

## Original Research Article

# A clinico-etiological evaluation and EEG correlation of neonatal seizures in a tertiary care hospital: a prospective cohort study

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## ABSTRACT

**Background:** Neonatal seizure is defined as a paroxysmal alteration in neurological function. The diagnosis of neonatal seizures is difficult to establish because of varied etiologies involved. The incidences vary from 1.5-3.7/1000 live births in term babies.

**Methods:** Hospital based observational study was conducted from December 1, 2016 till March 31, 2018. Universal sampling technique was followed. 93 neonates fulfilling the inclusion criteria were included in the study after consent from parents.

**Results:** This study results showed that 60.2% were males. Pre-term delivery occurred in 12.9% neonates. Most common etiology of neonatal seizures was birth asphyxia with 47.3% followed by metabolic abnormalities 32.3%. Abnormal EEG pattern was seen in 29% cases of neonatal seizures.

**Conclusions:** To conclude, the most common aetiology for neonatal seizures was birth asphyxia followed by metabolic abnormalities in which hypoglycaemia was the most common type. A significant association of seizures due to meningitis and metabolic abnormalities was observed with pre-term gestation while abnormal EEG pattern was observed with birth asphyxia and meningitis. EEG findings were found normal in majority of cases of neonatal seizure.

**Keywords:** Birth asphyxia, Electroencephalogram, Neonates, Seizures

## INTRODUCTION

Neonatal Seizures (NS) are the most frequent and distinctive clinical manifestation of neurological dysfunction in the new-born infant. The incidence of NS is 2.8 per 1000 in infants with birth weights of more than 2500 g; it is higher in preterm low birth weight neonates - as high as 57.5 per 1000 in very low birth weight infants.<sup>1</sup>

Infants with NS are at high risk of neonatal death or neurological impairment and epilepsy disorders in later Life. Seizures occur in 1% to 5% of infants during the first month of life (the neonatal period), which is one of

the highest-risk periods for seizures during the human life span.<sup>2</sup>

The most common cause of neonatal seizures is Hypoxic-Ischemic Encephalopathy (HIE), which occurs in approximately 1 to 2 per 1000 live births.<sup>3</sup> Other cerebrovascular disorders including arterial and venous stroke, intracerebral hemorrhage and subarachnoid hemorrhage also frequently present clinically with seizures.

Neonatal seizures also differ considerably from seizures observed in older children, principally because the

immature brain is less capable of propagating generalized or organized electrical discharges.<sup>4</sup>

The Neonatal seizures may be the first and perhaps the only, clinical sign of a central nervous system disorder in the newborn infant. Seizures in neonates may indicate the presence of a potentially treatable etiology and should prompt an immediate evaluation to determine cause and to institute early etiology-specific therapy. Hence, the clinical diagnosis, classification of neonatal seizures and the use of Electroencephalography (EEG) in clinical monitoring and management are critical for the neonate's care.

**METHODS**

The present study was conducted in NICU, Department of Pediatrics, Base Hospital, Delhi Cantonment. It is a tertiary care hospital of Armed Forces, which serves as referral center for the healthcare needs of defense personnel and their dependents. Guidelines provided by Indian Council of Medical Research for human research were followed strictly and clearance from Institutional Ethics Committee taken.

**Study population**

Neonates admitted to NICU of hospital with complaints of seizures during the study period.

Study design was hospital based observational Study. Universal sampling technique was followed, 93 neonates fulfilling the inclusion criteria were included in the study after consent from parents.

Study duration was December 1, 2016 till March 31, 2018.

**Inclusion criteria**

- Newborns till the age of 28 days with a diagnosis of neonatal seizures.
- Informed consent was given by the parents.

**Exclusion criteria**

- Congenital abnormalities
- Scalp swellings
- Critically ill and.
- Cases where no consent can be obtained

At the time of enrollment of the patient, all relevant clinical and demographic information was collected.

Demographic information like gender of the neonate, gestational age at which the neonate was born. Authors also elicited intrauterine growth status from the history obtained from the mother. Accurate clinical description of an event of seizure was noted for each enrolled patient.

To study the etiological profile of neonatal seizures in patients, authors obtained antenatal history from the mother, history of any infection, drug intake, hypertension, diabetes, hemorrhage and mode of delivery. History of consanguinity and family history of any Inborn Error of Metabolism (IEM) also taken.

EEG was performed in all patients. When required and if clinically indicated, patients underwent ultrasonography of the cranium, other hematology parameters, sepsis screen, blood culture, cerebrospinal fluid examination, VDRL, TORCH screen and other relevant investigations.

