International Journal of Contemporary Pediatrics
Sudia S et al. Int J Contemp Pediatr. 2015 Nov;2(4):389-394
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20150981

Research Article

Clinicoetiological profile and outcome of neonatal seizures

Sanjeev Sudia, Pramod Kumar Berwal, Niranjan Nagaraj*, Prathyusha Jeavaji, Sarika Swami, Ayush Berwal

Department of Paediatrics, SPMC, Bikaner, Rajasthan, India

Received: 21 August 2015
Accepted: 20 September 2015

***Correspondence:**
Dr. Niranjan Nagaraj,
E-mail: getniranjan806@yahoo.com

ABSTRACT

Background: Neonatal seizures are abnormal electrical discharge in the central nervous system of neonates, usually manifesting as stereotyped muscular activity or automatic changes. This study aims to determine the, clinical types, etiological factors and developmental outcome of neonatal seizures.
Methods: It is a prospective study conducted in NICU of PBM Hospital, Bikaner, India. Total 1278 neonates were admitted, out of which 150 had seizures. Details of history, examination and investigations were recorded on predesigned performa. Cases were followed at 6 months of age for developmental outcome.
Results: Intramural and extramural incidence of seizures was 1.42% and 10.16% respectively. Incidence in extreme low birth weight, very low birth weight and in low birth weight was 29.41%, 26.71% and 10.73% respectively. Male preponderance with male to female ratio was 1.73:1. 96 (64%) neonates born to primi and 54 (36%) were born to multiparous mother. Most common type of neonatal seizure is subtle 95 (63.33%) followed by generalized tonic 29 (19.33%), multifocal clonic 15 (10%), focal tonic and focal clonic 4 (2.67%) each and myoclonic 3 (2%). Most common cause of neonatal seizures is perinatal asphyxia 80 (53%) followed by metabolic causes 24 (16%), infections 15(10%), intracranial hemorrhage in 7 (4.66%), meconium aspiration syndrome (MAS) 5 (3.33%), bilirubin encephalopathy and polycythemia 2 (1.33%) each and 12 (8%) had undetermined etiology.
Conclusions: Most common type of neonatal of neonatal seizure is subtle, most common cause is perinatal asphyxia. Excellent outcome was seen in seizures due to electrolyte imbalance, MAS, neonatal septicemia, bronchopneumonia and polycythemia. Worst outcome was with HIE (Hypoxic ischemic encephalopathy) grade III and encephalitis.

Keywords: Neonatal seizures, Perinatal asphyxia, Bikaner, Outcome

INTRODUCTION

The occurrence of any manifestation of neonatal seizures (NS) indicates a primary or secondary dysfunctions of the central nervous system.[1-3] Thus, determination of etiology is critical, because it gives the opportunity to treat and to make a meaningful statement about the prognosis.[3-5] Nowadays, NS is defined by video - electroencephalographic monitoring, by clinical observation associated to ictal or interictal electroencephalogram (EEG), by electrographic discharge without associated clinical manifestation or by neonatal polysomnography[4,6-12]. However, in clinical practice at the pediatric or neonatal intensive care units (ICU), in developing countries where synchronized video-EEG monitoring is practically non-existent, clinical observation becomes the key to the diagnosis[3]. On the other hand, we know that seizure phenomenon in preterm infant (PN) is less organized than it is in Full-Term infant (FT).[3,13,14] Volpe[15] has classified seizures into five clinical types, viz. subtle, multifocal clonic, focal clonic, generalized tonic and myoclonic. Moreover, neonatal seizures are difficult to investigate

and consequently determination of etiology and initiation of therapy may be delayed resulting in poor neurological outcome. Neonatal seizures can be due to various causes such as hypoxic-ischemic encephalopathy, intracranial hemorrhage (ICH), meningitis, hypoglycemia, hypocalcemia, congenital malformation, etc.

Neonatal seizures are abnormal electrical discharge in the central nervous system of neonates, usually manifesting as stereotyped muscular activity or automatic changes.[16] Neonatal seizures by definition occur within the first 4 weeks of life in a full-term infant and up to 44 weeks from conception for premature infants[17] and are most frequent during the first 10 days of life.[18] Neonatal seizure is not uncommon cause of morbidity and mortality in later life, hence need of study is to find out causes of neonatal seizures which would help in early recognition and treatment of neonatal seizures and hence better prognosis in neonatal seizures.

