

# The clinical profile, etiology and short term outcome of neonatal seizures at Patan Hospital, Nepal

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## ABSTRACT

**Introduction:** The incidence of seizure is as high as 5/1000 live births and the mortality rate can be up to 15%. So this study was conducted to find out the clinical profile, causes and immediate outcome of neonatal seizures at Patan Hospital.

**Methods:** In this retrospective study, all neonates (aged 0-28 days) with seizure admitted to Patan Hospital over a period of one year from January 2015 to December 2015 were included. The data were obtained from hospital records and analyzed using SPSS 12.

**Results:** There were 32 cases of neonatal seizures admitted over the period of one year out of which 23 were born at Patan Hospital. The incidence of neonatal seizure was 2.9 cases of per 1000 live birth. Among neonates with seizure, 63% were male, 81% were term and 69% were of birth weight more than 2500gm. The cause of seizure was hypoxic ischemic encephalopathy in 25% of cases and no cause could be found in 15% of cases. Phenobarbitone alone controlled seizure in more than 50% of cases. The mortality rate was 9.3% with hypoxic ischemic encephalopathy being the most common cause.

**Conclusion:** The most common cause of neonatal seizure is hypoxic ischemic encephalopathy and is also the leading cause of death in neonates with seizure. Therefore improvement in healthcare during the delivery of newborns can decrease the incidence and death due to neonatal seizure.

**Keywords:** etiology, hypoxic ischemic encephalopathy, neonatal seizure

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## INTRODUCTION

Seizure is one of the medical emergencies in the neonatal period.<sup>1</sup> The decreased seizure threshold in the newborn reflects the developmental events active in the immature brain like the transient over development of excitatory systems compared to inhibitory systems. The incidence of seizure varies from 1-3.5/1000 live birth<sup>2-5</sup> while in NICU it can be upto 5/1000 live birth.<sup>6</sup>

The most common cause of neonatal seizure is hypoxic-ischemic encephalopathy.<sup>7</sup> Other causes include intracranial infections, metabolic disorders, CNS malformations, intracranial hemorrhage, birth trauma, drug withdrawal, and less frequent metabolic disorder such as inborn error of metabolism.<sup>8</sup> The mortality rate can go upto 27%<sup>9</sup> and commonly occurring in neonates with hypoxic ischemic encephalopathy.<sup>6,10,11</sup>

The primary objective of this study was to find the clinical profile, causes and immediate outcome of neonatal seizures at Patan Hospital.

## METHODS

This was a cross-sectional retrospective study. Charts of neonates discharged from the nursery, NICU and pediatric ward with the diagnosis of neonatal seizure were reviewed. Neonatal seizure was diagnosed on the basis of presence of seizure as seen by the treating doctor or sisters. All data were extracted from medical records and entered in a Performa. Investigations done to find out the cause of the seizure like sepsis screening, serum electrolytes, glucose, calcium, magnesium, lumbar puncture, cranial ultrasound/ MRI were reviewed from which the cause of neonatal seizure was found out. In this study, hypoxic ischemic encephalopathy was diagnosed by Apgar score <7 at 5 minutes of birth. Diagnosis of neonatal infection was based on the clinical manifestation, sepsis workup, and positive blood/urine culture. Bacterial meningitis was confirmed by CSF abnormalities. Metabolic disturbances were considered as hypoglycemia (blood sugar <40 mg/dl during the first 24 hours and <45 mg/dL after 24 hours of the birth), hypocalcemia (total serum Calcium <8 mg/dL in full term and Calcium <7 mg/dL in preterm neonates), and hyponatremia (serum sodium <135 mg/dL) and hypernatremia (serum sodium >145 mg/dL). Brain anomalies were determined by ultrasound cranium followed by magnetic resonance imaging if indicated. The statistical analysis was performed using SPSS-16 software. Also the type of anti-epileptics used in these neonates and the immediate outcome in terms of mortality or discharge was reviewed.

## RESULTS

There were 32 cases of neonatal seizure over the one year period out of which 23 cases were born at Patan Hospital and 9 were outborn cases. Out of 23 inborn cases, 4 cases were readmitted after discharge for seizure. While considering the

inborn cases, there were 2.9 cases of neonatal seizure per 1000 live birth. Distribution of cases according to gestational age and sex is given in Fig. 1 and Fig. 2 respectively. Sixty nine percent were of birth weight more than 2500 grams while thirty one percent were of birth weight 1500 to 2499 grams.

