

Original Research Article

Incidence and outcome of neonatal seizures at a tertiary care hospital

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ABSTRACT

Background: Seizures are associated with poor neuro developmental outcome if not diagnosed early and treated properly. During newborn period, seizures indicate underlying neurological disease. Neonatal seizures lead to increased morbidity and mortality usually found in neonatal intensive care unit. The objective of this study was to evaluate incidence and outcome of neonatal seizures.

Methods: Present study was hospital based prospective study conducted among 117 neonates of 0-28 days of age at a tertiary care hospital for a period of one year. The data like history, clinical examination and investigation findings was recorded in the pre-designed, pre-tested, semi structured questionnaire.

Results: The incidence of neonatal seizures was higher in male neonates. Subtle types of seizures were the commonest type of seizures. In term neonates, the birth asphyxia was the most common cause of neonatal seizures. The incidence of intra-ventricular hemorrhage (IVH) was significantly higher in preterm than term neonates. Out of biochemical abnormalities, the hypocalcemia was the most common cause of the neonatal seizures. Common causes of neonatal deaths in our center were severe birth asphyxia, intra-ventricular hemorrhage (IVH), septicemia and meningitis.

Conclusions: Most of the causes of neonatal seizures are preventable by good perinatal care and early interventions while metabolic seizures need a sharp vigilance and early suspicion.

Keywords: Birth asphyxia, complications, Neonatal seizures, Preterm

INTRODUCTION

It is a nightmare for the parents when the child develops convulsions. In convulsion, there is a repeated contraction of muscles which is involuntary and this is followed by confusion, deep sleep and a lot of weakness. During newborn period, seizures indicate underlying neurological disease and neonatal neurological disorder manifest as convulsions.

Neonatal seizures lead to increased morbidity and mortality usually found in neonatal intensive care unit.¹ For pediatricians, diagnosis and identification of types of

neonatal seizures is challenging. This statement is true especially when the diagnosis is attempted based on clinical findings. Neonatal seizure is a clinical emergency condition where rapid diagnosis and prompt treatment is required. Delay may result in poor neurological outcome.²

The incidence of neonatal seizures is around 1.8-3.5/1000 live births. The incidence is relatively more among premature and babies with low birth weight.³ The underlying reason for neonatal seizure is mostly abnormality of biochemical or cerebral. Among the patients admitted to Neonatal Intensive Care Unit the rate

of occurrence of neonatal seizures is 10-25%. Among these, the mortality rate is around 15. The incidence of poor neurological sequel is around 35-40%.⁴

The neonatal seizures have been defined as abnormal paroxysmal, stereotypic clinical events that are initiated by hyper-synchronous activity of neurons in the brain.⁵

The neonatal seizures can be due to withdrawal of drugs, or impaired cerebral inhibition. Sometimes clonus and jitteriness resemble seizure. By provoking stimulus, it can differentiate from seizures.⁶

Seizures are associated with poor neuro developmental outcome if not diagnosed early and treated properly. Hence this study has been done to evaluate incidence and outcome of neonatal seizures.

METHODS

Present study was hospital based prospective study conducted among 117 neonates of 0-28 days of age at a tertiary care hospital for a period of one year. Institutional Ethics Committee permission was obtained and informed consent was taken from eligible parents of neonates for the present study. Neonates of 0-28 days of both sexes having presented with seizure to the hospital in the present study during the study period and willing to give consent were included. They were followed till discharge and also for quite some time following the discharge. Neonates with doubtful seizures, cases which took discharge against medical advice and not willing to give consent were excluded from the present study.

The data was recorded in the pre- designed, pre- tested, semi structured questionnaire. The informant was either of parents or very close relative who could give the detailed history about the neonate's disease and specifically from mother in case of neonatal seizures i.e. age at onset of seizures, seizure activity with special emphasis on occurrence of 1st seizures, duration of seizures, number and type of seizures, associated autonomic changes, medications required to control seizures, response time to medications, and possible causes for determination of etiology. A detailed antenatal, natal and postnatal history was taken.

As per the semi structured questionnaire, data like investigations, management of the case details and the final outcome was recorded.

Neonatal seizure

Abnormal paroxysmal, stereotypic clinical events that are initiated by hyper-synchronous activity of neurons in the brain. The neonatal seizures were classified according to Volpe's classification into subtle, multifocal, clonic, focal clonic, tonic and myoclonic.²⁰

All required investigations were carried out and recorded. The outcome was noted down.

The data was entered in Microsoft excel worksheet and analyzed using proportions.