METHODS

This study was conducted in the Department of Paediatrics , Sardar Patel Medical College & Associated Group of Hospital, Bikaner (Rajasthan) from November 2013 to October 2014, with written ethical clearance from ethical committee of college. This study includes Neonatal seizures occurring in the first 4 weeks of life in a full term infant and up to 44 weeks from conception for premature infants and excludes Neonates with isolated subtle phenomenon, apnoea or paroxysmal autonomic changes i.e. only subtle motor movements or apnoea without tachycardia were excluded from the study, jitteriness, tetanic spasms.

Detailed antinatal history (age, parity of mother, history of ANC checkups, medical illness and obstetric complications like PIH, antepartum haemorrhage, oligo or polyhydramnios, preterm labour, obstructed labour), perinatal history (meconium staining of liquor, place and type of delivery, baby cried immediately or not, any resuscitation, Apgar score and medication given to the baby) and postnatal history were taken. Clinical details of each seizure episode reported by the mother and subsequently observed by resident doctors on duty were recorded, i.e. type, duration, number and consciousness during and between seizures were taken. Seizures were classified according to Volpe's classification into subtle, multifocal clonic, focal clonic, tonic and myoclonic[15]. General physical and systemic examination of neonate was done according to performa. Anthropometry recorded and gestational age assessed according to New Ballard Scoring. Following investigations was done for to determine the cause of seizure in neonates. Complete blood count, sepsis screening: CRP and blood culture if necessary. Blood sugar: Random blood sugar was done urgently with glucostick. Hypoglycaemia was diagnosed if RBS is <40 mg/dL. Serum electrolytes were done on emergency basis, serum Ca^{+2}, serum Na^{+1}, serum Mg^{+2} were done - hypocalcaemia defined when total serum calcium <8.0 mg/dl (2 mmol/L) or iCa below 1.0 mmol/L (4.0 mg/dl), hypomagnesaemia <1.5 mg/dL, hyponatremia when serum Na <135 mEq/L and hypernatremia when serum Na >150 meq/L. Chest X-ray, liver function test, blood urea and serum creatinine. In selected cases CSF analysis, USG, PT/APTT, blood group, ABG, EEG, CT-scan/MRI were done. Statistical analysis was done by using appropriate methods.

RESULTS

During our study total 6340 were live born, out of which 90 patients had seizures comprising 1.42%. Total 590 cases were referred from outside, out of which 60 patients had seizures. Total 1278 patients were admitted in NICU including inside as well as born outside, out of which 150 patients had seizures. Out of 1278, 480 were preterm, 774 were full term and 24 were post term 17 had ELBW (extreme low birth weight), 307 had VLBW (very low birth weight) and 354 had LBW (low birth weight) and 600 had normal weight. In our study, incidence of seizures is more in preterm (19.16%) than term (7.23%) and post term (8.33%). Maximum in ELBW 29.41% and minimum in cases with normal weight 4.16%. The total intramural incidence is 1.42%, preterm having more 4.33% than term 0.51%. Maximum in ELBW 10.52% and minimum in cases with normal weight 0.63%. The total extramural incidence is 10.16%. Post term having more incidence (50.50%) than pre term (14%) and term (5.59%). Maximum in ELBW (16.66%) and minimum in cases with normal weight (6.40%). out of total 150 cases, 92(61.33%) cases were preterm while 56 (37.33%) cases were term and only 1.33% cases were post term, 54.66% babies had very low birth weight while 25.33% babies had low birth weight, 16.66% had normal weight and 3.33% had extreme low birth weight, male preponderance over females where the male to female ratio was 1.73, 64% were born to primi gravida while 36% were born to multi gravida.

Table 1: Showing distribution of total cases admitted in NICU.

Patient	Total	PT	FT	Post T.	ELBW	VLBW	LBW	NW
With seizure	150 (11.73%)	92 (19.16%)	56 (7.23%)	2 (8.33%)	5 (29.41%)	82 (26.71%)	38 (10.73%)	25 (4.16%)
Without seizure	1128	388	718	22	12	225	316	575
Total	1278	480	774	24	17	307	354	600

Table 2: Distribution of cases according to type of seizures (n=150).