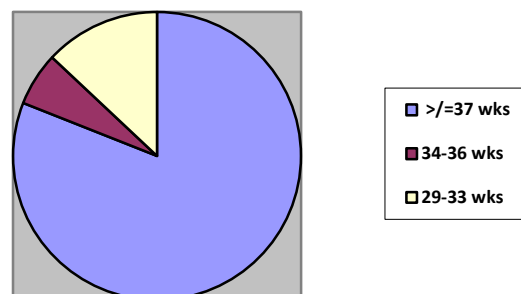


Fig. 1 Distribution of cases by gestational age

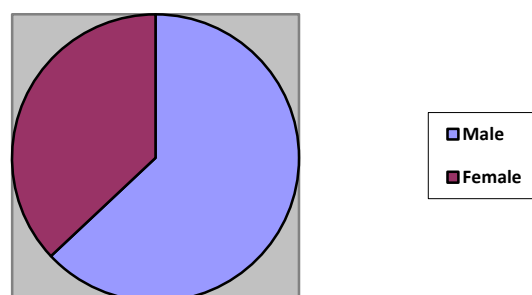


Fig. 2 Distribution of cases by sex

Out of 32 cases, 18 cases were delivered by LSCS while around 11 cases were delivered by SVD and there was 1 case delivered by vacuum and breech delivery each. About 70 % of newborn presented with seizure after 48 hrs. The cause of seizure is shown in Table 1. One case of hypoxic ischemic encephalopathy also had hypoglycaemia. One case with hypocalcemia also had hypomagnesemia while other had hypomagnesemia along with hypoparathyroidism.

Cause	Frequency(%)	Mortality(%)
Hypoxic ischemic encephalopathy	8(25)	2(6.3)
Hypocalcemia	5(15.62)	0
Hypoglycemia	3(9.37)	0
Meningitis	3(9.37)	
Sepsis	2(6.26)	0
Urinary Tract Infection	2(6.26)	0
Hyponatremia	1(3.12)	0
Congenital brain anomalies	1(3.12)	1(3.1)
Unknown	5(15.62)	0
Referred	2(6.26)	0

Table 1: Cause of neonatal seizure

The treatment given is shown in Fig 3. The other drugs used for seizure control was midazolam, calcium, magnesium and sodium valproate. USG cranium was not done in six cases and in rest of the 26 cases, 1 case showed Dandy Walker malformation, 1 case showed effacement of lateral ventricles and 1 case showed ischemia over temporal region due to hypoxic ischemic encephalopathy. There were 3(9.4%) mortalities out of which 2 cases had hypoxic ischemic encephalopathy. In the rest of 29 cases, 26 cases were discharged, 2 cases were referred to other centre for ICU care and 1 case left against medical advice.

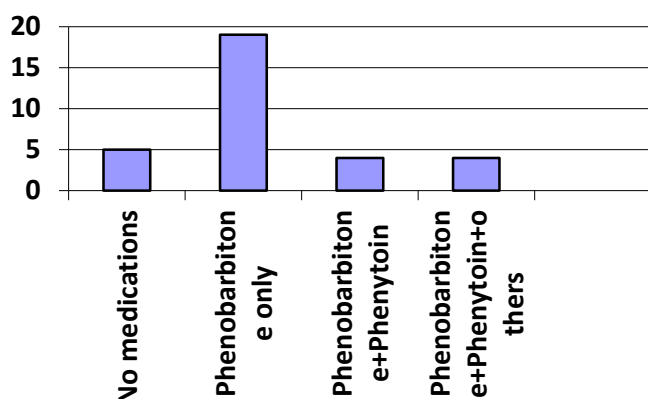


Figure 3: Response to treatment

## DISCUSSION

The incidence of neonatal seizure was 2.9 cases of neonatal seizure per 1000 live birth per one year. Various studies have shown the incidence to be 1- 3.5/1000 live birth.<sup>2-5</sup> The incidence was found to be 5/1000 live birth in a study done by Sadeghian et al<sup>6</sup> and Holden et al.<sup>12</sup> Sadeghian et al only included neonatal seizures in babies from NICU while Holden et al did the study in United States where there is better survival of preterm neonates in whom seizures are more common. The incidence in other studies by Najeeb et al was 0.95/ 1000 live birth. The incidence in this study was less than other studies as they studied babies only at discharge and included babies >36 weeks.<sup>13</sup>

Neonatal seizure was more common in male than in female similar to other studies.<sup>2,6,11,13-17</sup> Very few studies showed more females with neonatal seizures.<sup>10</sup>

Eighty one percent of the cases were term  $\geq 37$  weeks of gestation while thirteen percent were 29-32 weeks of gestation and six percent was 33-36 weeks of gestation. This finding was similar to a study by Sheth et al who found a parabolic effect of onset of seizure to gestational age.<sup>18</sup> Similar to the present study, term babies were more affected than the preterm babies in many other studies.<sup>2,13,14,16</sup> In other studies, seizure was more common in preterm babies. This difference might be because of the fact that these studies were done in NICU or developed countries where preterm survival has improved.<sup>11,17,19,20</sup>