RESULTS

Table 1 is showing that out of 117 neonates, 34 (29%) were preterm while 83 (71%) were term neonates. More than 70% of neonatal seizures were seen above 37 weeks.

Table 1: Age of gestation and sex wise distribution of neonatal seizures.

Age of gestation	Male	female	Total
<37 weeks	22 (64.7%)	12 (35.3%)	34 (29.06%)
>37 weeks	53 (63.86%)	30 (36.14%)	83 (70.94%)
Total	75 (64.10%)	42 (35.9%)	117 (100%)

Table 2 shows the relationship of types of seizures in preterm neonates. Out of 34 term neonates, 13 (38.23%) neonates had subtle seizures, 11 (32.35%) neonates had clonic seizures and 10 (29.41%) neonates had tonic seizures.

Table 2: Types of seizures in preterm neonates.

Type of seizure	No. of cases (n=34)	Percentage
Subtle	13	38.23
Focal clonic	08	23.52
Multifocal clonic	03	08.82
Tonic	10	29.41
Myoclonic	00	00.00
Total	34	100

Table 3 shows the relationship of types of seizures in term neonates. Out of 83 term neonates, 28 (33.73%) neonates had subtle seizures, 39 (47%) neonates had clonic seizures, 14 (16.86%) neonates had tonic seizures and 2 (2.4%) neonates had myoclonic seizures.

Table 3: Types of seizures in term neonates.

Type of seizure	No. of cases (n=83)	Percentage
Subtle	28	33.73
Focal clonic	21	25.30
Multifocal clonic	18	21.68
Tonic	14	16.86
Myoclonic	02	02.40
Total	83	100

Table 4 highlights common etiological factors leading to neonatal seizures in preterm neonates, out of 34 (29%) preterm neonates, 11 (32.35%) neonates had birth asphyxia, 07 (20.58%) neonates had septicemia and 01 (02.94%) neonates had meningitis. IVH was seen in 07

(20.58%) neonate, hypocalcemia in 03 (08.82%) neonates and hypoglycemia in 04 (11.76%) while 1 (02.94%) preterm neonate undiagnosed.

Table 4: Etiological classification of seizures in preterm neonates.

Aetiology	No. of cases (n=34)	Percentage
Birth asphyxia	11	32.35
Septicaemia	07	20.58
Meningitis	01	02.94
IVH	07	20.58
Hypocalcaemia	03	08.82
Hypoglycaemia	04	11.76
Others	01	02.94
Total	34	100

Table 5: Etiological classification of seizures in term neonates.

Etiology	No. of cases (n=83)	Percentage
Birth asphyxia	40	48.20
Septicaemia	15	18.00
Meningitis	09	10.84
IVH	01	01.20
Hypocalcaemia	10	12.04
Hypoglycaemia	07	08.43
Others	01	01.20
Total	83	100

Table 5 highlights common etiological factors leading to neonatal seizures in term neonates, out of 83 (71%) term neonates, 40 (48.20%) neonates had birth asphyxia, 15 (18%) neonates had septicemia and 9 (10.84%) neonates had meningitis. IVH was seen in 01 (01.20%) neonate, hypocalcemia in 10 (12.04%) neonates and hypoglycemia in 7 (08.43%) while 1 (01.20%) term neonate undiagnosed.

Out of the total number of neonates 34 (29.05%) developed seizures within 24 hours, 42 (35.91%) neonates had seizures between 25-48 hours, 27 (23.08%) neonates developed seizures between 2-7 days and 14 (11.96%) neonates developed seizures after 7 days.

Table 6: Day of onset of neonatal seizures.

Hours/days	No. of cases (n=117)	Percentage
0-24 hours	34	29.05
>24-48 hours	42	35.91
>2-7 days	27	23.08
>7 days	14	11.96

Out of 51 neonates of birth asphyxia 29 (56.87%) neonates had seizures within 24 hours, 21 (41.10%) neonates had seizures between 24-48 hours and 1 (1.96%) neonates had seizures between 2-7 days. In septicemia 9 (40.09%) neonates had seizures between 2-7 days and 8 (36.37%) neonates had seizures after 7 days.

Table 7: Time of onset of seizure in days with respect to etiology.