Type of seizures	No. of cases	Percentage
Subtle	95	63.33
G. tonic	29	19.33
MF clonic	15	10.00
F. tonic	4	2.67
Focal clonic	4	2.67
Myoclonic	3	2.00
Total	150	100.0

In our study, most common type of seizure was subtle (63.33%) followed by generalized tonic (19.33%), multifocal clonic (10%), focal tonic and focal clonic (2.67% each) while least common type of seizure was myoclonic only 2%. In this study, 80 (53.33%) cases had birth asphyxia/HIE while 24 (16%) cases had metabolic disorder, 15 (10%) cases had infection, 7 (4.66%) cases had intracranial haemorrhage, 5 (3.33%) had meconium aspiration syndrome, 3 (2.00%) had bronchopneumonia, 2 (1.33%) had bilirubin encephalopathy and polycythemia each while 12 (8%) cases had undetermined etiology. In our study, most common risk factor was preterm delivery while least common risk factor was diabetic mother and hypothyroidism where only 1.33% cases were found. In this study 69 cases had HIE grade II and out of them 16 (23.18%) patients were expired while 11 cases had HIE grade III and out of them 5 (45.45%) were expired. No case had HIE grade I. and 80 (53.33%) were completely recovered while 41 (27.34%) cases discharged with sequelae and 29 (19.33%) patients were expired. In present study six month follow up was done, out of 150 cases 29 were expired during hospital admission and 121 cases were discharged. Out of these 121, 6 cases did not come in follow up study.

Table 3: Shows distribution of cases according to etiology (n=150).

Etiology	No. of cases	%
Birth ashphyxia/HIE	80	53.33
Metabolic disorder	24	16.00
Hypocalcemia	9	6.00
Hypoglycemia	6	4.00
Hypocalcemiawith hypomagnesemia	3	2.00
Hyponatremia	3	2.00
Hypomagnesemia	2	1.33
Hypernatremia	1	0.66
Infections	15	10.00
Neonatal septicemia (nns)	11	7.33
Meningitis	3	2.00
Encephalitis	1	0.66
Intracranial haemorrhage	7	4.66
Intraventricular haemorrhage	4	2.66
Subgaleal haemorrhage	2	1.33
Subdural haemorrhage	1	0.66
Meconium aspiration syndrome	5	3.33
Bronchopneumonia	3	2.00
Bilirubin Encephalothy	2	1.33
Polycythemia	2	1.33
Undetermined etiology	12	8.00

Table 4: Showing developmental distribution of cases according to etiology.

Etiology	Total	Exp.	Follow-up cases	Norm. devel.	Global delay	Gross	Fine	Lang	Social
HIE II	69	16	53	42 (79.24%)	9 (16.98%)	0	0	1 (1.88%)	1 (1.88%)
HIE III	11	5	5	0 (0.0%)	5 (100%)	0	0	0	0
Hypocalcemia	9	0	9	7 (77.77%)	2 (22.22%)	0	0	0	0
Hypoglycemia	6	2	4	1 (25%)	2 (50%)	0	0	0	1 (25%)
Hypoca+Hypomg	3	0	2	2 (100%)	0 (0.00%)	0	0	0	0
Hyponatremia	3	0	2	2 (100%)	0 (0.00%)	0	0	0	0
Hypomg	2	0	2	2 (100%)	0 (0.00%)	0	0	0	0
Hypernatremia	1	0	0	-	-	-	-	-	-
NNS	11	0	10	10 (100%)	0 (0.00%)	0	0	0	0
Meningitis	3	0	3	1 (33.33%)	2 (66.66%)	0	0	0	0
Encephalitis	1	0	1	0 (0.00%)	1 (100%)	0	0	0	0
ICH	7	3	4	2 (50%)	2 (50%)	0	0	0	0
MAS	5	1	4	4 (100%)	0	0	0	0	0
Bronchopneumonia	3	0	3	3 (100%)	0	0	0	0	0
Polycythemia	2	0	2	2 (100%)	0	0	0	0	0
Bilirubin enceph.	2	0	2	0 (0.00%)	2 (100%)	0	0	0	0
Undetermined	12	2	9	3 (33.33%)	3 (33.33%)	0	0	2 (2.22%)	1 (1.11%)
Total	150	29+2*	115	83 (72.17%)	26 (22.60%)	0	0	3 (2.61%)	3 (2.61%)

