Doi: 10.32677/IJCH.2017.v04.i03.026

Original Article

Clinicoetiology profile of neonatal seizures in tertiary care Level II neonatal intensive care unit

Jyoti Bagla, Hariom Garg, R K Gulati, P P Gupta

From Department of Pediatrics and Neonatology, Government Medical College Kota & Associated Group of Hospitals, Kota, Rajasthan, India

Correspondence to: Dr. Jyoti Bagla, Department of Pediatrics, ESI PGIMSR, Basai Darapur, New Delhi, India.

E-mail: jyotibagla.dr@gmail.com

Received – 12 January 2017 Intial Review – 02 February 2017 Published Online – 05 June 2017

ABSTRACT

Objective: To study the incidence, etiology, and pattern of neonatal seizures and its relationship with age of onset, gestation, and other obstetrical factors. **Design:** Prospective observational descriptive study. **Setting:** Level II neonatal intensive care unit of a Government Medical College Hospital. **Participants:** 72 neonates with neonatal seizures admitted at our hospital and developed seizures before 28 days of life. **Results:** The incidence of neonatal seizure was 11.93/1000 live births. The seizures were more common in male babies and in term newborns (72%). Half of the babies with neonatal seizures were low birth weight (LBW), but seizures were significantly more in appropriate for gestation age in comparisons to small for gestation age babies. Seizure frequency was not different in babies born intramural or extramural and also in deliveries conducted by doctors, nurses, or TBAs. Subtle seizures were the most common pattern observed in both term and preterm newborns (38.9%) followed by generalized tonic (22.3%). Birth asphyxia was most common etiology followed by meningitis in our study. **Conclusion:** Birth asphyxia meningitis, hypocalcemia, and hypoglycemia are common etiology, and the majority present within the first 72 h of life. All the high-risk newborns (asphyxiated or LBW) should be monitored at least 72 h of birth for seizures.

Key words: *Asphyxia, Etiology, Neonatal seizures*

Neonatal seizures often herald potentially devastating form of brain injury. Recent advances in diagnostic technology have provided important insights into neonatal seizures and raised fundamental questions regarding the diagnosis, etiology, and the management of seizures in the newborn. Seizures occur in up to 3/1000 full-term infants and up to 60/1000 premature infants [1]. The reported incidence of neonatal seizures varies widely across studies, and this variability is primarily the result of inconsistent diagnostic criteria, subtle clinical manifestations of the neonatal seizures, and their potential confusion with non-epileptic neonatal behaviors.

It is critical to recognize and determine the etiology and pattern of neonatal seizures rapidly and treat them promptly for the following reasons: (1) They often reflect significant illness, and specific therapy may have profound effect on outcome, (2) neonatal seizures may be sustained for considerable period and interfere with important supportive measures such as alimentation and assisted respiration, (3) seizures *per se* may cause brain damage, (4) presence of neurological squeal correlates with possible etiology of seizures as well as its severity and age of onset of seizures, and (5) family counseling and anticipatory medical care after discharge [2]. This study was conducted to identify the incidence, etiologies, and patterns of neonatal seizures and its relationship with age of onset of seizures, gestational age, and other obstetrical factors.

METHODOLOGY

It was a prospective, observational study conducted in the Level II neonatal intensive care unit (NICU) of the Department of Pediatrics, Government Medical College. It included all the patients up to age of 28 postnatal days/4 weeks with seizures admitted in NICU irrespective of other associated illness/ conditions. A predesigned pro forma was used for recording details for each newborn that included taking the history from parents, attendants and treating doctor, findings of clinical examination and reports of investigations from patient bed-head ticket. Gestation was calculated from last menstrual period using Naegele's formula, available antenatal USG, or New Ballard Scoring System [3].

Obstetrical details including person conducting delivery, place of delivery, delayed cry, need for resuscitation and history of seizures in siblings during neonatal period were recorded. Clinical examination including neurological status, anterior fontanel, head circumference, significant congenital anomalies, neurocutaneous marker, any morbid condition such as neonatal septicemia, neonatal jaundice, necrotizing enterocolitis, meconium aspiration syndrome, apneic spells, kernicterus, and hypoxic ischemic encephalopathy as well as the stage of asphyxiated neonates was also noted. Details of seizures such as age of onset, duration, recurrence, and pattern/type of seizures recorded. The seizures

were classified in 4 essential seizure type, i.e., subtle, clonic, tonic, myoclonic; and 3 subtypes, i.e., focal, multifocal, and generalized seizures [2] as per history and observations of the parents, nursing staff, and treating doctor.

