



STUDY OF CLINICOINVESTIGATIVE PROFILE AND IMMEDIATE OUTCOME OF NEONATAL SEIZURES AT TERTIARY CARE HOSPITAL

Paediatrics

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ABSTRACT

Background- Neonatal seizure are abnormal electrical discharge in the central nervous system of neonates, usually manifesting as stereotyped muscular activity or automatic changes. Seizures in neonates are very different from those of older children and adults.

Objective

- To study the occurrence of neonatal seizures in rural tertiary care center.
- To study the clinical features and outcome of neonatal seizures

Design- Retrospective observational hospital based study **Study period-** January 2022- September 2022 **Setting-** Department of pediatrics of teaching hospital in rural india. **Methodology-** Neonates enrolled in this study with details of history, examination and investigation was recorded. Statistical analysis was done by SPSS 16 software. **Result-** out of 40 patients evaluated, males were 23(57.5%), and females were 17(42.5%). Male:female ratio was 1.35:1 . 33(82.5%) babies were born preterm and 7(17.5%) babies were born term. Majority 26(65%) were LBW, 20.8% were VLBW and 15% had normal birth weight. 71.8% neonates presented with convulsions within 48 hours of life. Most common type of neonatal seizures was subtle 62.8%, followed by focal clonic in 18%, generalized tonic 7% and remaining types were mixed(multifocal tonic, myoclonic) in 12% patients. Most common etiology of neonatal seizures was birth asphyxia in 54.8% neonates, followed by metabolic causes in 42.5% followed by meningitis and sepsis in 12.5% neonates. Among the metabolic abnormalities, hypoglycemia followed by hypocalcemia was commonest. 32% babies had abnormalities on neurosonography. Mortality was 7%. **Conclusion-** Neonatal seizures indicate significant underlying disease. Most common type of neonatal seizure is subtle and most common cause is perinatal asphyxia.

KEYWORDS

Neonatal seizures, birth asphaxia, neurosonography, hypoglycemia

INTRODUCTION:

In the newborn infant, seizures may occur due to an underlying cerebral and biochemical abnormality. Seizures are more common in newborn period than in any other phase of human life. Their incidence varies from 0.5% to 0.8% in term babies and 6-12% in babies weighing less than 1500g. Newborn babies do not manifest febrile convulsions. Developmental immaturity influences many aspects of diagnosis, management, and prognosis of seizures in the newborn: (i) Clinical seizure patterns in the neonate reflect the "reduced connectivity" in the neonatal brain, with prominence of focal ictal characteristics and rarity of generalized patterns of clinical seizures. (ii.) The balance of excitatory and inhibitory processes in the immature brain are weighted toward excitation with an excess of glutamatergic synapses over inhibitory (usually gamma-aminobutyric acid (GABA)-ergic) synapses.

Cause	Frequency
Hypoxic-ischemic encephalopathy	30-50%
Metabolic disorders Hypoglycemia, Hypocalcemia Hypomagnesemia, Hypo/hypnatremia	5-20%
Intracranial hemorrhage	5-15%
CNS malformation	6-15%
Meningitis (Fetal and neonatal)	2-15%
Cerebral infarction	4-12%
Inborn error of metabolism	3-5%
Acute bilirubin encephalopathy	1-2%
Maternal drug withdrawal	1%
Benign idiopathic neonatal seizures	1%
Neonatal epilepsy syndromes	<1%
Idiopathic	4-5%

Etiology:

The details of the pregnancy, birth history, maternal history, and family history are most important in directing the initial evaluation: For instance, a history of traumatic delivery, with good APGAR scores in a term infant, raises the possibility of intracranial hemorrhage (ICH).

Hypoxic-ischemic encephalopathy (HIE), which is the single most common cause of neonatal seizures, usually causes seizures within the first 24 hours of life. Focal seizures in the setting of a well-appearing non-encephalopathic newborn raises suspicion of perinatal infarction.

When seizures present after the first 48 hours of life, and particularly after a period of initial well-being, infection and metabolic disorders should be considered.