DISCUSSION

In During our study total 6340 were live born, out of which 90 patients had seizures comprising 1.42%. Total 590 cases were referred from outside, out of which 60 patients had seizures, comprising 10.16%. Total 1278 patients were admitted in NICU including inside as well as born outside, out of which 150 patients had seizures comprising 11.73%. In our study over all incidence of neonatal seizure by clinical observation is 11.73%. Intramural incidence is 1.42% and extramural incidence is 10.16%. Bhatt et al.[19] found 1% intramural and 18% extramural incidence, Kumar et al.[20] found 1.17% intramural incidence and Sahana et al.[21] found 14% extramural incidence of neonatal seizures which is comparable with our study. In present study as per table no.4, seizures in preterm 61.33% (92) have more as compared to term 37.33% (56) cases and post term 1.33% (2) cases. As per Table 1 overall incidence among term is 7.23% and in preterm is 19.16% as most of cases were referred from outside with birth asphyxia. Intramural incidence of seizures in preterm is 4.33%, in full term is 0.51%. case of neonatal seizure with very low birth weight baby are 54.66% (82), with low birth weight are 25.33% (38) and with normal birth weight are 16.66% (25) and with extreme low birth weight are 3.33% (5). In our study over all incidence in ELBW is 29.41% (5 cases out of total 17), in VLBW is 26.71% (82 cases out of total 307), in LBW is 10.73% (38 cases out of total 354). As per table no.2 intramural incidence among ELBW is 16%, in VLBW is 10.52%, in LBW is 2.00% and in cases with normal weight is 0.63%. Kumar et al.[20] found 10.14% incidence in very low birth weight, 1.51% in low birth weight and 0.59% in normal birth weight, Bhatt et al[19] and Eghbalian et al.[22] found intramural incidence of neonatal seizures in LBW 2.8% and 6% respectively which is comparable with our study. Extramural incidence among ELBW is 16.66%, in VLBW is 12.50%, in LBW is 13.8% and in cases with normal weight is 6.40%. Seizure were more common in male 63.33% (95) newborn as compared to female 36.66% (55) with male to female ratio 1.73:1 which is comparable with study by Bhatt S et al.[19] in which male to female ratio was 2.37:1, Eghbalian et al.[22] found slightly higher male to female ratio 3:1. Neonatal seizure are more common in neonates born to primi 64% (96) than in neonates born to multiparous women 36% (54) due to prolonged labor, difficulties in delivery and difficulties in feeding leading to delayed feeding. In our study most common type of neonatal seizure is subtle type 95 (63.33%) followed by generalized tonic 29 (19.33), multifocal clonic 15 (10%), focal tonic and focal clonic 4 (2.67% each) and myoclonic 3 (2%). Mizrahi and Kellaway,[10] Scher et al.,[11] also found subtle type as most common type seizure which is comparable with our study. In our study perinatal asphyxia 80 (53.33%) was most common cause of neonatal seizure followed by metabolic causes 24 (16%), infections 15 (10%), intracranial hemorrhage in 7 (4.66%), meconium aspiration syndrome 5 (3.33%), bronchopneumonia 3 (2.00%), bilirubin encephalopathy and polycythemia each 2 (1.33%) while 12 (8%) cases had undetermined etiology. Sood et al.