factor for their seizures)

Clinical type of neonatal seizures: Overall, there were 139 events of seizures. The most common type of seizure was subtle seizures (n=41, 29.5%), followed by focal clonic seizures (n=37, 26.6%), multifocal clonic seizures (n=29, 20.9%) and myoclonic seizure (n= 18, 12.9%). The least common type of seizures was tonic seizures (n= 14, 10.1%). 13 neonates had more than 1 clinical type of seizure during their hospital stay.

**Table 2: Clinical characterization of the seizure episode**

Type of seizure	Number of events	Percentage
Subtle seizures	41	29.5%
Focal clonic seizures	37	26.6%
Multifocal clonic seizure	29	20.9%
Myoclonic seizures	18	12.9%
tonic seizures	14	10.1%

**Time of presentation of seizures:** Of the 139 events of neonatal seizures occurring in these 104 neonates, 47(33.8%) events of NS occurred before 12 hours of life, 34(24.5%) between 12 hours to 24 hours of life, 23(16.5%) between 24 hours to 72 hours of life and 35(25.2%) after 72 hours of life. Overall, 104 events (74.8%) were reported before 72 hours of age and the rest 35 (25.2%) were reported after 72 hours of age

**Table 3: Age of occurrence and the risk factor for neonatal seizure:**

Age of onset of Seizure	Etiology of Seizure	Number	Percentage
Less than 12 hr of life (Total no. of events=47)	HIE	36	25.9%
	Hypoglycemia	7	5.0%
	Hypocalcemia	4	3.2%
12 to 24 hr of life (Total no. of events= 34)	HIE	23	16.5%
	Septicemia- Meningitis	4	2.9%
	Hypoglycemia	3	2.1%
	Hypocalcemia	2	1.4%
	Hyponatremia	1	0.7%
	Unknown etiology	1	0.7%
24 to 72 hr of life (Total no. of events= 23)	HIE	3	2.1%
	Septicemia- Meningitis	12	8.6%
	Hypoglycemia	2	1.4%
	Hyponatremia	2	1.4%
	Hypocalcemia	2	1.4%
	Bilirubin encephalopathy	1	0.7%
	Unknown etiology	1	0.7%
More than 72 hrs (Total no. of events= 35)	Hypocalcemia	6	4.3%
	Hyponatremia	4	2.9%
	Hypoglycemia	3	2.1%
	Septicemia- meningitis	17	12.2%
	Kernicterus/Bilirubin encephalopathy	3	2.1%
	Unknown etiology	2	1.4%

**Outcome:** In neonates with seizure, mortality was 31 (29.8%), mean duration of hospital stay was 9.7 days (SD= 2.81 days). In univariate analysis, neonatal seizure in term neonates was associated with a significantly higher duration of hospital stay and delay in commencement of oral feeds but there was no significant increase in mortality, need of ventilator support or inotrope support in such neonates as compared to term neonates without seizures.

**Table 4: Univariate analysis of short-term outcome**

Sl no.	Parameter studied	Term neonates with seizure (n=104)	Term neonates without seizure (n=412)	P value
01	Mortality	29.8%	24.1%	0.30
02	Hospital stay (days)	Mean 9.7, SD 2.8	Mean 8.9, SD 2.6	<b>0.002</b>
03	Ventilator support	15.4%	21.8%	0.20
04	Inotrope support	13.4%	14.1%	0.70
05	Enteral feeds starting after admission (days)	Mean 6.3, SD 2.6	Mean 5.4, SD 2.1	<b>0.001</b>

## DISCUSSION

Seizures are usually the first indicators of an underlying metabolic or neurological disorder. They are powerful predictors of long term cognitive and developmental impairment. The time of onset of seizures has a correlation with the etiology of seizures and prognosis. Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as associated abnormalities and are often underdiagnosed.<sup>6</sup> This study attempts to determine etiology, biochemical abnormalities and short-term outcome in neonatal seizures which would help in early recognition and treatment and hence better prognosis in neonatal seizures.

In our study subtle seizures was the commonest seizure type (29.5%) followed closely by focal clonic seizures (26.6%) while tonic seizures were the least common (10.1%). *Silverstein et al.*<sup>7</sup> showed subtle seizures as the commonest type of seizures occurring in approximately 50% of neonates which is somewhat higher than our findings. Moreover, the comprehensive work of *Mizrahi et al.*<sup>8</sup> and *Scher et al.*<sup>9</sup> also reports subtle seizures as the most common type of neonatal seizures. Subtle seizures can be easily mistaken to be hunger cry or other baby activities. The somewhat lower incidence of subtle seizure in our study can also be attributed to the sicker neonates admitted in our NICU.

In our study 104 (74.8%) of seizures presented within the first 72 hours of life and most of them could be attributed to perinatal asphyxia (59.6% of these events). *Rose et al.*<sup>10</sup> also found early onset seizures in 50.33% babies whereas *Coen RW et al.*<sup>11</sup> found that 81% of babies had early onset seizures. In a study done by *Ajay et al.* in New Delhi, 52 neonates developed seizures within 48 hours of life, out of which 20 neonates had seizure in less than 12 hours of life.<sup>12</sup> These are comparable to our findings and emphasizes being vigilant for occurrence of seizures during the early hours of life of a neonate, more so when dealing with sick neonates.

In our study the most common etiology of neonatal seizure was perinatal asphyxia (47.1% neonates), followed by sepsis-meningitis in 30.8% neonates. Metabolic disturbances (hypoglycemia, hyponatremia, hypocalcemia) were also seen in 31.7% neonates. In a study done by *Sahana et al.*<sup>13</sup> on clinical profile of neonatal seizures in 109 neonates, 63 had perinatal asphyxia as the main etiology (57.80%),

second major common etiology was infection (14.67%). In another study, *Shah et al.*<sup>14</sup> showed that the major etiology of seizures was birth asphyxia (44%), septicemia (11%), meningitis (11%), hypocalcemia (11%), and hypoglycemia (22%). These figures correlate with our findings and re-emphasizes the frequent occurrence of neonatal seizures in asphyxiated neonates which require prompt recognition and management to improve the immediate as well as later neurodevelopmental outcome of these unfortunate neonates.

The short-term outcome of such neonates was compared with term neonates without seizures. In univariate analysis, neonates with seizures were found to have a significant longer duration of hospital stay as well as significant delay in starting oral feeds. However, there was no significant increase in mortality, need of ventilator support or inotrope support. This may be explained by the higher proportion of asphyxiated neonates in seizure group who frequently have multiple organs involvement requiring more interventions owing to their perinatal depression.

## CONCLUSION

Hypoxic ischemic encephalopathy was the commonest etiology of neonatal seizures in the present study, followed by sepsis-meningitis. Together, these two problems are accountable for three-fourths of all neonatal seizure cases. Subtle seizures were the commonest clinical type of seizure which can be easily missed by untrained eyes. Most of the seizure events started within 72 hours of life. Relatively earlier occurrence of seizure and a high burden of asphyxia indicate that there is a pressing need to improve the quality of care these neonates receive during their prenatal period. Occurrence of neonatal seizure in term neonate seems to significantly increase duration of hospital stay and delay the commencement of oral feeds without increasing mortality.

### Limitations

First limitation is inherent in the study design that this is a single centre study. Second, EEG correlation with the seizures was not done and so it is likely that the true incidence of seizures was not reported. Third, long term follow up of these neonates was not done.

**Conflict of interest:** None

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