1. HIE

This is the most common cause of neonatal seizures, accounting for 50-75% of cases. In perinatal asphyxia, the seizures occur in the context of a newborn who has a history of difficulty during labour and delivery with alterations of the fetal heart rate, decreased umbilical artery Ph, and APGAR score <5 at 5 minutes.

2. Perinatal stroke

This is the second most common cause of seizures in the newborn period accounting for up to 20% of neonatal seizures.

3. ICH

ICH are responsible for 10-15% of neonatal seizures. In the term infant, primary subarachnoid hemorrhage (not due to extension of a deeper cerebral or intraventricular hemorrhage) is probably more common than realized. In the preterm infant, germinal matrix, intraventricular and parenchymal hemorrhages are the prototypic neurologic complications of premature hypoxic injury.

Classification of neonatal seizure

- Subtle seizure
- Focal clonic
- Focal tonic
- Myoclonic
- Generalised tonic

Material and methods

- Source- All neonates presenting with seizure admitted to the NICU at tertiary care hospital PRH LONI in last 8 months
- Study duration- January 2022- August 2022.
- Methods of collection of data- The data for study is collected from neonates fulfilling inclusion criteria and admitted to the NICU at tertiary care hospital PRH LONI in last 8 months.
- Type of study- Descriptive observational hospital based study.
- Sample size- 40 patients
- Inclusion criteria- All inborn neonates developing seizure in PRH LONI

- Exclusion criteria- All outborn neonates

Methodology

- Written consent was obtained from the parents of neonates included in our study.
- Details history of inborn neonates with seizure and through clinical examination were recorded
- Common biochemical parameters were estimated like blood sugar level, serum calcium, serum magnesium.
- Basic finding in convulsive neonate like weight, gestational age, sex and anthropometric measurement were noted
- Radiological study were done in all surviving neonates

Results

Table-1-Male and female distribution

	Preterm	Term	Total	Percentage
Male	19	4	23	57.5%
Female	14	3	17	42.5%
Total	33	7	40	100%

NUMBER OF CASES AS PER GESTATIONAL AGE



Fig 1-Preterm and term distribution

TOTAL NUMBER OF CASES ACCORDING TO WEIGHT

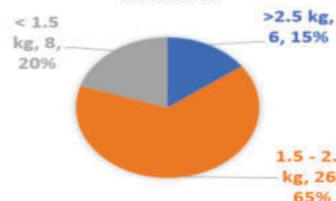


Fig 2-Birth weight distribution

Out of 40 patients, 23 (57.5%) were male patients and 17 (42.5%) were female patients, out of which 19 (82.60%) were preterm male and 14 (82.35%) were preterm female and 4 (17.39%) were term male, and 3 (17.64%) were term female patients. Male to female ratio was 1.3:1. In neonatal seizure male are more affected than female.

Out of 40 neonatal seizure patients 33 (82.5%) were preterm and 7 (17.5%) term patients were affected. In total 40 patients of neonatal seizures 6 (15%) were weight more than 2.5kgs, 26 (65%) were weight between 1.5-2.5kgs and 8 (20%) were weight below 1.5kgs. Low birth weight babies has more number of neonatal seizure percentage followed by very low birth weight babies. Out of 40 neonates, 28 (71.8%) presented with early onset neonatal seizures (i.e. within 48 hours of birth). 12 (28.2%) neonates presented with onset of seizure after 48 hours.

Table 2 Clinical assessment of patient with neonatal seizure

Parameter	Total	Percentage
Seizure activity	40	100%
Hypothermia	32	80%
Icterus	28	70%
Absent neonatal reflex	26	65%
Hypotonia	13	32.5%
Irritability	12	30%
Poor suck	16	40%
Petechial Hemorrhage	7	1.7%
Bleeding Tendency	7	1.7%
Tachycardia	34	85.5%
APGAR score 1 < 8 at end of 1 min	18	45%
APGAR score 2 < 8 at end of 5 min	18	45%

