

ORIGINAL RESEARCH

The etiology, clinical type and short outcome of neonatal seizures in term babies at tertiary care hospitalSudesh Singh¹, Rohit Chib²

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ABSTRACT

Background: The outcome of neonates with neonatal seizures has changed in recent years due to improved prenatal care, better obstetrical care and intensive neonatal care. Neonates with seizures are at an increased risk of mortality, and the survivors are at risk of neurological sequelae as developmental delay, epilepsy and cognitive impairment. Present study was aimed to study etiology, clinical type and short outcome of neonatal seizures in term babies at tertiary care hospital. **Material and Methods:** Present study was retrospective observational study, conducted in neonates admitted with diagnosis of neonatal seizure (Clinically apparent convulsions, history of convulsions or who developed convulsions during hospitalization), admitted in NICU. **Results:** Among 74 cases, majority of neonates were born to mothers of 21-25 years age (37.84 %) & 26-30 years age (32.43 %), were male neonates (56.76 %), had gestational age 37-40 weeks (55.41 %), had birthweight of 2.5-4 kg (51.35 %) & were delivered vaginally (71.62 %). Among majority of neonates common type of seizure was subtle seizures (47.3 %) followed by focal clonic type (24.32 %), generalised tonic (13.51 %), multifocal clonic (8.11 %), myoclonic (4.05 %) & focal tonic (2.7 %). Among neonates with seizures, common etiology noted was birth asphyxia/hypoxic ischemic encephalopathy (29.73 %) followed by hypoglycemia (17.57 %), septicemia (17.57 %), hypocalcemia (10.81 %) & 11 neonatal seizures were of idiopathic etiology (14.86 %). Majority neonates were discharged uneventfully (82.43 %) while 4 neonates (5.41 %) took discharge against medical advice. Mortality was noted in 12.16 % (majority had septicemia/ intraventricular hemorrhage, with low birth weight). **Conclusion:** Birth asphyxia/hypoxic ischemic encephalopathy, hypoglycemia, septicemia & hypocalcemia were major causes of neonatal seizures. Common clinical type was subtle seizure and short outcome was good of neonatal seizures.

Keywords: neonatal seizure, birth asphyxia, hypoglycemia, septicemia.

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INTRODUCTION

A seizure is defined as paroxysmal electrical discharge from the brain which may manifest as motor, sensory, behavioral, or autonomic dysfunctions.¹ The neonatal central nervous system

is particularly susceptible to seizures due to a combination of enhanced excitability, and low levels of the inhibitory neurotransmitter gamma amino butyric acid (GABA).²

The outcome of neonates with neonatal seizures has changed in recent years due to improved prenatal care, better obstetrical care and intensive neonatal care.³ Neonatal seizures are clinically significant as they may be suggestive of an underlying disorder or primary epileptic condition. The occurrence of seizure may be the first indication of a neurological disorder, and the time of onset of seizure has a relationship with the etiology of seizures and prognosis.³

Several prognostic factors for adverse outcome of seizure are well known, namely brain immaturity, abnormal cranial ultrasonography (USG) findings, low Apgar score, early onset of seizure or prolonged duration of seizure. Neonates with seizures are at an increased risk of mortality, and the survivors are at risk of neurological sequelae as developmental delay, epilepsy and cognitive impairment.^{5,6} Present study was aimed to study etiology, clinical type and short outcome of neonatal seizures at tertiary care hospital.

MATERIAL AND METHODS

Present study was retrospective observational study, conducted in department of Paediatrics, at Government medical college & hospital, Kathua, India. Study duration was of 10 months (from 1st January to 31st October 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Term neonates admitted with diagnosis of neonatal seizure (Clinically apparent convulsions, history of convulsions or who developed convulsions during hospitalization), admitted in NICU.

Exclusion criteria

- Preterm neonates,
- Seizures occurring after 1 month of age,
- Neonates with obvious congenital malformation e.g., anencephaly, large occipital meningocele, microcephaly, multiple malformations, dysmorphic features with “syndromic appearance”, etc.