[23] and Kumar[20] found birth asphyxia as etiology of neonatal seizure 48.27% and 45.71% respectively which are comparable with our study. Hypocalcaemia was in 9 (6%) and hypoglycemia in 6 (4%). Out of 9, 8 were preterm in hypocalcemic seizure and only one was term. So prematurity is important risk factor for hypocalcemic seizure. Incidence of hypocalcemic seizure range from 1.1-22%.[18,19] Sood et al.[23] found hypoglycemia and hypocalcaemia as most common metabolic etiology of neonatal seizure which are comparable with our study. Infections were detected in 15 (10%) cases as an etiology of neonatal seizures. Out of these 11 (7.33%) were neonatal septicemia, 3 (2.00%) were meningitis and 1 (0.66%) was encephalitis. So most common infectious cause of neonatal seizure is neonatal septicemia. Kumar et al.[20] found 9 (7.77%) cases due to neonatal infections which is comparable with our study. Intracranial hemorrhage (ICH) etiology was in 7 (4.66%) cases. Out of which 4 (2.66%) were intraventricular hemorrhage (IVH), 2 (1.33%) were subgaleal hemorrhage and 1 (0.66%) was subdural hemorrhage. Out of 7 cases due to IVH, 5 were preterm and 2 were term. So prematurity is important risk factor for neonatal seizure due to IVH. Sahana et al.[21] found 6 (5%) and Bushra et al.[24] found 9% case due to intracranial hemorrhage as a etiology of neonatal seizure which are comparable with our study. In present study incidence of undetermined neonatal seizure is 8%. Possible causes could be non-availability of pyridoxine, bed side cranial USG and EEG and short survival interval between seizure episode and death. Sahana et al.[21] found 4.58% undetermined etiology of neonatal seizures which is comparable with our study. The most common risk factor associated with neonatal seizure is prematurity (60%). Other risk factor associated with seizures are like delayed cry (50.67%), resuscitation required (19.33%), meconium stained liquor (12%), Fetal distress (8%), family history of similar complain (6%), family history of neurological disorder (5.33%), obstructed labor (4.67%), polyhydro-mnious and oligohydromnious (3.33% each), while PIH and history of drug injection lignocaine (2.67% each), according to HIE Grade, 69 cases had HIE grade II and out of them 16 (23.18%) patients were expired while 11 cases had HIE grade III and out of them 5 (45.45%) were expired. So mortality is more in HIE III as compared to HIE II. In present study out of 150 cases 29 were expired during hospital admission and 121 cases were discharged. Out of these 121, 6 cases did not come in follow up study. In HIE grade II etiology, 79.24% (42) cases had normal development, 16.98% (9) cases had global developmental delay and 1.88% (1) case had isolated language and social developmental delay in each group. In HIE grade III, encephalitis and Bilirubin encephalopathy etiology, all (5) cases had global developmental delay. In Hypocalcaemia etiology, 7.77% (7) cases had normal development, 2.22% (2) cases had global developmental delay. In hypoglycemia etiology, 25% (1) cases had normal development, 50% (2) cases had global

