



A study of Clinicoetiology & Outcome of Neonatal Seizure in NICU in HI-Tech Medical College & Hospital, Bhubaneswar

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Abstract

Background: Seizures are the most important indicator of significant neurological dysfunction in neonatal period. The incidence of neonatal seizure in India is around 1.8-3.5/1000 live births. The clinical diagnosis of neonatal seizure is very challenging as a high proportion of these seizures are subclinical. Without early diagnosis and treatment they lead to death and poor neurodevelopmental outcomes.

Objective: To identify different types of neonatal seizures and to determine the natural history, etiology, time of onset and short term outcome of seizures among neonates admitted to NICU of HI-Tech Medical College and Hospital, Bhubaneswar.

Methods: This prospective study was conducted in the NICU of HI-Tech Medical College and Hospital, Bhubaneswar. It was done from November 2017 to October 2019. All the neonates developing clinically identifiable seizures were included in the study. A detailed antenatal history, evidence of fetal distress, APGAR score, baseline data like gender, birth weight, gestational age and type of delivery was noted in a predesigned format. Etiology, time of onset and type of seizure was also noted and outcome was described in terms of number of deaths and neonates discharged with or without anti-epileptic drugs.

Results: Out of 1096 neonates admitted to NICU during the study period 81(7.4%) developed seizure. 35 out of 732(4.7%) inborn and 46 out of 364(12.6%) outborn neonates had seizure. Male to female and term to preterm ratio was 1.25:1 and 3.2:1 respectively. Mean birth weight was 2483 +/- 806 gms. 24 Out of 81 neonates were delivered by emergency LSCS. Antenatal history showed 18 had preeclampsia, 4 had diabetes mellitus, 2 had chorioamnionitis, 1 had abruption placentae and 1 had past history of unexplained neonatal death. 69 out of 81(85.2%) had onset of seizure within 72 hrs. Most common cause of seizure was perinatal asphyxia 42 out of 81(51.8%) followed by metabolic abnormality 20 out of 81(24.7%) and meningitis 15 out of 81(18.5%). Other causes included 2 cases of neural tube defects, 1 had Intra cranial haemorrhage and 1 was polycythemic. Most common cause of metabolic abnormality was hypocalcemia followed by hypoglycaemia. Most common cause of early onset neonatal seizure (<72hrs) was perinatal asphyxia followed by metabolic abnormality. Subtle seizure was the commonest type of seizure in 51.8% cases followed by clonic seizure in 24.7% cases. Other type of seizures were tonic and myoclonic. 53 out of 81(65.4%) were discharged without medication, 18 out of 81(22.2%) were discharged with medication and 10 out of 81(12.3%) died. Most common cause of death was perinatal asphyxia (4 out of 10). Other causes of death included galactosemia, meningitis, intracranial hemorrhage and neural tube defects.

Conclusion: Perinatal asphyxia was the most common cause of neonatal seizure and it is associated with high morbidity and mortality. In case of metabolic abnormality early detection and proper intervention leads to good outcome.

Keywords: Neonatal seizure, perinatal asphyxia.

Introduction

Seizures are the most important indicator of significant neurological dysfunction in neonatal period. The incidence of neonatal seizure in India is around 1.8-3.5/1000 live births⁽¹⁾. The clinical diagnosis of neonatal seizure is very challenging as a high proportion of these seizures are subclinical. It is defined as paroxysmal alteration in neurologic function which includes motor, behaviour and autonomic functions. It includes epileptic, non-epileptic and EEG seizures⁽²⁾. They occur more frequently in neonatal period than other time of life. The incidence of neonatal seizures in NICU can be as high as 10-25%, with death rate of 15% and poor neurological outcome in 35-40%⁽³⁾.

Subtle seizure, clonic seizure, tonic seizure and myoclonic seizure are commonly seen in neonates⁽⁴⁾. HIE, hypoglycaemia, hypocalcemia and meningitis are the most common causes of neonatal seizure^(5,6). Early onset seizures are usually associated with HIE, intracranial haemorrhage and metabolic abnormality while late onset seizures are associated with sepsis, meningitis, developmental defects and metabolic abnormality^(7,8).