All maternal & neonatal details were retrieved from case records. Detailed antenatal history (maternal age, past medical history, parity, gestational age, history of illness during pregnancy, medication during pregnancy), afterbirth events such as, any evidence of fetal distress, Apgar score, type of delivery and medication given to mother during delivery were noted. Baseline characteristics of convulsing neonate (sex, gestational age, anthropometry), clinical details of each seizure episode (age at onset of seizures, duration of seizure, number and type of seizure) were recorded. Type of seizure (subtle, focal clonic, multifocal clonic, tonic, myoclonic) was noted.

Investigations such as blood glucose, total serum calcium levels, Na⁺, K⁺, and magnesium, complete blood counts, blood culture, USG cranium, MRI/CT, and CSF analysis were noted. Treatment details, clinical course & outcome was noted. Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS

Total admissions from 0 to 28 days of life in NICU during 10 months were 940. Out of 940 babies admitted to NICU 74 had to be studied for seizures. Majority of neonates were born to mothers of 21-25 years age (37.84 %) & 26-30 years age (32.43 %), were male neonates (56.76 %), had gestational age 37-40 weeks (55.41 %), had birthweight of 2.5-4 kg (51.35 %) & were delivered vaginally (71.62 %). Among majority of neonates common type of seizure

was subtle seizures (47.3 %) followed by focal clonic type (24.32 %), generalised tonic (13.51 %), multifocal clonic (8.11 %), myoclonic (4.05 %) & focal tonic (2.7 %).

Table 1: General characteristics

Characteristics	Number of patients	Percentage
Maternal Age (years)		
≤20	7	9.46
21-25	28	37.84
26-30	24	32.43
31-35	11	14.86
>35	4	5.41
Neonatal gender		
Male	42	56.76
Female	32	43.24
Gestational age (weeks)		
34-37	27	36.49
37-40	41	55.41
>40	6	8.11
Birth weight		
< 2.5 kg	31	41.89
2.5 – 4 kg	38	51.35
>4 kg	5	6.76
Mode of delivery		
Vaginal (vertex)	53	71.62
Lower segment caesarean section	18	24.32
Instrumental	3	4.05
Type of seizures		
Subtle	35	47.3
Focal clonic	18	24.32
Generalized tonic	10	13.51
Multifocal clonic	6	8.11
Myoclonic	3	4.05
Focal tonic	2	2.7

Among neonates with seizures, common etiology noted was birth asphyxia/hypoxic ischemic encephalopathy (29.73 %) followed by hypoglycemia (17.57 %), septicemia (17.57 %), hypocalcemia (10.81 %), intraventricular hemorrhage (4.05 %), kernicterus (2.7 %), hypercalcemia & hypomagnesemia (1.35 % each). In present study 12.93 % neonates had idiopathic etiology (9.5 %). We noted that 11 neonatal seizures were of idiopathic etiology (14.86 %).

Table 2: Suspected etiology

Etiology	Number of patients	Percentage
Birth asphyxia / HIE	22	29.73
Hypoglycemia	13	17.57
Septicemia	13	17.57
Idiopathic	11	14.86
Hypocalcemia	8	10.81
Intraventricular hemorrhage	3	4.05

Kernicterus	2	2.7
Hypercalcemia	1	1.35
Hypomagnesemia	1	1.35

Majority of neonates responded to phenobarbitone alone (81.08 %) followed by Phenobarbitone & Phenytoin combination (16.22 %), while 2 neonates required combination of Phenobarbitone + Phenytoin + Levetiracetam (2.7 %). Additionally, dextrose (17.57 %) & calcium gluconate (10.81 %) were used to treat hypoglycemia & hypocalcemia respectively.

Table 3: Pharmacological treatment

Pharmacological Treatment	Number of patients	Percentage
Phenobarbitone	60	81.08
Phenobarbitone + Phenytoin	12	16.22
Phenobarbitone + Phenytoin + Levetiracetam	2	2.7
Dextrose	13	17.57
Calcium	8	10.81

Majority neonates were discharged uneventfully (82.43 %) while 4 neonates (5.41 %) took discharge against medical advice. Mortality was noted in 12.16 % (majority had septicemia/ intraventricular hemorrhage, with low birth weight).