developmental delay and 25% (1) case had isolated social developmental. In patients with following etiology all cases had normal development: hypocalcaemia with hypogmagnesaemia, hyponatremia, hypomagnesemia, MAS, NNS, Bronchopneumonia and polycyhemia.

In meningitis etiology out of 3, 2 cases had global developmental delay and 1 had normal development. In intracranial haemorrhage etiology, 50% (2) cases had normal development, 50% (2) cases had global developmental delay. In undetermined etiology, 3.33% (3) cases had normal development, 3.33% (3) cases had global developmental delay and 2.22% (2) case had isolated language and 1.11% (1) had social developmental delay. Over all 70.43% (81) cases had normal development, 24.34% (28) cases had global developmental delay, 2.61% (3) had isolated language and social developmental delay each group. Iype et al. found 68% normal development and 32% abnormal developmental outcome in follow up study of neonatal seizures which is comparable with our study. Excellent outcome was seen in cases with seizure due to electrolyte imbalance, MAS, bronchopneumonia and polycythaemia (100% normal development in each category). Worst outcome was in cases seen with HIE grade III, encephalitis and bilirubin encephalopathy (100% global developmental delay in each group).

CONCLUSION

Most common type of neonatal seizure is subtle followed by generalized tonic and multifocal clonic. So vigilant monitoring in NICU would lead to early recognition of neonatal seizures specially subtle seizures. Most common cause of neonatal seizure is perinatal asphyxia/HIE. Hypocalcaemia and hypoglycemia are most common metabolic causes of neonatal seizure. Prematurity and low birth weights are important risk factors of neonatal seizure. Most common risk factor associated with seizures is Preterm delivery followed by delayed cry. Excellent outcome was seen in cases with seizure due to electrolyte imbalance, NNS, MAS, bronchopneumonia and polycythaemia. Worst outcome was in cases seen with HIE grade III, encephalitis and bilirubin encephalopathy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Lanska MJ, Lanska DJ, Baumann RJ, Kryscio RJ. A population- based study of neonatal seizures in Fayette County, Kentucky. Neurology. 1995;45:724-32.
2. Scher MS. Neonatal seizures and brain damage. Pediatr Neurol. 2003;29:381-90.
3. Volpe JJ. Neonatal seizures. In: Volpe JJ, eds. Neurology of the Newborn. 4th ed. Philadelphia: Saunders; 2001: 178-214.
4. Mizrahi EM. Neonatal seizures: problems in diagnosis and classification. Epilepsia. 1987;28(Suppl 1):S46-55.
5. Patrizi S, Holmes GL, Orzalesi M, Allemand F. Neonatal seizures: characteristics of EEG ictal activity in preterm and fullterm infants. Brain Dev. 2003;25:427-37.
6. Caravale B, Allemand F, Libenson MH. Factors predictive of seizures and neurologic outcome in perinatal depression. Pediatr Neurol. 2003;29:18-25.
7. Holmes GL, Lombroso CT. Prognostic value of background patterns in the neonatal EEG. J Clin Neurophysiol. 1993;10:323-52.
8. McBride MC, Laroia N, Guillet R. Electrographic seizures in neonates c o r relate with poor neurodevelopmental outcome. Neurology. 2000;55:506-13.
9. Lombroso CT, Holmes GL. Value of the EEG in neonatal seizures. J Epilepsy. 1993;6:30-70.
10. Mizrahi EM, Kellaway P. Characterization and classification of neonatal seizures. Neurology. 1987;37:1837-44.
11. Scher MS. Eletroencephalography of the newborn: normal an abnormal features. In: Niedermeyer E, Lopes da Silva F, eds. Eletroencephalography: Basic Principles, Clinical Applications and related Fields. 4th ed. Baltimore: Williams & Wilkins; 1999: 886-946.
12. Oliveira AJ, Nunes ML, da Costa JC. Polysomnography in neonatal seizures. Clin Neurophysiol. 2000;111(Suppl 2):S74-80.
13. Hughes JR, Fino J, Gagnon L. The use of the electroencephalo-gram in the confirmation of seizures in pre mature and neonatal infants. Neuropediatrics. 1983;14:213-9.
14. Legido AC. Convulsions neonatales: comentarios sobre aspectos controvertidos. An Esp Pediatr. 1991;1:1-8.
15. Volpe J. Neonatal seizures. N Engl J Med. 1973;289(8):413-6.
16. Volp JJ. Neonatal seizures. In: Volp JJ, eds. Neurology of Newborn. 4th ed. Philadelphia: WB Saunders; 2000: 178-216.
17. Singh M. Neurology disorders. In: Singh M, eds. Textbook of Care of Newborn. 2nd ed. Delhi: Sagar Publication; 1999: 340-344.
18. Vigavano F. Benign familial infantile seizures. Brain Dev. 2005;27:172.
19. Bhatt S, Raju N, Phanse S, Patel SV, Madan G, Mehta S, et al. Clinico-etiological and EEG profile of neonatal seizures. Ind J Clin Pract. 2013;24(1):69-75.
20. Kumar A. Clinicoetiological and EEG profile of neonatal seizure. Indian J Paediatr. 2002;74(1)33-7.
21. Sahana G, Anjaiah B. Clinical profile of neonatal seizures. Int J Med Applied Sci. 2014;3(1):21-7.

22. Eghbalian F, Monsef A. Neonatal seizures: etiology and frequency. Iran J Child Neurol. 2007;2(1):39-42.
23. Sood A, Grover N, Sharma R. Biochemical abnormalities in neonatal seizures. Indian J Pediatr. 2003;70:221-4.
24. Bushra AM, Butt MA, Shamoon M, Tehseen Z, FAthima A, Hashmat N. Seizures etiology in the newborn period. J Coll Physicians Surg Pak. 2005;15(12):786-90.

Cite this article as: Sudia S, Berwal PK, Nagaraj N, Jeavaji P, Swami S, Berwal A. Clinicoetiological profile and outcome of neonatal seizures. Int J Contemp Pediatr 2015;2:389-90.