Investigations were carried out to establish possible etiology of seizures and required for the diagnosis and management plan of the individual patients. The blood investigations (complete blood counts, C-reactive protein, blood sugar, serum electrolytes (sodium, potassium, calcium, and magnesium), blood urea, serum creatinine, serum ammonia, and cerebrospinal fluid examination were done. Cranial ultrasonography was done by radiologist in all babies. Computed tomography scan and ECG were done wherever required. In each case, an effort was made to find out the etiological cause of seizures wherever possible. In case of having findings of more than one etiological factor, the probable cause of seizures was identified on clinical ground. Wherever apparent cause of seizure was not found, seizures were designated as idiopathic.

The data were subjected to statistical analysis by Chi-square test, Pearson's coefficient of correlation, and analysis of variance using the Statistical Package of Social Science for Window. A value of $p<0.05$ (for Chi-square test) and $r=-1$ (for Pearson's coefficient of correlation) was considered statistically significant.

RESULTS

The present study comprised 72 neonates suffering from convulsive disorders of varied etiology. Total admission during the study was 6032 live births (4942 Vaginal and 1090 lower segment cesarean section [LSCS] deliveries) making the incidence of neonatal seizure 11.93/1000 live births. Of 72 cases, 50 (69.4%) were male and 22 (30.6%) were female ($p<0.05$). 50 (55.6%) babies were weighing <2.5 kg (34 low birth weight [LBW], 4 very LBW [VLBW], and 2 extremely LBW [ELBW]). There was no significant difference in the seizure incidence in babies weighing <2.5 and >2.5 kg ($p>0.05$). Majority 52 (72.2%) of the cases were full term, while 16 (22.2%) were preterm and 4 (5.6%) were post-term. Term babies had significantly more seizure episodes ($p<0.05$). In addition, incidence of seizures was more ($p<0.05$) in appropriate for gestation age (AGA) than in small for gestation age babies. The incidence of seizures in vaginal (vertex) delivered babies was higher ($p<0.05$) than vaginal (breech) or LSCS delivered babies. The majority of the cases belong to primipara (46, 63.9%) mothers ($p<0.05$). There was no significant difference between seizure incidence and place of delivery or person conducting delivery as shown in Table 1.

Subtle seizures were the most common pattern observed in both term and preterm newborns (38.9%) followed by generalized tonic (22.3%). The incidence of generalized tonic seizures was higher in preterm babies than in term babies ($p<0.05$). In our study, majority of the seizures in newborns were observed in early days of life as more than half of the cases occurred in the first 3 days of life, and 22.2% cases occurred on the first day of life. The incidence of seizures was significantly higher in the 1st week of life than in later weeks of neonatal period ($p\leq0.05$) (Table 3).

Table 1: Baseline characteristics of cases

Characteristics	n (%)	p value
Male:female (n=72)	2.27:1	
Parity		
Primi	40 (55.6)	p<0.05
Multi	32 (44.4)	
Weight for gestation		p<0.05
SGA	20 (27.8)	
AGA	52 (72.2)	
Birth weight		
VLBW (<1.5 kg)	6 (8.3%)	
LBW (1.5-2.5kg)	34 (47.2)	
Normal weight (>2.5 kg)	32 (44.4)	
Mode of delivery		p<0.05
Vaginal (vertex)	58 (80.6)	
Vaginal (breech)	6 (8.3)	
LSCS	8 (11.1)	
Place of delivery		p>0.05
Intramural hospital	26 (36.1)	
Extramural hospital	22 (30.6)	
Extramural home	24 (33.3)	
Person conducting delivery		p>0.05
Doctor	28 (38.9)	
Nurse	28 (38.9)	
TBA/other	16 (22.2)	

LBW: Low birth weight, AGA: Appropriate for gestation age, SGA: Small for gestation age, LSCS: Lower segment cesarean section, VLBW: Very low birth weight

The most common cause for neonatal seizures was birth asphyxia (36.1%) followed by meningitis (22.2%). Other common causes were hypoglycemia (8.3%), hypocalcemia (5.6%), intracranial hemorrhage (ICH) (2.8%), kernicterus (2.8%) as shown in Table 2. Although birth asphyxia, meningitis, and hypoglycemia were more common etiologies in term than in preterm babies, there was no significant statistical correlation for etiological frequency in both the groups. Similarly, there was no significant correlation for etiological frequency difference in male and female, indicating that gender has no etiological predilection. The incidence of different etiologies in relation to age of onset after birth was found statistically significant (Pearson's coefficient of correlation) in the case of asphyxia ($r=-1.0$), hypoglycemia ($r=-1.0$), meningitis ($r=-0.4$), and unknown causes ($r=-0.8$). In other etiologies, significance could not be calculated due to small number of cases.

