

CLINICO-ETIOLOGICAL PROFILE AND OUTCOME OF NEONATAL SEIZURES - A HOSPITAL-BASED CROSS-SECTIONAL STUDY IN WESTERN NEPAL

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ABSTRACT

INTRODUCTION

Neonatal seizure, a common problem encountered in neonatal intensive care unit (NICU) setting, is an important determinant of outcome of neurological disorders in newborn period. The aim of the study was to study the clinical and etiological profile of neonatal seizures along with their outcomes.

MATERIAL AND METHODS

A prospective observational study was conducted in the NICU of Department of Pediatrics at Universal College of Medical Sciences, Bhairahawa, Nepal from November 2019 to March 2021. Babies with neonatal seizures were enrolled in the study after obtaining written consent from parents.

RESULTS

Out of 870 admitted neonates, 9.7% (n=85) developed clinical seizures where 62.4% were males. Most cases (87.1%) had seizures within 48-hour of life with subtle seizures (92.9%) being the commonest. About 43.5% cases had single episode of seizure followed by multiple episodes. Perinatal asphyxia (92.9%) either alone and/or associated with hypocalcemia (80%) followed by sepsis (40%) and hyponatremia (18.8%) were common etiologies for neonatal seizures. Most of the seizures (76.5%) were aborted with the use of single anti-epileptic drug. About 86% (n=73) survived and rest expired.

CONCLUSION

Subtle seizures were common and perinatal asphyxia was the predominant etiology for neonatal seizures. Thus, strengthening the healthcare facility during delivery of the newborn, proper newborn care and nutrition must be emphasized to decrease the incidence of seizures in developing nations like Nepal.

KEYWORDS

Neonatal seizure, Perinatal hypoxia, Outcome

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INTRODUCTION

Neonatal seizure is a common neonatal emergency of neurological dysfunction associated with high mortality and morbidity even with advanced perinatal care. Seizures occur most commonly in the neonatal period than any other time of life due to the developmental immaturity.¹

The incidence of neonatal seizures ranges from 1-5% and occur in response to an identifiable etiology in many cases.^{1,2} Focal seizures are more prominent than generalized seizures due to reduced connectivity between cerebral hemispheres in the neonatal brain.³ Subtle seizures have mild clinical manifestations and are often missed and sometimes may only present with autonomic features.³ Clonic seizure is manifested as rhythmic movement of muscle groups which occurs unilaterally, sequentially in different limbs or simultaneously but asynchronously, and has fast contraction phase and slow relaxation phase.¹ Tonic seizure is characterized by sustained flexion or extension of axial or appendicular muscle group, tonic horizontal eye deviation or asymmetric tonic truncal postures.

Myoclonic seizures manifest as single or multiple lightning fast jerks usually of both lower limbs and less of upper limbs. It is distinguished from clonic seizure by its more rapid speed, absence of slow return and predilection for flexor muscles.¹

Perinatal asphyxia, infection including meningitis, intracranial hemorrhage, and metabolic or electrolyte disturbances are the common identified etiologies.^{2,4} There are a number of problems in diagnosis and management of neonatal seizures underscoring the dynamic nature of the study of neonatal seizures.⁵

Although there is an increasing trend towards the use of electro-diagnostic techniques to diagnose neonatal seizures; traditionally, the incidence of neonatal seizures has been estimated using clinical observation of abnormal movements. The clinical presentation of seizures in the neonatal period is subjective, with wide inter-observer variations.⁶

Overall, data on incidence, clinico-etiological profile and outcome of neonatal seizures is still sparse in Nepal. Apart from this, we do not have any such studies conducted from western region of Nepal. Therefore, we conducted this prospective observational study to identify the clinico-etiological profile of seizures in newborn along with their outcomes.

MATERIAL AND METHODS

A hospital-based cross-sectional study was conducted in the neonatal intensive care unit (NICU) at Universal College of Medical Sciences, Bhairahawa, Nepal from Nov 2019 to Mar 2021. The study was approved by the institutional review committee of the institute (Ref. no. UCMS/IRC/207/19). A total of 85 babies with neonatal seizures were enrolled in the study after calculating the sample size ($n = z^2pq/d^2$) at 95% confidence interval with estimated prevalence of 5.5%² and allowable error of 5%.