Etiology	No. of cases	0-1 day	>1-2 days	>2-7 days	> 7 days
Birth asphyxia	51 (43.59%)	29 (56.87%)	21 (41.1%)	1 (01.96%)	00
Septicaemia	22 (18.80%)	01 (04.56%)	4 (18.18%)	9 (40.09%)	08 (36.37%)
Meningitis	10 (08.55%)	01 (10.00%)	4 (40.00%)	3 (30.00%)	02 (20.00%)
IVH	08 (06.84%)	00 (00.00%)	3 (37.50%)	2 (25.00%)	03 (37.50%)
Hypocalcaemia	13 (11.11%)	02 (15.38%)	4 (30.70%)	6 (46.15%)	01 (07.70%)
Hypoglycaemia	11 (09.40%)	01 (09.09%)	5 (05.55%)	5 (05.55%)	00
Others	02 (01.71%)	00 (00.00%)	1 (50.00%)	1 (50.00%)	00
Total	117 (100%)	34 (29.06%)	42 (35.9%)	27 (23.8%)	14 (11.96%)

Table 8: Causes of mortality in neonatal seizures.

Causes of death	No. of cases (n=21)	%
Birth asphyxia	10	47.6
Septicaemia	03	14.28
Meningitis	03	14.28
IVH	05	23.80
Total	21/117	17.95

The majority of seizures due to birth asphyxia were observed in first 48 hours life (early onset) while in infection, seizures were observed after 7 days of life (late onset). Among metabolic abnormalities, hypocalcemia

was seen within 1st to 7th day of life in 10 out of 13 i.e. 77% neonates while as 10 out of 11 i.e. 99.9% hypoglycemia cases were within 1st to 7th day of life. So, most of the metabolic abnormalities were seen after 24 hours of life. Out of 117 neonates, 96 (82.05%) survived while 21 (17.95%) neonates died. The common cause of neonatal death was birth asphyxia 10 (47.6%). On the other hand, no mortality was seen with metabolic abnormalities.

DISCUSSION

The overall incidence of neonatal seizure in present study was found to be 12.66%. Sandhu R et al studied 80

neonates and his incidence was 14.2%. Grover N studied 59 neonates and his incidence was 1.5%-14%.^{7,8}

In the present study, out of 117 cases, 75 (64.10%) were male and 42 (35.90%) were female neonates. The male to female ratio was 1.79:1 suggesting that the incidence of neonatal seizures was higher in male neonates than female neonates. The exact cause of this is not known. Similar results were also observed in study conducted by Holden et al and Powell et al.^{9,10} Holden et al studied 227 neonates of which 157 (56.77%) neonates were male and 120 (43.32%) neonates were female.⁹ Powell et al studied total of 24 cases of which 17 (70.83%) were male neonates and 7 (29.16%) were female neonates.¹⁰

In the present study, full term neonates were 83 (71%) and 34 (29%) neonates were preterm. The term neonates showed predominance for seizure activity. The possible higher incidence in term neonates can be explained by the fact that most of the neonates in this group were intrauterine growth retardation (IUGR). The incidence of birth asphyxia is higher in IUGR neonates; this might be a contributing factor for the high incidence of seizures in this group. Similar findings were also observed in the study conducted by Legido et al and Kumar et al.^{11,12} Legido et al studied 40 neonates out of which 28 (70%) were term neonates and 12 (30%) were preterm neonates and Kumar et al studied 35 neonates, out of which 30 (85.71%) neonates were term neonates.^{11,12}

Of all the seizures in neonates, subtle seizure is the commonest in majority of the studies. In the present study among the term group, subtle seizures were found in 28 (33.73%) neonates followed by clonic seizures in 39 (47%) neonates which were the commonest type of seizures observed. Tonic seizures were seen in 14 (16.86%) neonates followed by myoclonic in 2 (2.40%) neonates. In preterm neonates the subtle seizures were found 13 (38.23%) neonates followed by clonic seizures in 11 (32.35%) neonates which were the commonest type of seizures observed. Tonic seizures were observed in 10 (29.41%) neonates. Similar result was also shown by studies conducted by Ross et al and Soni et al.^{13,14} Rose et al studied 118 neonates, out of which 48 (40.60%) neonates had subtle, 42 (35.59%) neonates had clonic, 10 (8.9%) neonates had generalized tonic and 28 (27.78%) neonates had myoclonic type of seizures.¹³ In a study conducted by Soni et al the commonest type of seizures in term group was tonic seizures which were seen in 15 (37.5%) neonates and subtle seizures in 10 (25%) neonates.¹⁴ In the preterm group also the commonest type of seizures observed were tonic (41.6%) seizures followed by subtle seizures (33.3%).

In the present study, out of 83 term neonates, 40 (48.20%) neonates had birth asphyxia, 24 (28.84%) neonates had infection, and 1 (1.20%) neonate had intra-ventricular hemorrhage followed by hypocalcemia in 10 (12.04%) neonates, hypoglycemia in 7 (8.43%) neonates. Among 34 preterm neonates, 11 (32.35%) neonates had

birth asphyxia, 8 (23.53%) neonates had infection. Intra-ventricular hemorrhage (IVH) was seen in 7 (20.58%) neonates followed by hypocalcaemia in 3 (8.82%) neonates, hypoglycemia in 4 (11.76%) neonates.