Sixty nine percent were of birth weight more than 2500 grams while thirty one percent were of birth weight 1500- 2499 grams. More babies with birth weight more than 2500 gram was also found in other studies.<sup>10,11,13</sup> Unlike our study, other studies have shown seizure to be more common in LBW especially in VLBW babies. We did not have any VLBW babies with seizure. This could be because of better survival of VLBW babies in developed countries and might be the cause of less LBW babies in our study.<sup>13, 19,21</sup>

In our study the mode of delivery was LSCS in more than half of the cases. Similar findings with more delivery by LSCS was seen in other a study done by Yildiz et al.<sup>16</sup> While more babies was delivered by SVD in a study by Eghbalian et al.<sup>10</sup>

About 70 % of newborn presented with seizures after 48 hours. Unlike our findings, most of the studies had seizure onset less than 48 hours.<sup>2,6,11,13,22</sup> This might be due to the fact that most of the babies were with the mother at the time of seizure and the mother might have had difficulty recognising the seizure due to lack of knowledge about seizure in neonates. The difference might also be due to the fact that very few cases were included in the study.

Most common cause of neonatal seizure was hypoxic ischemic encephalopathy.<sup>2,6,7,22,10,11,13-15,17,23,24</sup> The second most common cause was metabolic abnormality out of which hypocalcemia was the most common abnormality.<sup>10,11,14,22,24,25</sup>

Out of 30 cases that had all the initial workup done, 5 cases (16.6%) had no obvious cause for seizure. Various studies have shown unknown cause of seizure to be from 5-31%.<sup>10,14,26,27</sup> In other studies, the cause of seizure was diagnosed in almost all the cases.<sup>15,24</sup> The cause of more unknown diagnosis in our case might be because of our limitation of investigation. A study done by Lauren et al showed that MRI was an important tool in the diagnostic process of neonatal seizures. If not done a diagnosis or important imaging abnormalities would have been missed in 11.9% of infants and MRI added significantly to the information obtained in 39.8% of infants.<sup>15</sup> We had MRI done in only one case.

More than 50% of the cases responded to phenobarbitone. A study by Pathak et al also showed phenobarbitone to be better than phenytoin in controlling neonatal seizure irrespective of the cause<sup>28</sup> which was the first choice in all of the patients in this study.

The mortality rate was 9.3 % (3 cases). In the rest of 29 cases, 26 cases were discharged, 2 cases were referred to other centre for ICU care and 1 case left against medical advice. The mortality rate was comparable to various studies.<sup>6,9-11,15,17,23</sup> Out of the 3 mortalities, 2 patients had hypoxic ischemic encephalopathy and 1 had Dandy Walker malformations. In various studies, the most common cause of death was hypoxic ischemic encephalopathy.<sup>6,10,11</sup>

## CONCLUSIONS

The higher number of unknown causes of neonatal seizure points to a the need of more diagnostic evaluation in these cases. The most common cause of neonatal seizure is hypoxic ischemic encephalopathy and is also the leading cause of death in neonates with seizure. Therefore improvement in healthcare during the delivery of newborns can decrease the incidence and death due to neonatal seizure.