The present study included all newborns having seizures unprovoked by stimulation and not abolished by restraint only after obtaining informed and written consent from the parents. Those newborns whose parents refused to give consent, those who succumbed to death or went on leave against medical advice (LAMA) were excluded from the study. Babies with poor documentation regarding perinatal events or having benign sleep myoclonus, tremors, jitteriness and no video recording of abnormal body movement were also excluded from the study.

The data was collected by filling the information from the record, interviewing the mothers and taking the required measurements and examining the newborns. All data were entered in an excel sheet and SPSS version 16 software was used for analysis. Mean, percentage and standard deviation was calculated using descriptive analysis.

RESULTS

Out of total 870 admissions during the study period, 85 babies had seizures comprising the incidence of neonatal seizure to be 9.7%. Among the babies with neonatal seizures, 82.4% (n=70) patients were Hindu in religion whereas 17.6% (n=15) were Muslim. Majority of the cases were from Rupandehi district (51.8%) followed by Kapilvastu (35.3%).

The baseline characteristics of the babies with neonatal seizures are given in Table 1. Majority of the babies (68.2%, n=58) in the present study were born by vaginal delivery followed by lower section caesarean section (31.8%).

Table 1. Baseline characteristics of babies with neonatal seizures

Variables	Mean ± SD	N (%)
Sex		
Male		53 (62.35)
Female		32 (37.65)
Gestation (weeks)	38.7 ± 1.8	
Preterm (<37 weeks)		3 (3.5)
Term (37 to <42 weeks)		76 (89.4)
Post-term (≥42 weeks)		6 (7.1)
Birth weight (gm)	2752.2 ± 471.8	
Length (cm)	50.0 ± 2.5	
Head circumference (cm)	33.6 ± 1.6	
Mode of delivery		
Vaginal delivery		58 (68.2)
Caesarean section		27 (31.8)
APGAR (mean ± SD)		
At 1-minute		
0-3		35 (41.2)
4-6		44 (51.8)
7-10		6 (7.1)
At 5-minute		
0-3		4 (4.7)
4-6		53 (62.3)
7-10		28 (32.9)
Resuscitation		
Dry stimulation		35 (41.2)
AMBU		37 (43.5)
ET with PPV		13 (15.3)

SD- Standard Deviation; N- Number; ET- Endotracheal Intubation; PPV- Positive Pressure Ventilation

Table 2 shows various causes of neonatal seizures reported in the present study with perinatal asphyxia (92.9%) being the most common cause. There were 34 cases of neonatal sepsis out of which 14 had meningitis. Among the babies with meningitis, 12 cases had concomitant perinatal asphyxia. No cases with meningitis succumbed to death. No etiology was revealed in 4 (4.7%) cases.

Table 2. Etiological profile of neonatal seizures

Causes	N (%)
Perinatal asphyxia	79 (92.9)
Hypocalcemia	68 (80)
Sepsis	34 (40.0)
Hypnatremia	16 (18.8)
Intracranial hemorrhage	7 (8.2)
Hypoglycemia	2 (2.3)
Unknown	4 (4.7)

Total 50 cases (58.8%) had mixed diagnosis. Perinatal asphyxia alone was seen in 35 cases (41.1%). Perinatal asphyxia along with sepsis was seen in 32 cases (37.6%).

Table 3 shows the seizure profile in the enrolled neonates. Most of the cases had seizures within first 48 hours of life. Subtle seizure was the most common type of the seizure observed (92.9%), followed by clonic seizure (4.7%). However, no cases of tonic seizure were observed.