In present study the birth asphyxia as a cause of seizures was seen in 40 (48.20%) term neonates and 11 (32.35%) preterm neonates. The similar result was also shown by Eriksson studied 77 neonatal seizure cases out of which 48% were due to birth asphyxia.¹⁵ Legido A et al studied 40 neonatal seizure cases out of which 35% were due to birth asphyxia.¹¹

Twenty-four term neonates had infections, out of which 9 (10.84%) neonates had meningitis and 15 (18%) neonates had septicemia. In preterm group 7 (20.58%) neonates had septicemia and 1 (2.94%) neonate had meningitis. The diagnosis of septicemia was made on the basis of clinical signs and laboratory parameters. The comparative studies are Taksande AM, et al studied 110 cases of neonatal seizures out of which 28.2% were infectious origin.¹⁶

In the present study, 8 (6.83%) neonates had intra-ventricular hemorrhage out of which 1 (1.20%) neonate was term while 7 (20.58%) neonates were preterm. The incidence of intra-ventricular hemorrhage was higher in preterm neonates than term neonates. Peri-ventricular or intra-ventricular hemorrhage is the most common cause of intracranial bleeding and neurological damage in low birth weight and preterm neonates. The similar results were also shown by studies conducted by Taksande AM et al out of 110 neonatal seizure cases 7 (6.36%) neonates develop seizures due to IVH.¹⁶

Hypocalcemia is one of the important metabolic causes of neonatal seizures. In the present study neonatal seizures due to hypocalcaemia was observed in 13 (11.11%) neonates, out of which 10 (76.92%) neonates were term and 3 (23.08%) neonates were preterm. Most neonates fed with the non-human milk have lower calcium and higher phosphate concentration on sixth day of life than breast fed neonates. This can be the possible cause for late onset seizures. The similar result was also shown by studies conducted by Kumar et al out of 35 neonatal seizure cases 14.28% were due to hypocalcaemia.¹² Taksande AM et al out of 110 neonatal seizure cases 13 (11.81%) neonates develop seizures due to hypocalcaemia.¹⁶

Hypoglycemia occurs in both term and preterm neonates and particularly in neonates of diabetic mother. In our present study, hypoglycemia as a cause of neonatal seizures was observed in 11 (9.40%) neonates, out of whom 7 (63.64%) neonates were term and 4 (36.36%) neonates were preterm. The similar result was also shown by studies conducted by Legido A et al out of 40 neonatal seizure cases 9.5% were due to hypoglycemia.¹¹ Taksande AM et al out of 110 neonatal seizure cases 9

(8.18%) neonates develop seizures due to hypoglycemia.¹⁶

In the present study, out of total 117 neonatal seizure cases, 103 (88.04%) neonates had seizures within 7 days of life, mostly constituted by the birth asphyxia (early onset). Similar result was also observed in a study conducted by Ronen GM et al who reported 83% of seizures in the 1st week of the life and by Taksande AM et al out of 110 neonatal seizure cases 94 (85.45%) neonates develop seizures in the 1st week of the life.^{16,17} Most common cause was found to be birth asphyxia, seen in 50 neonates (98.04%) occurring within 48 hours, and with the study conducted by Kumar et al he found 45 (97.83%) within 48 hours, Holden R et al found all cases of birth asphyxia i.e. 16 (100%) neonates had onset of seizures within the first 48 hours of life.^{9,12}

In present study 14 (11.96%) neonates had convulsions after 8 days of life, out of which 8 (57.14%) neonates had septicemia. In the study conducted by Holden et al 36 (13%) neonates had convulsions after 8 days, which were due to sepsis and meningitis.⁹

Among the metabolic seizures, 3 (12.5 %) neonates presented seizures within 24 hours, while 21 (87.5%) neonates after 24 hours of life. There was a significant biphasic distribution of seizures with first peak formed by birth asphyxia and second peak formed by metabolic abnormalities and septicemia at the end of first week. Similar results were also observed in the studies conducted by Kumar A et al and Sandhu R et al.^{7,12}

CONCLUSION

The early recognition and treatment of neonatal seizures is essential for optimal management and satisfactory outcome, as seizures in neonatal period are associated with high mortality and morbidity. Most of the causes of neonatal seizures are preventable by good perinatal care and early interventions while metabolic seizures need a sharp vigilance and early suspicion.

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