Neonatal seizures lead to high morbidity and mortality without early diagnosis and treatment. So this study was conducted to evaluate incidence, etiology, natural history and outcome of neonatal seizure.

Methods

This prospective study was conducted in the NICU of HI-TECH Medical College and Hospital, Bhubaneswar. The neonates developing clinically identifiable seizures before 28 days of life were included in the study. The conditions mimicking seizure like jitteriness, benign sleep myoclonus and apnea were excluded. Baseline data including gender, gestational age and weight were recorded at admission. A detailed antenatal history including history of maternal illness during pregnancy, natal history, labor records for evidence of fetal distress and Apgar score, type of delivery

was recorded on a predesigned format. The diagnosis of neonatal seizures was based on clinical observation. Description of the type of seizures and time of onset of seizures were noted. Family history of seizures, neonatal death was recorded. A complete clinical examination of neonates including head circumference, dysmorphic features, vitals, CNS and other systemic examination were done. Blood glucose, total serum calcium and magnesium levels were done immediately after neonate had seizure and before starting of any specific treatment. The seizure etiology diagnosis was based on positive clinical data, laboratory findings, brain imaging studies (Cranial ultra-sound. CT scan. MRI) and Inborn error of metabolism screening in specific cases. For diagnosing neonatal infection sepsis workup and for suspected meningitis CSF study was done. In case of icterus, serum bilirubin was sent. Finally, the outcome was established in terms of number of deaths and neonates discharged with or without anti-epileptic drugs. Data was analysed by using proportions and Microsoft excel was used for calculation of mean and standard deviation.

Results

Out of 1096 neonates admitted to NICU during the study period 81(7.4%) developed seizure. 35 out of 732(4.7%) inborn and 46 out of 364(12.6%) outborn neonates had seizure. Male to female and term to preterm ratio was 1.25:1 and 3.2:1 respectively. Mean birth weight was 2483+/- 806 gms. 24 Out of 81 neonates were delivered by emergency LSCS. Antenatal history showed 18 had preeclampsia, 4 had diabetes mellitus, 2 had chorioamnionitis, 1 had abruption placentae and 1 had past history of unexplained neonatal death. Table 1 shows demographic characteristics.

Table 1: Demographic characteristic of neonates with seizure

| Characteristics | | No. of neonates | Percentage |
|------------------|------------------------------|-----------------|------------|
| Gender | Male | 45 | 55.5 |
| | Female | 36 | 44.5 |
| Birth weight | 2500 or more | 60 | 74 |
| | <2500 | 21 | 26 |
| Gestational age | Term | 62 | 76.5 |
| | Preterm | 19 | 23.5 |
| Mode of delivery | Spontaneous vaginal delivery | 30 | 37.1 |
| | Assisted vaginal delivery | 13 | 16.1 |
| | Elective LSCS | 14 | 17.2 |
| | Emergency LSCS | 24 | 29.6 |
| Maternal disease | Preeclampsia | 18 | 22.2 |
| | Diabetes mellitus | 4 | 5 |
| | Chorioamnionitis | 2 | 2.5 |
| | Abruptio placentae | 1 | 1.2 |
| Family history | Seizure | 2 | 2.5 |
| | Neonatal death | 1 | 1.2 |

69 out of 81 (85.2%) had onset of seizure within 72 hrs. We found that 31(38.3%) neonates had first seizure within 24 hours of birth, 38 (46.9%)

neonates within 24 to 72 hours and 12(14.8%) neonates after 72 hours (late onset) of birth. (Table-2)

Table 2: The time of onset of seizures

| Onset type | Time of onset | No. of neonates | Percentage |
|-------------|----------------|-----------------|------------|
| Early onset | <24 hours | 31 | 38.3 |
| | 24 to 72 hours | 38 | 46.9 |
| Late onset | >72 hours | 12 | 14.8 |
| Total | | 81 | 100 |