Table 3. Clinical profile of neonatal seizures

Variables		N (%)
Onset	<48 hours	74 (87.1)
	>48 hours	11 (12.9)
Types	Subtle	79 (92.9)
	Clonic	4 (4.7)
	Tonic	0 (0.0)
	Myoclonic	2 (2.3)
Episodes	Single	37 (43.5)
	Two	18 (21.2)
	Multiple	30 (35.3)
AED requirement	Single (1)	65 (76.5)
	Multiple (≥2)	20 (21.2)

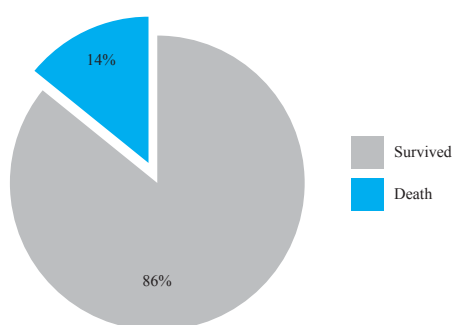


Figure 1. Showing the outcome of babies with neonatal seizures

Out of 85 neonates with seizures, 73 cases (86 %) survived and 12 died (14 %) as shown in figure 1. There were no LAMA cases during the study period.

DISCUSSION

The clinical presentation and recognition of neonatal seizures is mainly subjective in resource poor countries leading to variations in the incidence rate. The incidence of neonatal seizures in the present study was 9.7% which was similar to a study done by Mwaniki et al.⁷ A study done by Kumar et al found the overall incidence of neonatal seizures to be as low as 1.1% with higher incidence in preterm babies (6.14%) in contrast to only 0.69% in term babies. The incidence of neonatal seizures in their study was calculated in total live birth neonates whereas in the present study, the incidence was calculated in total NICU admitted babies. This could be the reason of higher incidence of neonatal seizures in the present study.⁸ Another study from India found higher incidence of neonatal seizures in extramural babies in comparison to intramural babies (7.3% versus 0.77%).⁹ In contrary, a study conducted by Anand and Nair found the incidence to be 5.5%. This lower incidence in their study could be because of majority of them being preterm (58.3%) in comparison to our study where majority of the cases were term (89.4%).²

The proportion of neonatal seizures in the present study was more common in males (62.35%) than in females (37.65%) similar to other studies done. The higher incidence of seizures in males compared to females could be due to prominent occurrence of opening of chloride channels in male brain compared to females, which are excitatory in premature brain resulting in depolarizing the cells.^{2,10}

The mean birth weight in the present study was almost similar to the studies conducted by Garfinkle and Shevell¹¹ and Yildiz et al¹⁰ whereas Loman et al¹² had mean weight of 3490 gm which was higher than the present study. A recent study from Iran (2018) conducted by Nemati et al showed that more than two-third cases with neonatal seizures had normal birth weight (>2500 gm) with mean weight being 2890±580 gm.¹³

In the present study, 68.2% cases had vaginal delivery and 31.8% had caesarean delivery. This was almost similar to studies from Canada and Iran conducted by Garfinkle and Shevell¹¹ and Eghbalian et al¹⁴ respectively. Similar study done by Amare and Amare showed that 23% babies of neonatal seizures were delivered by caesarean section which was lower than the present study.¹⁵ The mean APGAR score at 1 minute and 5-minute in the present study was 4.0±1.5 and 5.9 ± 1.50 respectively which was almost similar to the study done by Nunes et al who recorded APGAR of 5 ± 0.3 at 1-min and 7.1 ± 2.5 at 5-min.¹⁶

Most of the cases (87.1%) in our study had occurrence of seizures within the first 48 hours of life. Studies done by Pasi et al¹⁷ found that 94.7% of neonatal seizures occurred within 7th day of life whereas in a study conducted by Calciolari et al,¹⁸ 90% of seizures occurred within 48 hours of life which was similar to the present study. In the present study, 43.5% of all recruited babies with neonatal seizures had single episode of seizures. The proportion of babies having single episode of seizure in a study conducted by Pasi et al was 36.8% which was slightly less than the present study.¹⁷

Subtle seizure was the most common type of the seizure observed, followed by clonic seizures and myoclonic seizures in the present study. A study conducted in Ethiopia showed

subtle seizure to be around 60% which was much lesser than the present study.¹⁵ Masduzzaman et al found subtle seizure occurrence even lesser (58.3%) than Amare and Amare with around one-third having clonic seizures but no myoclonic seizures.¹⁹ Various researchers too have demonstrated the predominant occurrence of subtle seizures in their studies.^{18,20} The important reason for the occurrence of the variation could be due to inter-observer variation in seizure classification.