EEG was performed as early as possible after a seizure but within 24 hours of the event. EEG recordings were done as per the specifications of the American Clinical Neurophysiology Society. The EEG was reviewed by the neurologist, who was blinded to the neonate's clinical status.

**Statistical analysis**

The quantitative data was represented as their mean±SD. Categorical and nominal data was expressed in frequency and percentage. The t-test was used for analysing quantitative data while nonparametric data was analysed by Mann Whitney test. Categorical data was analysed by using chi-square test. The significance threshold of p-value was set at <0.05. All analysis was carried out by using SPSS software version 21.

**RESULTS**

The present hospital based observational study revealed the following results.

The study population included neonates of which the majority 60.2% were males while remaining 39.8% were females. It was found that pre-term delivery occurred in 12 (12.9%) neonates while remaining 81 (87.1%) were term gestation (Table 1).

**Table 1: Distribution of study population based on gender and gestation.**

Sex	Frequency	Percent
Male	56	60.2%
Female	37	39.8%
<b>Gestation</b>		
Full term	81	87.1%
Pre-term	12	12.9%

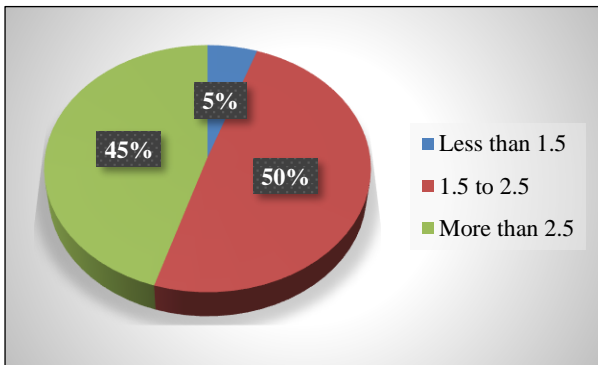
The weight of neonates was measured, Low birth weight was seen in 51 cases (54.9%) while the remaining neonates were of normal weight (Figure 1).

The clinically diagnosed cases showed that most common etiology of neonatal seizures was birth asphyxia (47.3%) followed by metabolic abnormalities (32.3%). Other

etiologies included: hyper-bilirubinemia (7.5%), meningitis (3.2%), hypoxia (2.2%) and structural malformations (2.2%) and no etiology could be identified in 5.4% cases (Table 2).

**Table 2: Distribution of study population based on etiology of seizure.**

Aetiology	Frequency	Percent
Birth asphyxia	44	47.3%
Metabolic	30	32.3%
Hyperbilirubinemia	7	7.5%
Hypoxia	2	2.2%
Meningitis	3	3.2%
Structural Malformation	2	2.2%
Unknown	5	5.4%
Total	93	100.0%



**Figure 1: Distribution of study population based on birth weight.**

Among the metabolic abnormalities being the cause of seizures, 16 (53.3%) had hypoglycaemia while 12 (40%) had hypocalcaemia. And 2 (6.7%) neonates had both hypoglycaemia and hypocalcaemia (Table 3).

**Table 3: Distribution of study population based on type of metabolic abnormalities.**

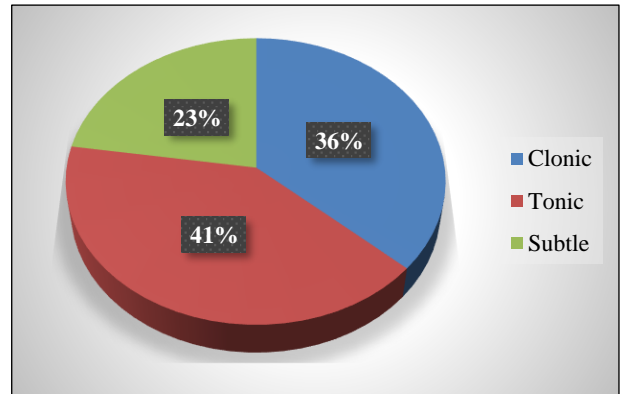
Metabolic Abnormalities	Frequency	Percent
Hypoglycaemia	16	53.3%
Hypocalcaemia	12	40.0%
Both	2	6.7%
Total	30	100.0%

The seizures among the neonates were tonic type in majority 38 (40.9%) followed by clonic type in 34 (36.9%) and subtle type of seizures were present in minority of 21 (22.6%) cases (Figure 2).

