

Profile and Short Term Outcome of Seizures in Term Neonates

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ABSTRACT

Introduction: Neonatal seizures are common neurological problem and they are often the first sign of neurological dysfunction. Neonatal seizure carries a high risk of mortality as well as neurological impairment/epilepsy in later life. Common causes include hypoxic-ischemic encephalopathy, meningitis, hypoglycemia, hypocalcemia etc. **Study aimed** to study the clinico-aetiological profile & short term outcome of neonatal seizure in term neonates.

Material and methods: We conducted this observational study in NICU of NMCH, Patna over 1 year period from June 2019 to May 2020 including term neonates of less than 1 month age with seizure who stayed for >24 hours. Parameters studied were risk factors, seizure type, time of onset of seizure & short term outcome.

Results: Of the 81 neonates studied, male: female ratio was 1.25:1. Mean gestational age was 38.9±1.3 weeks and mean admission weight was 3.12±0.52 Kg. Perinatal asphyxia was the commonest risk factor (46.9%) followed by septicemia-meningitis (32.1%) and metabolic disturbances (32.1%). Subtle seizure was the commonest seizure type (37.2%) followed by clonic seizures (36.1%). 66% of the events were reported before 72 hours of age. In neonates with seizure, mortality was 28.4% and mean duration of hospital stay was 8.4± 2.7 days. There was a significant increase in duration of hospital stay and delay in commencement of oral feeds without 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 neonatal seizure cases. Subtle seizures were the commonest seizure type. Majority of seizures occurred within 72 hours of life. Occurrence of seizure in term neonate significantly increases duration of hospital stay and delays the commencement of oral feeds without increasing mortality.

Keywords: Hypoxic Ischemic Encephalopathy, Neonatal Seizure, Term Neonates, Seizure Type.

INTRODUCTION

Neonatal seizure (NS) is defined as a paroxysmal alteration in neurological function i.e. motor, behavior and/or autonomic function¹ in infants less than 4 weeks of age. Neonatal seizure is a common neurological problem, infant 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.² 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 and often subtle.

Seizures in newborn are different from those in older children.³ Common causes of neonatal seizures include hypoxic-ischemic encephalopathy, intracranial hemorrhage, meningitis, hypoglycemia, hypocalcemia, congenital malformation etc. Neonatal seizure carries a high risk of mortality as well as neurological impairment/epilepsy disorders in later life.⁴ With advances in neonatology, mortality from NS has decreased considerably from 40% to about 20% over the years, but occurrence of long-term neurodevelopment problems hasn't changed much and hovers around 30%.⁵ This can be partly due to delay in diagnosis as well as improper and inadequate management of seizures.

Based on this background and considering the frequent occurrence of this entity at our tertiary care level teaching hospital, we intended to conduct this study for better understanding of the clinico- etiological profile of neonatal seizures. As we cater to sick term neonates referred from nearby districts, we decided to include only term neonates in the present study.

Study aimed to study the clinico-aetiological profile & short term outcome of neonatal seizure in term neonates with the objectives to study clinical profile and risk factors for seizures in term neonates, to characterize the type of seizures in them and to study time of onset of seizures and short term outcome of seizures in these neonates.

MATERIAL AND METHODS

Hospital based prospective observational study was done in N.I.C.U of deptt of Pediatrics N.M.C.H Patna for 1 year, from June 2019 to May 2020.

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 obvious

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congenital malformation were excluded from the present study.

Study technique: After obtaining written informed consent, we enrolled cases in this study. All cases were subjected to thorough physical and neurological examination and focused history taking from guardians. Information so obtained and data regarding 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 (serum glucose <45mg/dl), hypocalcemia (total serum Calcium <7mg/dl), hypomagnesemia (serum magnesium levels < 1.5 mg/dl), hypernatremia (serum sodium >150 meq/dl), hyponatremia (serum sodium <130 meq/dl), hypokalemia (serum potassium <3.5 meq/dl), hyperkalemia (serum potassium >5.5 meq/dl), hyperphosphatemia (serum phosphorus >8 mg/dl) etc. X-ray chest, X-ray skull, 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.

Etiology of seizures	Number of patients	Percentage
HIE 2	30	37.1
HIE 3	8	9.8
Septicemia and meningitis	26	32.1
Hypocalcemia	11	13.6
Hypoglycemia	9	11.1
Hyponatremia	6	7.4
Hyperbilirubinemia kernicterus	2	2.5
Unknown	2	2.5
(13 neonates had more than 1 risk factor for their seizures)		

Table-1: Profile of risk factors for neonatal seizures:

STATISTICAL ANALYSIS

Pertaining data 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.

RESULTS

Incidence of NS was 18.6% in term neonates admitted in our NICU. Out of the 81 neonates in the study, 36 (44.4%) were female and 45(55.5%) were male. Mean GA was 38.9 weeks, SD 1.3 weeks and mean admission weight was 3.12 Kg, S.D 0.52 Kg. Out of them 48 (59.25%) were referred to us from peripheral institutions (outborn), while 33(40.7%) neonates were born in our institution (inborn).

