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Clinical Profile of Neonatal Seizures Admitted In a Teaching Hospital in North-East India

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Abstract:
Background : *Neonatal seizures are defined as paroxysmal alteration in motor activity, behavior or autonomic function that results from abnormal electrical activity of brain in the neonatal period. Seizures are the most frequent sign of neurological dysfunction in the neonatal period. Seizures during the neonatal period are relatively common, occurring in approximately 1.1 to 8.5 per 1000 live births, with greater frequency in premature or low birth weight babies as compared to term babies.*
Methods: *The aim was to determine the various etiological factors associated with neonatal seizures, describe the clinical profile of neonatal seizures and study the short term outcome. It was a hospital based prospective cross-sectional study conducted in the Department of Pediatrics, RIMS Imphal on 71 neonates with < 28 days of life with seizures.*
Results: *Neonatal seizures were higher in term babies (66.2%) than preterm (33.8%) babies and more common among male (53.5%) neonates as compared to females (46.5%) with male to female ratio of 1.15:1. Most babies were born to primigravida mothers by normal vaginal deliveries (74.7%). Subtle seizures (45%) were the most common type of seizures seen in both term and preterm babies, followed by multi-focal clonic seizures (39.5%). 77.5% of cases had seizures within first 3 days of life and 52.1% cases occurred within 1 day of life. Birth asphyxia was the prominent etiology causing 59.2% of seizure followed by septicaemia (29.6%) and metabolic causes (25.6%) viz – hypoglycaemia and hypocalcaemia.*
Conclusion: *Overall incidence of neonatal seizures was 4.96%, majority being term neonates. Subtle seizure was the predominant type and birth asphyxia was the most frequent cause of seizure followed by septicaemia and metabolic abnormalities. USG cranium findings were found to be abnormal in 3 cases.*
Key words: *Seizures, neonate, term, cranium*

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I. Introduction

Neonatal seizures are defined as paroxysmal alterations in motor activity, behaviour or autonomic function that results from abnormal electrical activity of brain in the neonatal period.[1] Seizures during the neonatal period are relatively common, occurring in approximately 1.1 to 8.5 per 1000 live births, with greater frequency in premature or low birth weight babies as compared to term babies [2] and are usually classified in the following types: subtle, multifocal, focal, clonic, tonic, myoclonic seizures. Subtle seizures are so termed because the clinical manifestations are mild and are often missed and are the commonest type, constituting about 50% of all seizures.[3]

Neonatal seizures are 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. A seizure discharge therefore cannot readily propagate throughout the neonatal brain to produce a generalized seizure.[4] In the newborn, seizures are always due to an underlying cerebral or biochemical abnormality and may have an adverse effect on neurodevelopment and may predispose to cognitive, behavioural or epileptic complications later in life.[5]

The commonest cause of neonatal seizures is perinatal asphyxia, more appropriately termed - Hypoxic ischaemic encephalopathy (HIE), which is an abnormal neurobehavioral state consisting of decreased level of consciousness and other signs of brain stem and/or motor dysfunction and seizures occur in up to 50% of neonates with HIE.[6] The overall mortality rate in perinatal asphyxia is 20% and the frequency of neuro-developmental sequelae in surviving neonates is 30%.[7] Seizures may also occur due to meningitis and meningo-encephalitis secondary to intrauterine infections (TORCH group, syphilis). Intracranial haemorrhages (ICH) - subarachnoid, intraparenchymal or subdural hemorrhage in term neonates and intraventricular hemorrhage (IVH) in preterm neonates contribute to neonatal seizures.[7] Biochemical disturbances e.g. hypoglycaemia,

hypocalcaemia and hypomagnesaemia, occur frequently in neonatal seizures either as an underlying cause or as associated abnormalities and are often underdiagnosed. Other rare causes include pyridoxine dependency and inborn errors of metabolism.[3,8]

This present study was planned to study the various etiological factors, clinical profile and short term outcome of seizures in the neonates < 28 days of postnatal life who were admitted in the Pediatric Ward of Regional Institute of Medical and Sciences (RIMS), Imphal, Manipur in North Eastern India.