Clinical assessment of patient with neonatal seizure

Thorough clinical assessment was done in all patients including general and systemic examination. clinical seizure activity was present

in all patients i.e. 100%. Hypothermia was present in 32 patients i.e. 80%. Icterus was present in 28 babies i.e. 70%. Absent neonatal reflex was present in 26 patients i.e. 65%. Hypotonia was present in 13 babies i.e. 32.5%. Irritability was present in 12 babies i.e. 30%. Poor suck was present in 16 babies i.e. 40%. Petechial hemorrhage was present in 7 babies i.e. 1.7%. Bleeding tendency was present in 7 babies i.e. 1.7%. Tachycardia was present in 34 babies i.e. 85.5%. Apgar score 1 < 8 at end of 1 min was present in 18 babies i.e. 45%. Apgar score 2 < 8 at end of 5 min present was 18 babies i.e. 45%. most common clinical presentation was seizure activity followed by tachycardia.

Table no 3- Patient distribution according to seizure type

Type of seizure	Total	Percentage
Subtle	25	62.8 %
Focal clonic	8	18 %
Generalized tonic	2	7 %
Mixed	5	12.2 %

Out of all seizure episode, most common type of neonatal seizure was subtle 25 (62.8%) followed by focal clonic in 8 (18%), generalized tonic 2 (7%) and remaining types were mixed (multifocal tonic, myoclonic). Most common type of seizure seen in preterm neonate was subtle followed by focal clonic seizure. In term neonate, most common type of seizure was focal clonic followed by subtle seizure. Most common etiology of neonatal seizures was birth asphyxia in 54.8% neonates, followed by metabolic causes in 32.5% followed by meningitis and sepsis in 12.5% neonates. Among the metabolic abnormalities, hypoglycemia followed by hypocalcemia was commonest.

METABOLIC ABNORMALITIES IN NEONATAL SEIZURE PATIENTS

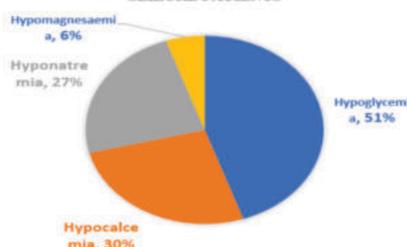


Fig 3- Metabolic abnormalities in neonatal seizure patients

Neurosonography was done in 37 patients in whom, total 13 (32%) patients have neurosonography abnormalities in which 5 (12%) patients showed diffuse cerebral edema, 8 (20%) shows minimal intraventricular hemorrhage and rest were normal. All 37 patients had got treated and discharged. Total mortality rate was 7% (3). 1 patient died due to severe septicemia and 2 due to severe HIE

DISCUSSION

Present Study is a descriptive cross sectional well designed study evaluating the Clinical and investigative profile and immediate outcome of Neonatal seizure patients admitted to Tertiary Rural medical College and Hospital in Neonatal Intensive Care Unit Patient. In Our study Males dominated in number being 23 out of 40, male to female ratio was 1.3:1. There was significant difference between term and preterm neonates in relation to gender. About 82.5% (33) Neonates were preterm and 17.5% (7) out of 40. There was no significant difference in term preterm distribution in relation to mode of delivery. In total 40 patients of neonatal seizures 6 (15%) were weight more than 2.5kgs, 26 (65%) were weight between 1.5-2.5kgs and 8 (20%) were weight below 1.5kgs. Out of all seizure episodes, most common type of neonatal seizure was subtle in 25 neonates. The commonest cause of seizure was birth asphyxia in 54.8% patients

In our study, seizures were more common in male 57.5% (23) newborn as compared to female 42.5% (17) with male to female ratio 1.3:1. This is comparable with study done by Bhatt S et al. in which male to female ratio was 2.37:1. G Sahana studied 109 neonates with seizures in 2014 and reported total number of male Neonates with seizures 57 (52.29%) as compared to female Neonates 52 (47.71%). In Study done by Sameer Kumar in 2014 on 102 neonates with seizures reported number of males 54 (53%) compared to females 48 (47%). This is consistent with our study. Glass et al (2002) who studied 426 neonates of which 56% were males. Manoel et al (2006) also showed 58% of males among 114 neonates.