## REFERENCES

1. Mwaniki M, Mathenge A, Gwer S, Mturi N, Bauni E, Newton CR, Berkley J, Idro R. Neonatal seizures in a rural Kenyan District Hospital: aetiology, incidence and outcome of hospitalization. *BMC Medicine*. 2010;8:16.
2. Talebian A, Jahangiri M, Rabjee M, Alavi NM, Akbari H, Sadat Z. The etiology and clinical evaluations of neonatal seizures in Kashan, Iran. *Iran j child neurol*. 2015;9(2):29-35.
3. Lanska MJ, Lanska DJ, Baumann RJ, Kryscio Rj. A population- based study of neonatal seizures in Fayette County, Kentucky. *Neurology*. 1995;45:724-32.
4. Saliba RM, Annegers FJ, Waller DK, Tyson JE, Mizrahi EM. Incidence of neonatal seizures in Harris County, Texas, 1992-1994. *Am J Epidemiol*. 1999;150:763-9.
5. Ronen GM, Penney S, Andrews W. The epidemiology of clinical neonatal seizures in Newfoundland: a population-based study. *J Pediatr*. 1999;134:71-5.
6. Sadeghian A, Damghanian M, and Shariati M. Neonatal Seizures in a Rural Iranian District Hospital: Etiologies, Incidence and Predicting Factors. *Acta Medica Iranica*, 2012;50(11):760-764.
7. Volpe JJ. *Neurology of the Newborn*. 4th edition, WB Saunders, Philadelphia, 2001.
8. Fakhraee SH. Neonatal seizures: A Review. *Iran J child Neurol* 2007;1(4):7-11.
9. Kuti BP, Oseni SB, and Owa JA. Pattern, etiological factors and determinants of mortality among sick newborns with seizures in Ilesa, Nigeria. *J Pediatr Neurosci*. 2015; 10(3): 227–234
10. Eghbalian F, Rasuli B, Monsef F. Frequency, Causes, and Findings of Brain CT Scans of Neonatal Seizure at Besat Hospital, Hamadan, Iran. *Iran J Child Neurol*. 2015;9(1):56-63.
11. Ghanshyambhai P, Sharma D, Patel A, and Shastri S. To study the incidence, etiology and EEG profile of neonatal seizures: a prospective observational study from India. *J Matern Fetal Neonatal Med*, 2016;29(4):554–558.
12. Holden KR, Mellits DE, Freeman JM. Neonatal seizures.I. Correlation of prenatal and perinatal events with outcomes. *Pediatrics* 1982;70:165-76.
13. Najeeb S, Qureshi AM, Rehman A, Ahmad F, Shah S, Khan AY, Siddiqui TS. Aetiology and types of neonatal seizures presenting at Ayub teaching hospital Abbottabad. *J Ayub Med Coll Abbottabad* 2012;24(1):33-37.
14. Malik AR, Quddusi AI, Naila. Neonatal seizures, experience at Children Hospital and Institute of Child Health Multan. *Pak J Med Sci* 2013;29(5):1128-1131.
15. Malik AR, Groenendaal F, Toet MC, Benders MJN, Nievelstein RA, Vanrooij LGM, De Vries LS. The aetiology of neonatal seizures and the diagnostic contribution of neonatal cerebral magnetic resonance imaging. *Developmental Medicine & Child Neurology* 2015;57:248–256.
16. Yildiz EP, Tatli B, Ekici B, Eraslan E, Aydinli N, Caliskan M, Ozmen M. Evaluation and etiologic and prognostic factors in neonatal convulsions. *Pediatric Neurology*. 2012;47:186-192
17. Anand V, Nair PMC. Neonatal seizures: Predictors of adverse outcome. *J Pediatr Neurosci*. 2014; 9(2): 97–99
18. Raj D. Sheth, MD Gerald R. Hobbs, PhD Martha Mullett, MD. Neonatal Seizures: Incidence, Onset, and Etiology By Gestational Age. *Journal of Perinatology* .1999;19(1):40–43.
19. Lanska MJ, Lanska DJ. Neonatal seizures in the United States: results of the National Hospital Discharge Survey, 1980-1991. *Neuroepidemiology*. 1996;15(3):117-25
20. Plouin P, Kaminska A. Neonatal seizures. *Handb Clin Neurol*. 2013; 111:467-76.
21. Rennie JM, Boylan GB. Seizure disorder of the neonate. In: Levene MI, Chervenak FA, Editors. *Fetal and neonatal neurology and neurosurgery*. 4<sup>th</sup> ed. Philadelphia: Elsevier; 2009.p. 698-710.
22. Calciolari GPerlman JM, Volpe JJ. Seizures in the Neonatal Intensive Care Unit of the 1980s. *Clinical Pediatrics*. 1988;27(3):119-23
23. Tekgul H, Gauvreau K, Soul J, Murphy L, Robertson R, Stewart J, Volpe J, Bourgeois B, du Plessis AJ. The current etiologic profile and neurodevelopmental outcome of seizures in term newborn infants. *Pediatrics*. 2006;117(4):1270-80.
24. Loman AM, ter Horst HJ, Lambrechtsen FA, Lunsing RJ. Neonatal seizures: aetiology by means of a standardized work-up. *Eur J Paediatr Neurol*. 2014 May;18(3):360-7.
25. Sood A, Grover N, Sharma R. Biochemical abnormalities in Neonatal seizures. *Indian J Pediatr*. 2003;70(3):221-224
26. Dehdashtian M, Momen AA, Ziaei T, Moradkhani S. Evaluation of seizure etiology in convulsive neonates admitted to Imam Khomeini and Abozar hospitals of Ahvaz 2004 - 2007. *Jundishapur Scientific Medical Journal* 2009;8(2):163.
27. Ronen GM, Penney S, Andrews W. The epidemiology of clinical neonatal seizures in Newfoundland: a population based study. *Epilepsia* 1995; 36(suppl 4):28.
28. Pathak G, Upadhyay M, Pathak U, Chawla D, Goel SP. Phenobarbitone versus Phenytoin for treatment of Neonatal Seizures: An Open-label Randomized Controlled Trial. *Indian Pediatrics*. 2013;50:753-57