II. Materials And Methods

This prospective cross sectional study was conducted in the Pediatric Ward, Regional Institute of Medical Sciences (RIMS), Imphal for two years from October 2015 to September 2017. 71 neonates with seizures who fulfilled the inclusion criteria were taken up for study.

The Inclusion criteria are:

1. Neonates less than 28 days of postnatal life with clinically diagnosed seizures, admitted in Pediatric Ward, RIMS Hospital, Imphal.
2. Neonates who had birth weight ≥ 2000 grams or with gestational age of ≥ 35 weeks.

The Exclusion criteria are:

1. All critically ill neonates viz; severe respiratory distress syndrome, severe meconium aspiration syndrome, with gross congenital abnormalities. with low birth weight i.e. < 2000 gms or gestational age of < 35 weeks.
2. Parents/legal guardians declining consent.

Survey tools included detailed antenatal history, baseline characteristics of convulsive neonate including sex, gestational age, weight, length and head circumference. Clinical details of each seizure episode reported by the mother and subsequently observed by resident doctors on duty were recorded in a pre-designed proforma. Blood samples for complete blood count, sepsis screen, blood glucose, serum - calcium, magnesium, sodium, potassium, and chloride were collected as required. Ultrasonography (USG) cranium and magnetic resonance imaging (MRI) of brain were carried out as per indications. Management of the cases were carried out as per unit protocol. The purpose of the study was explained to the parents and informed consent was taken. Confidentiality and privacy was maintained. Interview in local language using structured questionnaire was done. Data collected was checked for completeness, consistency and after entering in SPSS 21.0 version summarized by using descriptive statistics like mean, percentages and standard deviation. Chi-square test and t-test was employed to test the association. P value of < 0.05 was taken as significant.

III. Results

Table - 1: D**emographic distribution of the neonates**

Parameters		Number	Percentage (%)
Age	< 24 Hr	37	52.1
	24 – 72 Hr	18	25.4
	>72hr – 7 Days	12	16.9
	>7 Days	4	5.6
Gender	Male	38	53.5
	Female	33	46.5
Gestation	Term	47	66.2
	Preterm	24	33.8
Parity	Primigravida	44	62.0
	Multi-gravida	27	38.0
Mode of delivery	Normal vaginal	53	74.7
	Instrumental	4	5.6
	Caesarean section	14	19.7

There were 71 neonates with seizures out of total 1432 admissions during the study period (incidence – 4.96%). Majority of the neonates presenting with seizures were less than 1 day of life (< 24 hours) consisting 52.1% of the cases, 53.5% of neonates were males and 66.2% were term as shown in the table-1.

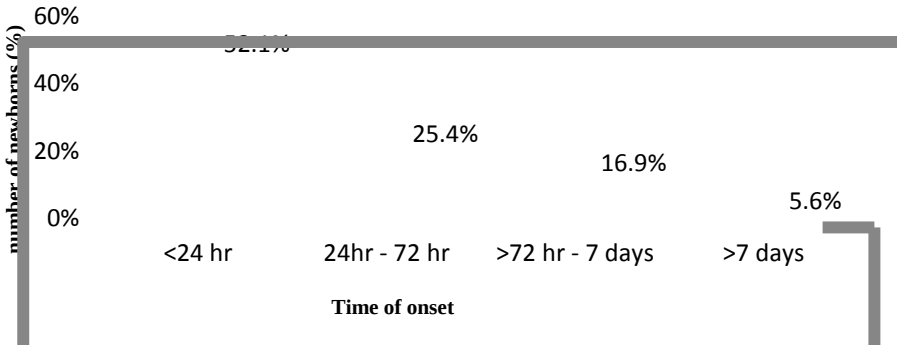


Figure - 1 : D**istribution of the neonates by time of onset of seizure**

Majority of the neonates had seizures on the 1st day of life consisting 37(52.1%) cases, 18(25.4%) cases occurred during 2nd and 3rd day of life and thereafter seizure percentage decreased as the age of the neonate increased as shown in figure-1.