Among the 81 neonates studied, perinatal asphyxia was the commonest risk factor for neonatal seizure (n=38, 46.9% of neonates). Among these HIE neonates, HIE stage -2 was seen in 37.1% (n =30) and HIE stage-3 was seen in 9.8% (n=8). Second to HIE was septicemia- meningitis (n=26, 32.1%). Other causes include- hypocalcemia (n=11, 13.6%), hypoglycemia (n=9, 11.1%), hyponatremia (n=6, 7.4%), hyperbilirubinemia kernicterus (n=2, 2.5%) and unknown

Type of seizure	Number of events	Percentage
Subtle seizures	35	37.2%
Focal clonic seizures	19	20.2%
Multifocal clonic seizure	15	15.9%
Myoclonic seizures	14	14.9%
tonic seizures	11	11.7%
(9 neonates had more than 1 clinical type of seizure during their hospital stay)		

Table-2: Clinical type of neonatal seizure:

Age of onset of Seizure	Etiology of Seizure	Number	Percentage
Less than 12 hr of life (Total no. of events=27)	HIE	21	22.3%
	Hypoglycemia	3	3.2%
	Hypocalcemia	3	3.2%
12 to 24 hr of life (Total no. of events= 23)	HIE	14	14.9%
	Septicemia- Meningitis	2	2.1%
	Hypoglycemia	2	2.1%
	Hypocalcemia	3	3.2%
	Hyponatremia	2	2.1%
24 to 72 hr of life (Total no. of events= 12)	HIE	3	3.2%
	Septicemia- Meningitis	6	6.4%
	Hypoglycemia	1	1.1%
	Hyponatremia	1	1.1%
	Hypocalcemia	1	1.1%
More than 72 hrs (Total no. of events= 32)	Hypocalcemia	4	4.2%
	Hyponatremia	3	3.2%
	Hypoglycemia	3	3.2%
	Septicemia- meningitis	18	19.1%
	Kernicterus/Bilirubin encephalopathy	2	2.1%
	Unknown cause-2	2	2.1%

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

Sl No.	Parameter studied	Term neonates with seizure (n=81)	Term neonates without seizure (n=354)	P value
01	Mortality	28.4%	23.1%	0.31
02	Hospital stay (days)	Mean 8.4, SD 2.7	Mean 7.5, SD 2.4	0.003
03	Ventilator support	15.1%	21.6%	0.19
04	Inotrope support	12.5%	14.1%	0.70
05	Enteral feeds starting after admission (days)	Mean 6.1, SD 2.3	Mean 5.2, SD 1.9	0.0003

Table-4: Univariate analysis of short term outcome

(n=2, 2.5%) (table-1).

Clinical type of neonatal seizures: Overall, there were 94 instances of neonatal seizures. The most common type of seizure was subtle seizures (n=35, 37.2%), followed by focal clonic seizures (n=19, 20.2%), multifocal clonic seizures (n=15, 15.9%) and myoclonic seizure (n= 14, 14.9%). The least common type of seizures was tonic seizures (n= 11, 11.7%) (table-2).

Time of presentation of seizures: Of the 94 events of neonatal seizures studied in these 81 neonates, 27(28.7%) events of NS occurred before 12 hours of life, 23(24.5%) between 12 hours to 24 hours of life, 12(12.8%) between 24 hours to 72 hours of life and 32(34%) after 72 hours of life. Overall, 62 events (66.%) were reported before 72 hours of age and the rest 32 (34%) were reported after 72 hours of age (table-3).

Outcome: In neonates with seizure, mortality was 23 (28.4%), mean duration of hospital stay was 8.4 days (SD= 2.7 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).

DISCUSSION

Seizures are usually the first indicators of 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.⁶ 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 (37.2%) followed closely by clonic seizures (36.1%) while tonic seizures were the least common (11.7%). Silverstein et al.⁷ showed subtle seizures as the commonest type of fits occurring in approx 50% of neonates which is only slightly higher than our findings. Moreover, the comprehensive work of Mizrahi et al⁸ and Scher et al⁹ also reports subtle seizures as the most common type of neonatal seizures.

In our study 62 (66%) of seizures presented within the first

72 hours of life and most of them could be attributed to birth asphyxia (61.3% of these events). Rose et al¹⁰ also found early onset seizures in 50.33% babies whereas Coen RW et al¹¹ found that 81% of babies had early onset seizures. In a study done by Ajay at 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.¹² These are in agreement to our findings and emphasizes the need to be more vigilant during the early hours of life of a neonate, more so when dealing with sick neonates.

In our study most common risk factor for neonatal seizure was perinatal asphyxia (46.9% neonates), followed by sepsis-meningitis in 32.1% neonates. Metabolic disturbances (hypoglycemia, hyponatremia, hypocalcemia) were also seen in 32.1% neonates. In a study done by Sahana et al¹³ on clinical profile of neonatal seizures in 109 neonates, 63 had perinatal asphyxia as the major common etiology (57.80%), second major common etiology was infection (14.67%). In another study, Shah et al¹⁴ showed that the major etiology of seizures were birth asphyxia(44%), septicemia (11%), meningitis (11%), hypocalcemia (11%), and hypoglycemia (22%). These figures correlate with our findings and reiterate the high burden of neonatal seizures in asphyxiated neonates which require prompt recognition and management of seizures to improve the outcome of these unfortunate neonates.

We also studied the short term outcome of such neonates and compared it 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 increase in mortality, need of ventilator support or inotrope support in such neonates. This however may be explained by the higher proportion of asphyxiated neonates in seizure group who require more interventions owing to their perinatal depression.

Limitations

First limitation is inherent in the study design, 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 couldn't be reported. Third, we couldn't do long term follow up of these neonates.

CONCLUSION

Hypoxic ischemic encephalopathy was the commonest etiology in our study, followed by sepsis-meningitis. Together, these two problems are accountable for approximately 75%

of total neonatal seizure cases. Subtle seizures were the commonest clinical type of seizure which can be easily missed by untrained eyes. Most of the neonates developed seizure within 72 hours of life. Relatively earlier presentation 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.

Abbreviations

GA: Gestational age; HIE: Hypoxic ischemic encephalopathy; NS: neonatal seizure; NICU: neonatal intensive care unit; SD: standard deviation;

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