Cranial USG showed ICH in 4, increased echogenicity of brain parenchyma in 4, ventriculitis in 1, infarct in 1, congenital hydrocephalus in 1, and periventicular leukomalacia in 1 newborn.

DISCUSSION

In our study, seizures were more commonly observed in: (1) males, (2) term babies, (3) LBW with AGA babies, (4) vaginally (vertex) delivered, and (5) babies born to primipara mothers. Subtle seizures were the most common pattern and majority of the

Table 2: Relationship of etiology of seizures versus gender, gestation and age at onset

Etiology	Total n=72 (%)	Sex		Gestation		Day 1	Day 2-3	Day 4-7	Day 8-28
		Male n=50	Female n=22	PT n=16	Term n=56				
Birth asphyxia	26 (36.1)	20	6	2	24	14	10	2	-
Meningitis	16 (22.2)	10	6	5	11	-	-	6	10
Hypoglycemia	6 (8.3)	4	2	2	4	-	4	-	2
Hypocalcemia	4 (5.6)	4	0	2	2	-	2	-	2
ICH	4 (5.6)	3	1	2	2	-	2	-	2
Kernikterus	2 (2.8)	0	2	1	1	-	-	2	-
Stroke	1 (1.4)	0	1	0	1	-	1	-	-
Congenital hydrocephalus	1 (1.4)	1	0	0	1	1	-	-	-
Idiopathic	12 (16.6)	8	4	2	10	1	3	2	6
Total	72 (100)	69%	31%	22%	78%	16 (22%)	22 (30%)	12 (16.6%)	22 (30%)

Table 3: Seizure pattern in relation to gestation

Pattern of seizure	Number of cases (%)	Preterm (%)	Term (%)
Subtle	28 (38.9)	6 (37.5)	22 (39.3)
Generalized tonic	22 (30.6)	8 (50)	14 (25.0)
Multifocal clonic	12 (16.6)	2 (12.5)	10 (16.4)
Focal clonic	6 (8.3)	0 (0)	6 (10.7)
Focal myoclonic	4 (5.6)	0 (0)	4 (7.1)
Total	72 (100)	16 (100)	56 (100)

cases occurred in the first 3 days of life. Birth asphyxia was most common etiology followed by meningitis. The overall incidence of neonatal seizure was 11.93/1000 live births, which was similar to the study done by Kumar et al. [4]. However, reported incidences are less (2.84 per 1000 live births) by Lanska et al. and (2 per 1000 live term births to 11.1 per 1000 live preterm births) by Ronen et al. [5,6]. In this study, there is an overall male sex preponderance which is consistent with other studies. Cockburn et al. and Fredrichsen and Intyrel et al. also reported male sex preponderance in their studies for which no plausible mechanism has been proposed [7-9]. The difference in sex may be attributed to some extent by male child preference in our society as male infants are better cared and treatment for any sickness is sought promptly in many families.

In the present study, majority of the cases were full-term AGA. The incidence of seizures was higher in term newborns in comparison to pre-term ($p \leq 0.05$) newborns contrary to observation of Ronen et al. and Kumar et al. [4,6]. This could be due to fact that 64% of babies among study group were born outside this hospital, and newborns with preterm gestation and significantly low weight (VLBW/ELBW) died before they seek the treatment at this hospital. The risk of seizure varies inversely with birth weight as reported by Lanska et al. and Kumar et al. [4,5]. Holden et al. and Taksande et al. found that the incidence of neonatal seizure were 63% in LBW and 37% in more than 2.5 kg [10,11]. We did not find any difference in seizure incidence between babies >2.5 kg and above 2.5 kg ($p \geq 0.05$). This could be due to fact that newborn of good birth weight with asphyxia (most common reason for convulsions) survived for longer time and could reach this hospital for management. Another observation was that the newborn with term gestation and good weight had more frequency of asphyxia (39.3%) in comparison to pre-term (25%) babies, probably due to the high incidence of obstructed labor in this group.

The 2/3rd (66.7%) of deliveries were conducted at hospitals, and 1/3 (33.3%) deliveries were conducted at home. Statistically, 'place of delivery' and 'person conducting delivery' did not have a significant effect on incidence of seizures ($p \geq 0.05$ for both). The incidence of seizures in vaginal (vertex) delivered babies was higher ($p \leq 0.05$) than vaginal (breech) or LSCS delivered babies. However, the number of vaginal (vertex) deliveries is much higher in study group in comparison to breech and LSCS, as its normal pattern of deliveries.