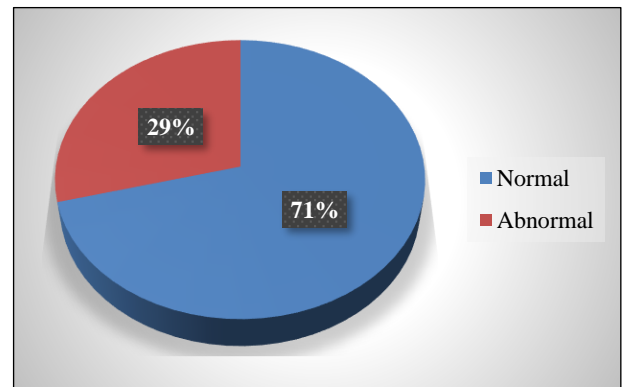
The abnormal EEG pattern was seen in 29% cases of neonatal seizures and the majority 69% of neonates had normal EEG study (Figure 3).

In the present study conducted on EEG, low voltage was observed in 21.5% cases while 7.5% cases had slow

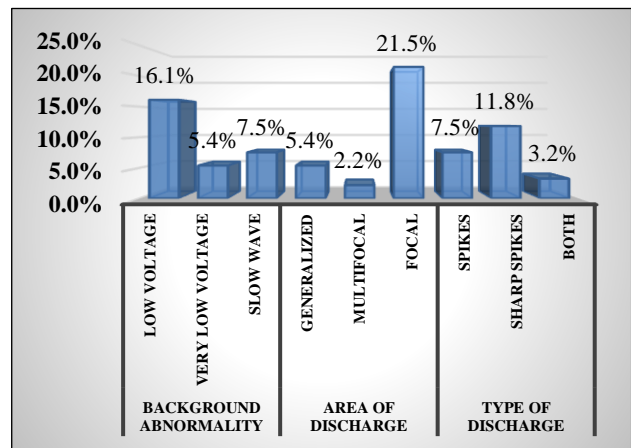
waves. Focal discharge was most commonly observed (21.5%) followed by generalized discharge (5.4%). Sharp spikes were observed in 11.8% cases (Figure 4).



**Figure 2: Distribution of study population based on type of seizures.**



**Figure 3: Distribution of cases as per EEG findings.**



**Figure 4: Distribution of cases as per pattern of EEG findings.**

A significant association was observed between birth asphyxia and meningitis with abnormal EEG patterns ( $p < 0.05$ ). The other factors such as metabolic abnormalities, hyperbilirubinemia, hypoxia and structural

malformations did not show association with p values >0.05 (Table 4).

**Table 4: Association of etiology of seizure with EEG findings.**

Etiology	EEG		Total	p-value
	Abnormal	Normal		
Birth asphyxia	17 38.64%	27 61.36%	44 100.00%	0.046
Metabolic	5 16.67%	25 83.33%	30 100.00%	0.089
Hyperbilirubinemia	1 14.29%	6 85.71%	7 100.00%	0.67
Hypoxia	0 0.00%	2 100.00%	2 100.00%	1.00
Meningitis	3 100.00%	0 0.00%	3 100.00%	0.03
Structural Malformation	0 0.00%	2 100.00%	2 100.00%	1.00
Unknown	1 20.00%	4 80.00%	5 100.00%	1.00
Total	27 29.03%	66 70.97%	93 100.00%	

## DISCUSSION

In the present study conducted it was found that, out of the total 93 neonates with seizures, 60.2% were males while 39.8% were females. These results are in accordance with the studies carried out by Moayed AR et al, in which 64 were male (58.2%) and 46 female (41.8%) and in study carried out by Eghbalian F et al, 25/34 (73.55%) were males and 9/34 (26.5%) were females.<sup>5,6</sup> A similar type of finding was seen in study done by Digra SK et al, in which 72 out of 102 neonates were males and remaining 30 were females.<sup>7</sup> Parvin R et al, in their study observed 76.5% males and 23.5% females in their study of 51 cases.<sup>8</sup> Pre-term delivery occurred in 12 (12.9%) neonates while remaining 81 (87.1%) were term gestation. These results are consistent with other studies like Marzoki J et al, in which 84 out of 88 (95.4%) full term neonates had seizures.<sup>9</sup> Parvin R et al, also observed 80.4% cases as term and 19.6% as pre-term.<sup>8</sup>

Low birth weight was seen in 51 cases (54.9%) while 45.1% neonates had normal birth weight i.e. >2.5 Kg. This was not consistent with other studies like Eghbalian F et al, Digra SK et al, and Marzoki J et al, in which the majority of neonates had the birth weights more than 2.5 kg.<sup>6,7,9</sup> Though this study has majority of full term (81/93) neonates, majority have intra uterine growth retardation which is the reason why being full term they have birth weight less than 2.5 kg.