Most common cause of neonatal seizure was perinatal asphyxia 42(51.8%) followed by metabolic abnormality 20(24.7%) : 12 of them were due to hypocalcemia, 7 due to hypoglycaemia and 1 due to inborn error of metabolism (galactosemia). Meningitis was found

in 15(18.5%), congenital malformation in 2(2.5%) ,1(1.2%) was due to intracranial hemorrhage and 1 due to polycythemia. Congenital malformation included one case of encephalocele and meningomyelocele each. (Table-3,4)

Table 3: Etiology of neonatal seizure

| Etiology | No.of neonates | Percentage |
|-------------------------|----------------|------------|
| Perinatal asphyxia | 42 | 51.8 |
| Metabolic abnormality | 20 | 24.7 |
| Meningitis | 15 | 18.6 |
| Congenital malformation | 2 | 2.5 |
| Intracranial hemorrhage | 1 | 1.2 |
| Polycythemia | 1 | 1.2 |
| Total | 81 | 100 |

Table 4: The metabolic etiological disorders of seizures

| Metabolic disorder | No. of neonates | Percentage of total etiologies |
|----------------------------|-----------------|--------------------------------|
| Hypocalcemia | 12 | 14.8 |
| Hypoglycaemia | 7 | 8.7 |
| Inborn error of metabolism | 1 | 1.2 |
| Total | 20 | 24.7 |

The relation between seizure onset time and etiological disorder showed perinatal asphyxia, polycythemia, intracranial hemorrhage and

congenital malformation were leading cause of early onset seizure. (Table-5)

Table 5: The relation of seizures onset time to etiological disorders

| | Early onset (<72 hrs) | | Late onset (>72 hrs) | | Total | |
|-------------------------|-----------------------|------|----------------------|------|-------|-----|
| | No. | % | No. | % | No. | % |
| Perinatal asphyxia | 40 | 95.2 | 2 | 4.8 | 42 | 100 |
| Metabolic abnormality | 17 | 85 | 3 | 15 | 20 | 100 |
| Meningitis | 8 | 53 | 7 | 47 | 15 | 100 |
| Congenital malformation | 2 | 100 | 0 | 0 | 2 | 100 |
| Intracranial hemorrhage | 1 | 100 | 0 | 0 | 1 | 100 |
| Polycythemia | 1 | 100 | 0 | 0 | 1 | 100 |
| Total | 69 | 85.2 | 12 | 14.8 | 81 | 100 |

Among type of seizures subtle seizure 42(51.8%) was commonest followed by clonic type

20(24.7%) then tonic 16(19.7%) and myoclonic 3(3.7%). (Table-6)

Table 6: Types of neonatal seizures

| Types of neonatal seizure | No. of neonates | Percentage |
|---------------------------|-----------------|------------|
| Subtle | 42 | 51.8 |
| Focal/multifocal clonic | 20 | 24.7 |
| Tonic | 16 | 19.7 |
| Myoclonic | 3 | 3.7 |
| Total | 81 | 100 |

In our study 53(65.4%) were discharged without medication, 18(22.2%) were discharged with

medication and mortality was in 10(12.3%) cases. (Table-7)

Table 7: The outcomes of neonatal seizures

| Outcomes | No. of neonates | Percentage |
|-------------------------------|-----------------|------------|
| Discharged without medication | 53 | 65.4 |
| Discharged with medication | 18 | 22.2 |
| Death | 10 | 12.3 |
| Total | 81 | 100 |

When we evaluated outcome of neonatal seizure as per the etiological disorder mortality was highest in perinatal asphyxia (4 out of 42) followed by infection (2 out of 15) and congenital brain malformation (2 out of 2). Both cases of congenital malformation were neural tube defects. One was a case of encephalocele and the other one meningomyelocele. Among perinatal asphyxia out of 42 cases 26 were discharged without medication and 12 were discharged with medication. Metabolic abnormalities carried good

prognosis as out of 20 cases 19 were discharged without medication and 1 died. The neonate with polycythemia was discharged without medication. Congenital brain malformation and intracranial hemorrhage carried worst prognosis 100% mortality. To summarize out of 81 cases 53 were discharged without medication, 18 with medication and 10 neonates died. (Table-8)