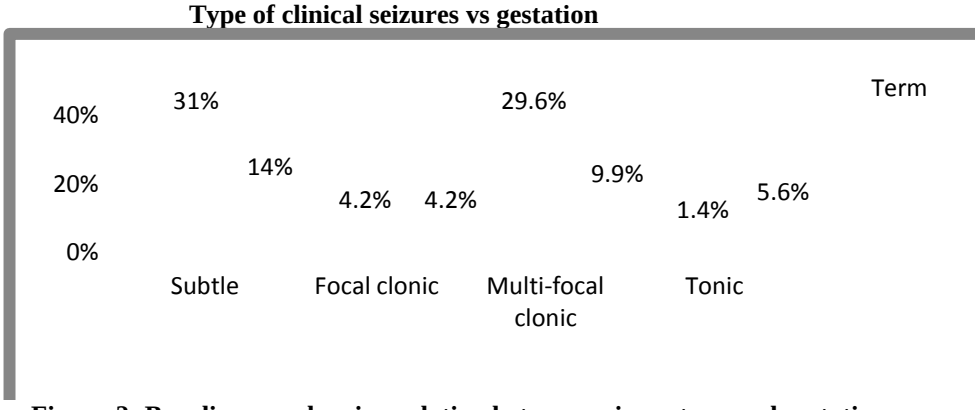


Figure-2: Bar diagram showing relation between seizure type and gestation

About two-third of neonatal seizures were present in term babies (66.2%) and one-third in preterm babies (33.8%). Subtle seizure was common in both term and preterm neonates seen in 32(45.0%) cases, followed by multi-focal clonic seizures being seen in 28(39.4%) cases as shown in figure-2. However, this finding was found to be statistically insignificant (p value - 0.088).

Table – 2: Relation between age of onset of seizure and type of seizure (n=71)

Age of onset	Type of seizure				Total (%)	P value
	Subtle (%)	Focal clonic (%)	Multi-focal clonic (%)	Tonic (%)		
<24 h	22 (59.5)	3 (8.1)	9 (24.3)	3 (8.1)	37 (52.1)	0.00
≥24h to 72 h	7 (38.9)	3 (16.7)	8 (44.4)	0	18 (25.4)	
>72 h to 7 days	1 (8.3)	0	11 (91.7)	0	12 (16.9)	
>7 days	2 (50)	0	0	2 (50)	4 (5.6)	

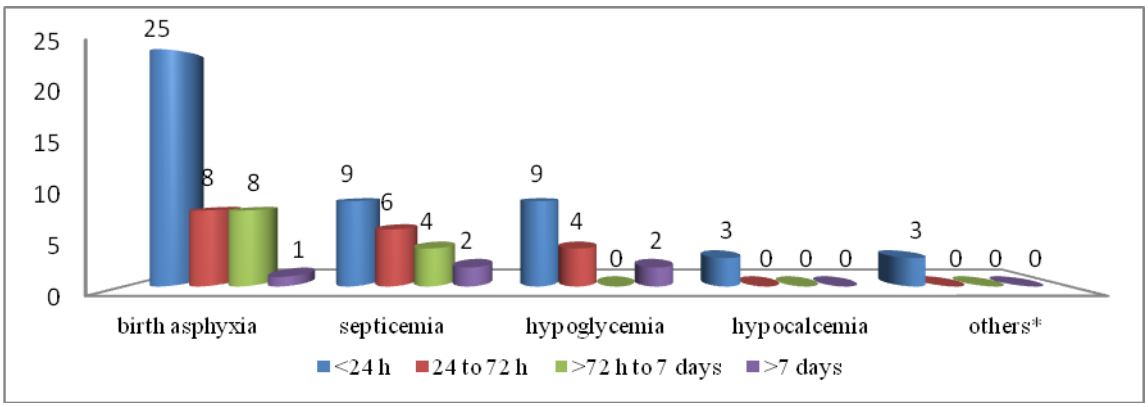
32(45.0%) cases had subtle seizure, followed by 28(39.4%) cases of multi-focal clonic seizure. Most of the seizures (37 cases;52.1%) started within 1 day of life (< 24 hours), with 22 neonates (59.5%) having subtle seizures and more than 70% occurred within 3 days of life as shown in table 2. This finding was found to be statistically significant with p value < 0.05.