Subtle seizure was the most common pattern in our observation as reported by other authors [12,13]. However, Kumar et al. found multifocal clonic seizure as the most common pattern [4]. The higher incidence of generalized tonic seizures in pre-term babies in comparison to term babies was found statistically significant ($p \leq 0.05$).

In the present study, asphyxia was the major cause for day 1 and day 2-3 onset seizures (87.5% and 45.5%) and meningitis for late-onset seizures. The high incidence of seizures in 1st week of life was found statistically significant ($p \leq 0.05$) in comparison to later weeks which is similar to the findings of Eriksson et al. [14]. High incidence of early onset neonatal seizures in our study can be explained by the fact that birth asphyxia was the most dominant factor contributing toward neonatal seizures in 2/3rd babies. The incidence of meningitis, hypoglycemia, and hypocalcemia was higher in preterm, while incidence of asphyxia and idiopathic seizures were higher in term babies as reported by others [4,15].

Our study being a prospective observational study had complete records and followed our unit's protocol for the diagnosis and management of neonatal seizures. However, we had limitations of small sample size, non-availability of in-house cerebral function monitor to confirm for abnormal electroencephalogram discharge in all the babies having subtle seizure. Further research with good sample size and neonatal seizures diagnosed not only clinically

but also electrical seizure will give better magnitude of the problem.

CONCLUSION

In our study, incidence of neonatal seizures was 11.93/1000 live births with overall preponderance of male sex, subtle seizures, early onset seizures, and birth asphyxia. Place of delivery and person conducting delivery did not have a significant effect on the incidence of seizures. All the high-risk newborns (asphyxiated or LBW) should be monitored at least 72 h of birth for clinical/subtle seizures.

REFERENCES

1. Adre JD, Cloherty JP, Eichenwald EC, Stark AR, editors. Neonatal Seizures in Manual of Neonatal Care. 5th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2004. p. 507-23.
2. Volpe JJ, editor. Neonatal seizures. Neurology of the New Born. 4th ed. Philadelphia, PA: W.B. Saunders; 2001. p. 178-216.
3. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. J Pediatr. 1991;119(3):417-23.
4. Kumar A, Gupta A, Talukdar B. Clinico-etiological and EEG profile of neonatal seizures. Indian J Pediatr. 2007;74(1):33-7.
5. Lanska MJ, Lanska DJ, Baumann RJ, Kryscio RJ. A population-based study of neonatal seizures in Fayette County, Kentucky. Neurology. 1995;45(4):724-32.
6. Ronen GM, Penney S, Andrews W. The epidemiology of clinical neonatal seizures in Newfoundland: A population-based study. J Pediatr. 1999;134(1):71-5.
7. Cockburn F, Brown JK, Belton NR, Forfar JO. Neonatal convulsions associated with primary disturbance of calcium, phosphorus, and magnesium metabolism. Arch Dis Child. 1973;48(2):99-108.
8. Fredrichsen C. Tetany in a sucking infant with latent osteitis fibrosa in the mother. Lancet. 1939;1:85-6.
9. Intyrel M, Boss S, Va T. Parathyroid hormones and magnesium homeostasis. Nature. 1963;198:1058-60.
10. Holden KR, Mellits ED, Freeman JM. Neonatal seizures. I. Correlation of prenatal and perinatal events with outcomes. Pediatrics. 1982;70(2):165-76.
11. Taksande AM, Vilhekar K, Jain M, Lakra M. Clinico-Biochemical Profile of Neonatal Seizures. Pediatric Oncall; 2005. p. 2. Available from: http://www.pediatriconcall.com/fordoctor/Medical_original_articles/neonatal_seizures.asp. [Last cited on 2010 Oct 01].
12. Mizrahi EM, Kellaway P. Characterization and classification of neonatal seizures. Neurology. 1987;37(12)1837-44.
13. Scher MS. Controversies regarding neonatal seizure recognition. Epileptic Disord. 2002;4(2):139-58.
14. Eriksson M, Zetterström R. Neonatal convulsions. Incidence and causes in the Stockholm area. Acta Paediatr Scand. 1979;68(6):807-11.
15. Kumar A, Gupta V, Kachhawaha JS, Singla PN. Biochemical abnormalities in neonatal seizures. Indian Pediatr. 1995;32(4):424-7.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Bagla J, Garg H, Gulati RK, Gupta PP. Clinicoetiology profile of neonatal seizures in tertiary care Level II neonatal intensive care unit. Indian J Child Health. 2017; 4(3):383-386.