More than three-fourth of the enrolled babies got their seizures aborted with the use of single drug (phenobarbitone monotherapy) in the present study. Studies conducted by Garfinkle et al¹¹ and Nunes et al¹⁶ also found majority of the babies having seizure control with phenobarbitone monotherapy.

Perinatal asphyxia followed by sepsis were the predominant etiological factors to be associated with neonatal seizures in the present study. A study conducted in India by Anand and Nair also found similar findings as ours.² Few studies from the Middle-East Asia²¹ and Europe^{12,22} also support our findings.

All the babies with hyponatremia in the present study had either perinatal asphyxia or both perinatal asphyxia and sepsis together. No other co-morbidities were associated with hyponatremia in the present study. Pasi et al also found almost similar findings as ours where isolated hyponatremia was not seen even in a single case and was always secondary to HIE alone or HIE with other co-morbidities. The reasons for asphyxiated babies having hyponatremia could be either due to fluid overload as a result of renal compromise or due to inappropriate secretion of anti-diuretic hormone (SIADH).¹⁷

The present study showed that 80% babies with neonatal seizures had hypocalcemia where almost all hypocalcemic cases had perinatal asphyxia alone and/or other co-morbidities. The possible reason for hypocalcemia in asphyxiated neonates could be due to increased phosphate load caused by tissue metabolism, renal insufficiency and increased serum calcitonin concentration. A study by Eghbalian et al showed that hypocalcemia was lesser than the findings in the present study.¹⁴ Similarly, a recent study from Bangladesh (2019) had almost 50% cases having hypocalcemia in those with metabolic disturbances.¹⁹ The vast difference in the incidence of hypocalcemia in the neonates with seizures could be due to fact that majority of the enrolled cases with seizures were asphyxiated in our study in contrast to their study.

Neonatal sepsis was associated with seizures in more than one-third of cases in the present study which was similar to a Indian study² and a study conducted in Bosnia by Heljic et al (35%).²² This could be because of poor NICU level and lack of aseptic precautions and proper handling of newborn in developing countries like ours.

Intracranial hemorrhage (ICH) was noticed in 8.2% cases in the present study which was similar to the studies conducted by Loman et al¹² and Eghbalian et al.¹⁴ In contrast to this, ICH was noticed to be more than 2-fold high in a study conducted by Yildiz et al.¹⁰ the reason for high occurrence of ICH could be have been due to majority of the babies being preterm in their study. In the present study, only three babies with

seizures were preterm.

No causes were identified in 4.7% cases which was similar to the study done by Garfinkle et al where causes were unidentified in 5% cases. The lack of facilities of investigations in many hospitals of resource poor countries to determine the causes contributing to seizures may limit the study of etiological profile.

The overall survival was seen in 86% babies and male babies predominantly succumbed to death. In studies conducted at India by Anand and Nair² and Pasi et al,¹⁷ the mortality rate was found to be higher (17.2% and 14.5% respectively) than the present study whereas an Iranian study conducted by Eghbalian et al¹⁴ showed a lower mortality rate (12.8%). The higher mortality rate in Nepal and India could be attributed to the quality of health facilities and other compounding factors.

Our study had few limitations. In this study, only clinically evident seizures were documented and subclinical seizures were possibly missed due to lack of EEG monitoring for newborn seizures in our centre. Secondly, it was a single centred hospital-based study and the findings may not represent to the whole population.

CONCLUSION

The incidence of neonatal seizure in the present study was 9.7%. Subtle seizure was the most common type of the seizure observed, followed by clonic seizures and myoclonic seizures. Perinatal asphyxia was a predominant cause of neonatal seizures.

CONFLICT OF INTEREST

None

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