In our study, out of 40 Neonates, 33 (82.5%) were preterm. This is in accordance with most of the studies showing higher incidence in preterm Neonates. Ronen et al found that neonatal seizures were six times more common in preterm (86%) than term (14%) neonates. Anand V et al studied 108 neonates with seizures and found that 58% were preterm. Manoel et al found that out of 114 Newborn studied, (74) 71.2% were term and (30) 28.8 were Preterm. This is comparable with our study.

Sanjeev Kumar et al studied 102 neonates with seizures found that 82.3% were term and 17.7% were preterm. Asif Aziz in 2013 studied 100 neonates with seizures and found 35 were preterm and 65 were term. These two studies are not comparable with our study. This may be due to higher number of preterm deliveries taking place in our hospital. Being a tertiary care center, most preterm deliveries are referred and preterm deliveries carry good prognosis in our hospital.

In our study, out of 40 neonates, 28 (71.8%) presented with early onset neonatal seizures (i.e. within 48 hours of birth) and 12 (28.2%) presented with late onset of seizures after 48 hours. This is comparable to study done by G Sahana who showed that out of 109 neonates, 75 (69%) developed seizures within 48 hours and 34 (31%) developed seizures after 48 hours. Rose et al. also found early onset seizures in 75 (50.33%) neonates whereas Coen RW et al. found in 81% of Neonates. Lombroso CT et al and others also found similar results. Essam et al (2007) found day of presentation of seizures within 48 hours in most of neonates. Ajay Kumar et al (2007) also found 57.8% neonates among 90 neonates studied, presented with seizures within 48 hours. These studies are comparable with our studies.

In our study, out of 40 Neonates, Majority 26 (65%) were Low birth weight, 8 (20%) were Very low Birth weight and 6 (15%) had normal birth weight. Mean average weight in our study was 1.89 Kg. Proportion of Preterm neonates was significantly higher in LBW and VLBW neonates. Shah GS in 2007 performed a study on 90 neonates with seizures, amongst them 60 (66%) were Low birth weight and 30 (33%) were normal birth weight. Sameer Kumar in 2014 performed a study on 102 neonates with seizures and found 42 cases (41.17%) Low birth weight and 60 (58.82) cases were normal birth weight. This is comparable with our study. Studies done by Sahana et al., Airede et al., Evan et al., and Scher et al. found that Seizures were common in Newborns with Low Birth weight as compared to Normal Birth weight.

Out of all seizure episodes in our study, most common type of neonatal seizure was subtle 25 (62.8%) followed by, focal clonic in 8 (18%), generalized tonic 2 (7%) and remaining types were mixed (multifocal tonic, myoclonic) in patients. Essam J et al found 61.2% subtle seizures which is comparable to our study and 12.9% multifocal clonic. Shah et al found 50% seizures were subtle with 25% focal clonic, 12.5% multifocal clonic, 7.5% tonic and 5% Myoclonic. Malik et al found 39.6% Subtle seizures, and Sabzehei found 38.2% subtle seizures. Essam J et al found 61.2% subtle seizures and 12.9% multifocal seizures. Shah et al, malik et al, sabzeiai et al, Jaseem et al found 50%,39.6%,38.2%,31.8% of subtle seizures. All these studies were comparable to our study.

In our study, the commonest cause of seizure was birth asphyxia in 54.8% of neonates followed by metabolic causes (32.5%). Among biochemical abnormalities the most common cause of seizure observed in our study was hypoglycemia (95%) and hypocalcaemia (5%) common cause leading to neonatal seizure. Neurosonography was done in all 37 patients, cerebral edema was seen in 5 (12%) patients and intraventricular hemorrhage (IVH) was seen in 8 (20%) patients. Our study is comparable with studies done by Mahjoob et al (4%), Sanjeev Kumar et al (6.9%), Mahmood et al (6.25%), Sabzehei (6.9%). Mishra (3%) respectively had Intraventricular hemorrhage.