Table-3: Distribution of the neonates by etiological-biochemical factors

Etiologies	Number of neonates	Percentage (%)
Isolated birth asphyxia	30	42.3
Birth asphyxia +sepsis	3	4.2
Birth asphyxia+ hypoglycaemia	2	2.8
Birth asphyxia+ hypocalcaemia	1	1.4
Birth asphyxia+sepsis+ hypoglycaemia	2	2.8
Birth asphyxia+sepsis+ hypoglycaemia+ hypocalcaemia	1	1.4
Birth asphyxia+ others*	3	4.2
Isolated sepsis	11	15.5
Sepsis + hypoglycaemia	3	4.2
Sepsis + hypocalcaemia	1	1.4
Isolated hypoglycaemia	7	9.9
Unknown	7	9.9

*Intracranial haemorrhage, ventriculomegaly, hydrocephalus

Table-3 shows that isolated birth asphyxia was the most common cause of neonatal seizures (42.3%), followed by isolated sepsis (15.5%).



*Intracranial haemorrhage, ventriculomegaly, hydrocephalus *p value > 0.05

Figure – 3: Bar diagram showing relation between etiology and time of onset of seizure

In majority of the cases, seizures started in the first day of life. 25(67.6%) of cases were associated with birth asphyxia, 9(24.3%) with infections and 9 (24.3%) with hypoglycaemia. Figure - 3 shows that seizures also occurred within 24 hours of life associated with other uncommon causes viz – hypocalcaemia, intraventricular haemorrhage, ventriculomegaly and hydrocephalus.

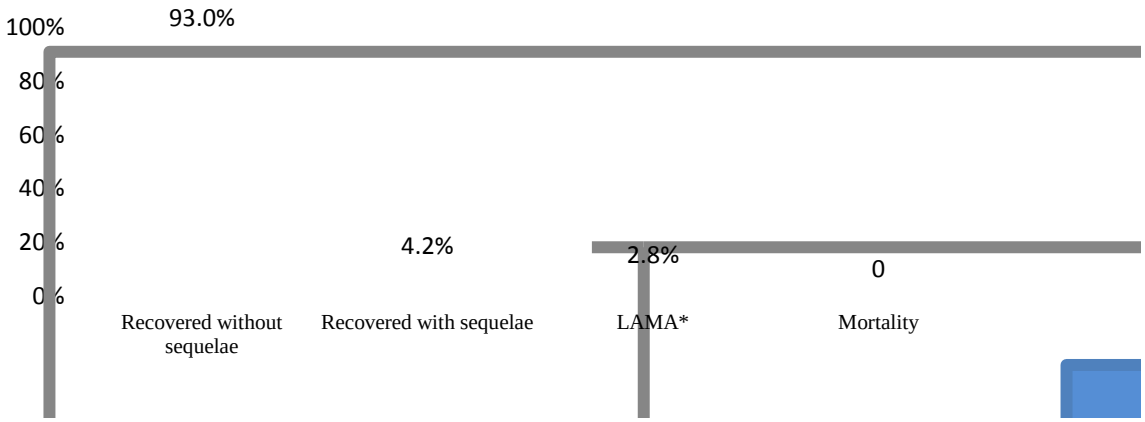


Figure - 4: Bar diagram showing outcome of the neonates

66(93%) neonates with seizures recovered with no abnormality; 3(4.2%) cases recovered with abnormality/sequelae and 2(2.8%) cases were discharged against medical advice as shown in figure - 4.

IV. Discussion

The total number of newborns admitted during the study period was 1432 with an incidence of 4.96%. Similar findings were observed by Khan M *et al*,[9] Aziz A *et al*[10] and Asindi AA *et al*[11] where incidence rates were 3.54%, 3.9% and 4.1% respectively. There were 47(66.2%) term and 24(33.8%) preterm neonates in the present study, comparable to a study by Aziz A *et al*[10] where 65% of neonates were terms and 35% preterms. Our finding might be attributed to patient enrolment characteristics and also due to high incidence of perinatal asphyxia, which is a more common cause of seizure in term newborns rather than preterms in whom interventricular hemorrhage and infections are the most frequent causes.[12]