Most common etiology of neonatal seizures was birth asphyxia (47.3%) followed by metabolic abnormalities

(32.3%). Other etiologies included: hyperbilirubemia (7.5%), meningitis (3.2%), hypoxia (2.2%) and structural malformations (2.2%). No etiology could be identified in 5.4% cases. Out of the 30 cases with metabolic abnormalities, 16 had hypoglycaemia while 12 had hypocalcemia. Two neonates had both hypoglycaemia and hypocalcemia.

In the study by Parvin R et al, half of the neonate had perinatal asphyxia (56.86%), followed by septicemia (15.67%), meningitis (11.76%), neonatal jaundice (kernicterus) (3.92%), neurometabolic disorder (3.92%), TORCH (Rubella infection 1.96%).<sup>8</sup> There were 1.96% neonates whom diagnosis could not be identified. Thirty-five neonates had biochemical abnormalities and most of them had hypoglycemia (19.5%) and hypocalcemia (15.7%). In the study by Kumar A et al, perinatal asphyxia was the most common etiology in pre-term and term babies (39% and 49%) respectively.<sup>10</sup> In another study done by Digra SK et al, birth asphyxia is the most common cause accounting for 67.65% cases followed by infections (septicemia and meningitis). Birth asphyxia was also the commonest cause of neonatal seizures reported by Soni et al, and Ronen et al.<sup>11,12</sup>

Most common type of seizures were tonic (40.9%) and clonic (36.9%) while subtle seizures were present in 22.6% cases. Parvin R et al, found majority of seizures was tonic (45.1%) in nature, followed by subtle seizure (35.3%), clonic (15.35) and mixed type (3.9%).<sup>8</sup> In a study of neonatal seizures by Brunquell J et al, subtle seizures were the commonest occurring in 51% (27 of 53), followed by focal clonic (42%), multifocal clonic (30%) and GTS (23%).<sup>13</sup> Lakra et al, also reported that subtle seizures were the commonest type.<sup>14</sup> But in the study of Soni et al, generalized tonic seizure was commonest type of seizure, followed by subtle seizures.<sup>11</sup>

Abnormal EEG pattern was seen in 29% cases of neonatal seizures. On EEG, low voltage was observed in 21.5% cases while 7.5% cases had slow waves. Focal discharge was most commonly observed (21.5%) followed by generalized discharge (5.4%). Sharp spikes were observed in 11.8% cases.

In a study by Parvin R et al, about half (43.1%) of the EEG findings were abnormal.<sup>8</sup> In background abnormality, 23.5% had low voltage; very low voltage was in 11.8%. In area of involvement of the discharges, it was mostly focal (31.4%). In the type of discharges, sharp spikes (15.7%) and spikes (11.8%) were predominant. Similarly, Kumar A et al, in their study observed abnormal EEG in 26.7% cases of neonatal seizures.<sup>10</sup> Rose and Lombroso and Mizarahi and Kellaway reported abnormalities in standard EEG in HIE in 70% and 46.3% cases respectively.<sup>16</sup>

In present study, a significant association was observed between birth asphyxia and meningitis with abnormal EEG pattern (p<0.05).

In the study by Pravin R et al, there was a statistically significant relationship of meningitis with background abnormality of EEG (low voltage recorded in 12 cases, very low voltage recorded and slow wave voltage recorded in 2 cases each), area of involvement of discharges of EEG (focal in 14 cases, generalized in 2 cases), and type of discharges (spike in 6 cases, sharp spike in 2 cases).<sup>8</sup> There was also a statistically significant relationship between abnormal EEG findings and the perinatal asphyxia of the neonates ( $p < 0.01$ ). Abnormal standard EEGs in meningitis has also been reported in 33.3% cases by Rose and Lombroso and 17% by Mizrahi and Kellaway which were consistent with these results.<sup>15,16</sup>

## CONCLUSION

Present study revealed that the most common aetiology seizures in this series was Birth asphyxia followed by metabolic abnormalities in which hypoglycaemia was the most common type. Males outnumbered females in present study and most common type of seizure was tonic type (focal) followed by clonic and then subtle seizures. A significant association of seizures due to meningitis and metabolic abnormalities was observed with pre-term gestation. A significant association of seizures due to meningitis and metabolic abnormalities was observed with pre-term gestation while abnormal EEG pattern was observed with birth asphyxia and meningitis. EEG findings were found normal in majority of cases of neonatal seizure.

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