Table 4: Neonatal outcome

Outcome	Number of patients (n= 116)	Percentage
Discharge	61	82.43
Mortality	9	12.16
Discharge against advice	4	5.41

DISCUSSION

The fundamental mechanisms of neonatal seizures are generally unknown, disturbance in energy production can result in a failure of Na⁺/ K⁺ pump. In addition to these cellular factors, differential development of neural systems may enhance the excitatory state of the immature brain and predispose to seizures. Other suggested mechanisms of injury include effects of nitric oxide synthase inhibition on cerebral circulation, which then contributes to ischemic injury.⁷

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.⁸ Neonates with seizures are at risk of death, whereas survivors are at risk of neurological sequelae, developmental delay, later epilepsy and cognitive impairment so, we need to initiate an early diagnostic work up to determine the causes, depending upon the facilities available.⁹

Abhishek CK et al., studied 81 neonates, 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.

Nair BK et al.,¹¹ studied 75 neonates admitted with neonatal seizure, 49 (65.33%) were male and 26 (34.60%) were female. Majority (52, 69.93%) were term babies. Subtle seizures (39.13%) were most common in both preterm babies (39.13%) and term (53.85%) babies. Age of onset was <24 h of life in 53.33% of the babies. Hypoxic- ischemic encephalopathy (HIE) was the most common cause (52%) of neonatal seizure.

Agrawal V et al.¹² studied 100 cases, majority of neonates had onset of seizure <3 days (<72 hours) 53% and remaining 47% neonates had onset of seizure >3 days (>72 hours). Most common type of neonatal seizure was subtle(75%), other types were tonic seizure (17.3%), clonic seizure (5.1%) and least common type was myoclonic (2.5%). Most common cause of neonates seizure noted was birth asphyxia (73%) second common cause is pyomeningitis and third common cause is hypoglycaemia. Most common cause of neonatal seizure both in full term (71.17%) and preterm (25%) is birth asphyxia. Second most common cause of neonatal seizure in full term is pyomeningitis (8.70%) and in preterm is pyomeningitis and hypoglycaemia (25%). Most common cause of neonatal seizure both in onset of seizure <3 days (<72 hours) 53% and in onset of seizure >3 days (>72 hours).

Dagar J et al.,¹³ studied 2990 neonates admitted, 87/2990 (2.9%) neonates had episodes of neonatal seizure. Out of 87 cases, 55 were male and 32 were female. Commonest type of seizures observed in this study were subtle (51.82%) followed by Clonic (48.92%), tonic (36.09%) and myoclonic (6.14%). The most common aetiology was perinatal asphyxia (54.02%), followed by metabolic disturbances (19.54%), infections (19.54%) and intra 77.01% (67/87) cases of neonatal seizures recovered completely. 5.74% (5/87) were lost during study (discharged against medical advice) and 17.24% (15/87) of cases of neonatal seizures expired.

Chesti MS et al.,¹⁴ studied 80 neonates with seizures, among them 48 were males and 32 were females. Majority of neonates (57.5%) developed seizures during first 72 hours of life due to birth asphyxia. Commonest types of neonatal seizures observed in our study were subtle observed in 46 cases, followed by tonic (21.2 %), clonic (14.9 %) and mixed (6.2%) seizures. Birth asphyxia was commonest cause (57.5%) of NNS, sepsis with meningitis (18.7%) followed by hypoglycemia (13.7%) and hypocalcemia (5%). Cases of birth asphyxia were associated with higher mortality (58.3%) as compared to cases with metabolic seizures.

Early identification of at risk delivers, institutional delivery with timely resuscitation is required to reduce morbidity and mortality related to neonatal seizure. Knowledge regarding most common organism causing neonatal sepsis and their antimicrobial resistance pattern is mandatory to choose most appropriate first line antibiotic, So that early diagnosis and treatment will lead to decrease morbidity and mortality due to neonatal sepsis. There are certain risk factors for emergence of antimicrobial resistance, such as irrational use of broad-spectrum antibiotics, poor infection control practice, lack of antibiotics stewardship policy, lack of nurse patient ratio and overcrowding.^{15,16} Hence, in any NICU, it is very essential to have annual review to define the current bacteriological profile and their sensitivity pattern.