In this study, seizure was observed in 38(53.5%) male neonates and 33(46.5%) female neonates with male to female ratio of 1.15:1 which was also observed by Tekgul H *et al*.[13] 53(74.7%) neonates were born normally, 4(5.6%) by instrumental delivery and 14(19.7%) born by caesarean section and most of the newborns were born to primigravidas (62%) and 38% to multi-gravida mothers (Table - 1). Onset of seizures on first day of life was seen in 37(52.1%) neonates. On second and third day of life, 18(25.4%) neonates developed seizures. The first three days of life together constituting the maximum cases (77.5%) of neonatal seizures ($p < 0.00$). Nawab *T et al*[14] had also found the correlation of day of onset (first three days of life) of convulsions with types of neonatal seizures to be statistically highly significant ($P < 0.05$). Seizures percentage decreased as age of the neonate increased (Figure-1) and late onset seizures (> 7 days of life) accounted only 5.6% cases. Kumar A *et al*[8] had also reported that 75% of the episodes occurred before 3rd day of life. Subtle seizure was the commonest seizure type observed in this study occurring in 45% of neonates; multi-focal clonic – 39.5%, focal clonic – 8.5% and tonic – 7% were the other seizures. Similar results were found by others.[15,16] Subtle seizures are often mild and easily missed and here is usually mild paroxysmal alteration in motor, behavior and autonomic function.[7] None of the babies had myoclonic seizures.

Birth asphyxia was the most common cause of seizures observed in our study accounting for 59.2% of neonates (Table – 3). Isolated cases of birth asphyxia were found in 30(42.5%) cases, associated with sepsis and hypoglycemia in 3(4.2%) and 2(2.8%) cases respectively. Similarly, Wagh SS *et al*[17] reported that birth asphyxia accounted for 61(46.2%) cases of seizures either alone or in combination with other etiologies. Isolated HIE was seen in 35(26.5%) cases and associated with sepsis in 16(12.1%) cases as also reported by others.[8, 18] Birth asphyxia alongwith sepsis, hypoglycaemia and hypocalcaemia were found in varying proportions (Table – 3). Isolated sepsis was seen in 11(15.5%) cases. Most of the mothers of the babies with sepsis had history of premature or prolonged rupture of membrane before hospitalization which might have contributed towards the incidence of septicemia. Wagh SS *et al*[17] also reported isolated sepsis in 32(24.2%) cases, 18(13.6%) cases associated with birth asphyxia and hypoglycaemia. There were 18(25.4%) neonates with metabolic abnormalities including hypoglycemia and hypocalcaemia. Hypoglycemia, alone or in association with others contributed to 15(21.1%) of the cases. This finding was not significant ($p > 0.05$). Sood A *et* al[18] and Malik BA *et al* [19] demonstrated that hypocalcaemia and hypoglycemia were the most common metabolic abnormalities, and this trend was also observed in our study as shown in Table - 3 and Figure - 3.

Ultrasonography (USG) cranium was conducted on affected newborns and 3(4.2%) neonates had abnormal findings, each with intracranial haemorrhage, ventriculomegaly and hydrocephalus. 66(93%) neonates recovered with no abnormalities or sequelae; 3(4.2%) cases were discharged with sequelae and 2(2.8%) left against medical advice. In a study conducted by Alyasiri AA *et al*,[20] 69(56.6%) neonates got discharged without sequelae; 32(26.2%) had neurological sequelae and 21(17.2%) died. The non-observance of mortality in our study may be due to the exclusions of all severely ill neonates or hemodynamically unstable neonates.

There are certain limitations in the present study. The exclusion of early preterms precludes a better understanding of seizure pattern in these babies. The inclusion of neonates based on clinical criteria without supportive electroencephalogram evidence is another limitation. A larger study with long-term follow up of affected neonates with better neuro-imaging facilities will be of immense benefit in better understanding of neonatal seizures and their management.

V. Conclusion

Seizures are one of the commonest causes of neonatal morbidity and mortality. Birth asphyxia followed by infections and metabolic abnormalities are the main etiological factors. Meticulous care of the expectant mothers, initiating with good antenatal and perinatal care, alongwith careful monitoring and observation of high risk neonates will be helpful in prognosis and treatment.

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