Table 8: The outcomes according to etiological disorders

| Etiology | No. & percentage | Outcome | | |
|-------------------------|------------------|-------------------------------|----------------------------|-------|
| | | Discharged without medication | Discharged with medication | Death |
| Perinatal asphyxia | 42 (51.8) | 26 | 12 | 4 |
| Metabolic abnormalities | 20 (24.7) | 19 | 0 | 1 |
| Meningitis | 15 (18.6) | 7 | 6 | 2 |
| Congenital malformation | 2 (2.5) | 0 | 0 | 2 |
| Intracranial hemorrhage | 1 (1.2) | 0 | 0 | 1 |
| Polycythemia | 1 (1.2) | 1 | 0 | 0 |
| Total | 81 (100) | 53 | 18 | 10 |

Discussion

In our study the incidence of seizure among NICU admitted cases was 7.4% which is comparable to Sahana et al⁽⁹⁾ study (8.38%). It is also similar to Sabzehei et al⁽¹⁰⁾ study (9.1%) and Mwaniki et al⁽¹¹⁾ study (9.0%). But it is higher than study by Alyasiri⁽¹²⁾. Higher incidence in our study is because it was done in NICU admitted cases which is high around 10-25%⁽³⁾. But study by Alyasiri included both general ward and neonatal care cases.

We found that seizures are more common in babies weighing more than 2500 gm and term neonates. This is similar to result obtained by Sahana et al and study by Alyasiri. Al-marzoki⁽¹³⁾ and Yader⁽³⁵⁾ also got similar results. The incidence of seizure was more in male than female which goes with Alyasiri⁽³²⁾ (63.9%), Al-marzoki⁽³⁴⁾ (54.5%), Yader⁽³⁵⁾ (53.4%) study. Similar results were also obtained in Sahana et al⁽²⁹⁾ (52.3%) and Sabzehei et al⁽³⁰⁾ study (57%).

We had 69 out of 81 (85.2%) neonates developing first onset of seizure within 72 hours of birth. This is similar to finding of Sahana et al⁽²⁹⁾ 78%. Faiz et al⁽³³⁾ also got 59.6% of neonates developing early onset seizure. Al-marzoki⁽³⁴⁾ found that most of the seizures are late onset which may be because most of the cases in their study were due to metabolic abnormality but in our study most common cause was perinatal asphyxia.

The most common cause of seizure in our study is perinatal asphyxia 42(51.8%) cases which is comparable to Sahana et al study⁽²⁹⁾ 57.8%. Perinatal asphyxia was also leading cause of neonatal seizure in studies by Alyasiri⁽³²⁾ 33.6%, Kumar et al⁽³⁶⁾ 44.4%, Amar et al⁽³⁷⁾ 42.7% and

Sabzehei et al⁽³⁰⁾ 34.3%. Metabolic abnormality 20(24.7%) was the second most common cause of neonatal seizure in our study. Similar results were obtained by Alyasiri⁽³²⁾ 29.5%, Kumar et al⁽³⁶⁾ 23.33% and Amar et al⁽³⁷⁾ 20%. In Sahana et al⁽²⁹⁾ study metabolic abnormality was also the second most common cause of neonatal seizure but it accounted for 15.5%. In Sabzehei et al⁽³⁰⁾ second most common cause of seizure was infection in 24.5% cases. Mwaniki et al⁽³¹⁾ study showed infection 60% was the leading cause of seizure followed by perinatal asphyxia in 21% cases. This may be because this study was conducted in rural Kenyan district hospital where chances of sepsis is more.

Meningitis was associated with 15(18.5%) cases. It is similar to studies by Alyasiri⁽³²⁾ and Sahana et al⁽²⁹⁾ with results of 16.4% and 14.6% respectively. But studies by Sabzehei et al⁽³⁰⁾ and Faiz et al⁽³³⁾ showed higher infection rates 24.5% and 28.7% which may be due to better maintenance of asepsis and early use of antibiotics in our hospital.

Other causes of seizure in our study were encephalocele, meningomyelocele, intracranial hemorrhage and polycythemia each accounting for one case.