The mortality rate observed in our study was 7%. Out of 40 patients, 3 patients died; 2 (5%) had HIE and 1 (2%) died due to septicemia. Mortality rates in studies done by Ronen et al was 9%, Mahjoob et al was 8%, Mwaniki et al was 9.1% which is quite comparable to our study.

CONCLUSION

Out of 40 patients evaluated- Males were 23 and females were 17. Male:female ratio was 1.35:1. 33 babies were born preterm and 7 babies were born term. Majority 26 were LBW, 20.8% were VLBW and 15% had normal birth weight. 71.8% neonates presented with

convulsions within 48 hours of life. Most common type of neonatal seizures was subtle 62.8%, followed by focal clonic in 18% , generalized tonic 7% and remaining types were mixed(multifocal tonic, myoclonic) in 12% patients. Most common etiology of neonatal seizures was birth asphyxia in 54.8% neonates, followed by metabolic causes in 32.5% followed by meningitis and sepsis in 12.5% neonates. Among the metabolic abnormalities, hypoglycemia followed by hypocalcaemia was commonest. 26% babies had abnormalities on neurosonography with most common was diffuse cerebral edema. Mortality was 7%. So vigilant monitoring in NICU would lead to early recognition of seizure like subtle and early treatment causing less morbidity and mortality in patients with seizure.

REFERENCES:

- Aberman et al. Cerebral palsy and severe educational subnormality in LBW. *Lancet*, 1982;1:606-8.
- Adam Francis: Translation from Greek; The genuine work of Hippocrates "on sacred disease." 1832:374-380.
- Adeebah A. Alyasiri. Etiology And Short Outcome Of Neonatal Seizures In Babylon Gynecology And Pediatrics Teaching Hospital. *Alyasiri A. A., Med. Res. Chron.*, 2015, 2 (1), 30-40.
- Airede KL. Neonatal seizures and two year neurological outcome, *J Trop Pediatr* 1991;37:313-17.
- Ajay Kumar, Ashish Gupta, Bibek Talukdar. Clinico-Etiological and EEG Profile of Neonatal seizures. *Indian J Paediatr* 2007;74(1): 33-37.
- Alcover-Bloch E, Campistol J, Iriando-Sanz M. Neonatal seizures, our experience. *Rev Neurol* 2004;38:808-12.
- Amit Upadhyay. Seizures in the newborn. *IJP*. Vol 68, Oct 2001: 967-972.
- Anand V, Nair P. Neonatal seizures: Predictors of adverse outcome. *J Pediatr Neurosci* 2014; 9:97-9.
- Arvind Sood, Neelam Grover and Roshan Sharma, Biochemical abnormalities in neonatal seizures. *IJP*: Vol 70, 2003:221-4
- Asif Aziz Wani. Spectrum of biochemical abnormalities in neonatal seizures at tertiary care hospital. *Int Journal of Development and Research* 2015; 5:4311-15.
- Azam M, Jamal M. Neonatal seizures; classifications, diagnosis and treatment.
- Aziz A, Gattoo I, Aziz M, Rasool G. Clinical and etiological profile of neonatal seizures: a tertiary care hospital based study. *Int J Res Med Sci* 2015;3:2198-203.
- Ballard JL, Khoury JC, Wedig K, et al. New Ballard Score, expanded to include extremely premature infants. *J Pediatrics* 1991; 119:417-423.
- Bergman I, Painter MJ, Hirsch RP, et al. Outcome in neonates with convulsions treated in an intensive care unit. *Ann Neurol* 1983; 14:642-647. 15. 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.
- Bredt EM: *Pediatric neurology*, 1st edition Churchill livingstone, 1983
- Brown JK, Cockburn F and Forfur JO. Clinical and chemical correlate in convulsion of newborn. *Lancet*. 1992; 1:135-138.
- Bushra AM, Butt MA. Seizure etiology in the new-born period. *Journal of College of Physicians and Surgeons Pakistan* 2005;15:786-90.
- Coen RW, McCutchen CB, Wermer D, Snyder J, Gluck FE. Continuous monitoring of EEG following perinatal asphyxia. *J Pediatr* 1982;100:628-30.
- Dehan M, Quilleron D, Naveley et al. Les convulsions. Du cinquieme jour de vie: Unoureal syndrome? *Arch Fr Pediatr* 1977; 34: 730-42.
- Dennis J, Chalmers I. Very early neonatal seizures rate - a possible epidemiological indicator of the quality of perinatal care. *Br J obstet Gynaecol* 1982;89:418-26
- E. M. Breet: *Epilepsy and Convulsions*. A textbook of Pediatric neurology, 3 ed. 331-341.
- Eghbalian F, Monsef A. Neonatal seizures: etiology and frequency. *Iran J Child Neurol*. 2007;2(1):39-42
- eMedicine. Neonatal seizure: Article by Raj. D. Seth, MD: 1-12.
- Essam J. Al-Zwaini, Mohammed M. Al-Ani, Alwan H. Mengal, The epidemiology of clinical neonatal seizures in Ramadi city. *Neurosciences* 2007; Vol. 12 (2)
- Evans D, Levene M, Neonatal Seizures. *Arch. Dis. Child. Fetal Neonatal Ed*. 1998;78:F70-75.
- Fenichel GM. Hypoxic Ischemic Encephalopathy in the newborn. *Arch Neurol*. 1983; 40:261-266.
- Francis and Foster. The epilepsies and convulsive disorders in clinical neurology. 1st Ed. Baker A B. Harper and Row, 1987:1-3
- GB Boylan, R B Panui. Cerebral blood flow during neonatal seizures *IJP*; vol 80, 1999
- G Sahana, B Anjaiah. Clinical Profile of Neonatal Seizures. *International Journal of applied and Medical sciences*. 2014;3(1):21-27.
- Glass HC, Pham TN, Danielsen B, Townner D, Glidden D, Wu YW. Antenatal and intrapartum risk factors for seizures in term newborns: A population-based study, *California* 1998-2002. *J Pediatr* 2009; 154:24-28. el.
- Goldberg HJ. Neonatal convulsions-10 year review. *Arch Dis Child* 1983; 57: 633- 635.
- J. H. Keen and D Lee Sequal of neonatal convulsions. *Archives of disease in childhood* 1973, 48: 542-546.
- J. H. Keen. Significance of hypocalcaemia in neonatal convulsions. *Arch Dis. Children*, 1969, 44: 356-361.
- J.K. Brown, J. O. Forfar, F. Lockburn. Clinical and chemical correlates in convulsion in newborn. *The lancet*, Jan 15, 1972:135-139.
- Jan Goddard-Finegold. Seizures and other paroxysmal Disorders in Avery's Disease of newborn. Ed 7. 1988:871-876
- Jankovic et al. Eponyms and Epilepsy. *Srpiki archive a celukupno lekarstov*, 1996, 124:217-227.
- Jasim M. AL. Marzoki. Clinico-Biochemical Profile of Neonatal Seizures, 2010. *QMJ VOL.6 No.10*.
- Jin S, Hahn MD, Donald M, Olson MD. Etiology of neonatal seizures. *Neo Reviews* 2004;5(8):e327-35.
- Karbowski K, Neveka A. Right midtemporal sharp EEG transients in healthy newborns. *Electroencephalography Clin. Neurophysiol*, 1980; 48: 461-469.
- Kellaway P, Hrachovy RA. Status epilepticus in newborns: a perspective on neonatal
- Kellaway P, Mizrahi EM. Neonatal seizures in textbook of Pediatrics Ed. Nelson 16th ed. 2000:1825-27
- Kohelet D. *J Child Neurol*-2004 Feb; 19(2): 123-8.
- Kumar A, Gupta V, Singla, Kachhawaha: Biochemical abnormalities in neonatal seizures. *Indian Paed*. 1995;32(4):424-8.
- Lanska M. *J Neurology*. 1995 April; 45(4): 724-32.
- Legido A. Clancy RR. Neurologic outcome after EEG proven neonatal seizures. *Paediatrics* 1991;88:583-96.
- Lennox WG: *Epilepsy and related disorders*. London JA and Churchill, 1960