Limitations of present study were retrospective nature of study, unavailability of video EEG, ictal EEG, and seizure semiology confirmation was lacking in this study. Also, details of other causes contributing for seizures like inborn error of metabolism could not be specified due lack of investigations. We recommend large sample, multicentric studies for better understanding of this crucial topic.

CONCLUSION

Birth asphyxia/hypoxic ischemic encephalopathy, hypoglycemia, septicemia & hypocalcemia were major causes of neonatal seizures. Common clinical type was subtle seizure and short

outcome was good of neonatal seizures. Early identification and treatment are likely important for long-term outcomes in acute symptomatic seizure.

REFERENCES

1. Mikati M, Kliegman R, Behrman R, Stanton B. Nelson Textbook of Paediatrics. 19th ed. Philadelphia: WB Saunders; 2011
2. Jin S.Hahn, Donald M.Olson,"Etiology of neonatal seizures", Neo Reviews, 2004; 5(8):327.
3. Arpino C, Domizio S, Carrieri MP, Brescianini S, Sabatino G, Curatolo P. Prenatal and perinatal determinants of neonatal seizures occurring in the first week of life. *J Child Neurol.* 2001;16(9):651-6.
4. Sankar MJ, Agarwal R, Aggarwal R, Deorari AK, Paul VK. Seizures in the newborn. *Indian J Pediatr* 2008;75:149- 55.
5. Silverstein FS, Jensen FE. Neonatal seizures. *Annals of neurology.* 2007 Aug;62(2):112-20.
6. van der Heide MJ, Roze E, van der Veere CN, ter Horst HJ, Brouwer OF, Bos AF. Long-term neurological outcome of term-born children treated with two or more anti-epileptic drugs during the neonatal period. *Early human development.* 2012 Jan 1;88(1):33-8.
7. Takei Y, Takashima S et al. Effects of nitric oxide synthase inhibition on the cerebral circulation and brain damage during kainic acid induced seizures in newborn rabbits. *Brain Dev* 1999; 21: 253-259.
8. Kumar A, Gupta A, Talukdar B. Clinico-etiological and EEG profile of neonatal seizures. *Indian J Pediatr.* 2007;74:33-7.
9. World Health Organization, "Guidelines on neonatal seizures", Italy -Villaggio Cristo Redentore srl, 2011.
10. Abhishek CK, Jha G, Singh BK, Kumar S. Profile and short term outcome of seizures in term neonates. *International Journal of Contemporary Medical Research* 2020;7(12):L1-L4.
11. Nair BK, Sharma J, Chaudhary S. Clinicoetiologiical profile of neonatal seizure in a newborn care unit of a tertiary care teaching hospital in Northern India. *J Clin Neonatol* 2020;9:27-31.
12. Agrawal V, Bagri DR, Sharma J.N., Singh R. Clinico-aetiologiical profile and Outcome patterns of neonatal seizures at a tertiary care centre. *Int J Contemp Pediatr* 2020;7:316-20
13. Jaiom Dagar, Suryakant Ingale, Chandershekhar Aundhakar, Allapa Koppad, Siddharth Singh. Etiology and outcome of neonatal seizures in NICU, KIMS, Karad 1. *International Journal of Recent Trends in Science and Technology*, September 2015; 6(2): 344-347
14. Chesti MS, Shahzad N, Chaman S, Gazala S. Clinical profile, etiology, type and outcome of neonatal seizures: a hospital-based study. *Int J Contemp Pediatr* 2022;9:104-8.
15. Bhat YR, Lewis LE, Vandana KE. Bacterial isolates of early onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: An audit from a center in India. *Ital J Pediatr.* 2011;37:32.
16. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicaemia and antibiotic susceptibility pattern of the isolates. *J Nat Sci Biol Med.* 2013;4(2):306-09.