Out of 20 metabolic causes hypocalcemia was found in 12, hypoglycemia in 7 cases and one was a case of galactosemia. Hypocalcemia as a cause of seizure was seen in preterm and infant of diabetic mother. Few cases of perinatal asphyxia were associated with hypocalcemia. But hypocalcemia as a cause of seizure in such cases is not certain as many babies with similar degree of hypocalcemia did not manifest seizure. Several

studies like Sahana et al⁽²⁹⁾, Kumar et al⁽³⁶⁾ and Alyasiri⁽³²⁾ also got hypocalcemia and hypoglycaemia as leading cause of metabolic abnormality associated with neonatal seizure. Type M et al⁽²²⁾ found perinatal asphyxia, hypoglycaemia, hypocalcemia and meningitis were most common causes of seizure which is comparable to our study.

Now in relationship of etiology with time of onset of seizure we found that 40 out of 42(95.2%) cases of perinatal asphyxia, 17 out of 20(85%) cases of metabolic abnormality developed early onset neonatal seizure. Meningitis cases were almost equally distributed among early and late onset neonatal seizure. Polycythemia, intracranial hemorrhage and neural tube defects developed early onset seizure. Volpe JJ⁽²⁰⁾, Rennie JM⁽³⁸⁾ and Laroia N⁽³⁹⁾ also stated similar findings that is onset of seizure within 72 hrs were commonly due to perinatal asphyxia, metabolic abnormality, intracranial hemorrhage and beyond 72 hrs were associated with sepsis, meningitis.

Most common type of seizure in this study was subtle seizure(51.8%). Other types of seizure observed were clonic (24.7%), tonic(19.7%) and myoclonic(3.7%). Sabzehei et al⁽³⁰⁾ and Al marzoki⁽³⁴⁾ also found similar result. Volpe JJ⁽²⁰⁾ also stated subtle seizure to be the commonest one. But in Sahana et al⁽²⁹⁾ and Kumar et al⁽³⁶⁾ clonic seizure was the commonest seizure.

In terms of outcomes of neonates with seizure we found that 53(65.4%) neonates were discharged without medication, 18(22.2%) were discharged with medication and 10(12.3%) neonates died. Metabolic abnormalities had most favourable outcome as out of 20 cases 19 were discharged without medication and only 1 baby died. Among other causes of death 4 were due to perinatal asphyxia, 2 due to meningitis, 2 due to congenital malformations and 1 was due to intracranial hemorrhage. Alyasiri⁽³²⁾ in his study found that 56.6% neonates were discharged without sequel, 26.2% were discharged with sequel and 17.2% neonates died. These findings are similar to our study. In Sahana et al⁽²⁹⁾ 49.54% neonates were

discharged without sequel, 32.11% neonates discharged with sequel and 18.35% neonates died. In Sabzehei et al⁽³⁰⁾ 14.7% neonates died. In Alyasiri and Sahana et al study relatively higher percentage of deaths could be due to severity of the etiological factors as they had cases of cerebral dysgenesis, holoprosencephaly and kernicterus etc. Moreover the outcomes of our study is also as per the results obtained by Uria-Avellanal et al⁽⁴⁰⁾. They found out mortality ranges from 7 to 16% and neurodevelopmental sequel ranges from 27 to 55% in neonatal seizure.

Conclusion

Perinatal asphyxia is the leading cause of neonatal seizure. Hypocalcemia and hypoglycaemia are common metabolic disorders associated with seizure. Perinatal asphyxia and metabolic abnormalities are common causes of early onset neonatal seizure. Among different type of seizures subtle seizure is the commonest type of neonatal seizure. Outcome of neonatal seizure depends on etiology with metabolic abnormalities carrying most favourable and intracranial hemorrhage, congenital malformations carrying worst prognosis. Neurological sequelae are commonly observed in perinatal asphyxia and meningitis.

Recommendation

Improvement in antenatal, obstetric care and appropriate neonatal resuscitation is necessary. Always look for metabolic abnormality first and if present immediate intervention needs to be done. Finally a long term prospective study is necessary to evaluate neurodevelopmental outcomes.

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