ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 04 | April - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF CLINICO-ETIOLOGICAL, BIOCHEMICAL, MICROBIOLOGICAL AND NEUROSONOGRAM FINDING IN NEONATAL SEIZURES AT A TERTIARY HEALTH CARE CENTER IN CENTRAL INDIA

Paediatric Medicine

Dr. Ajay Keshwani Professor and Head Department of Paediatrics Shri VNGMC Yavatmal

Dr Ujvala Gulab Girhe* Junior Resident Department of Paediartics, SVNGMC Yavatmal *Corresponding Author

Dr. Harish Tambekar Assistant Professor SVNGMC Yavatmal

Dr. Balkishan Chaudhari Assistant Professor SVNGMC Yavatmal

ABSTRACT

Background: Neonatal seizures (NS) are common neurological finding in neonatal period. Biochemical disturbances and meningitis occur frequently in NS either as an underlying cause or as an associated abnormality. The present study was undertaken to study clinico-etiological biochemical, microbiological and neurosonogram finding in NS at tertiary health care center in central India. **Method:** A total 256 neonates (first 28 days of life) admitted in NICU with at least one of the clinical types of seizure were enrolled to study the clinico-etiological biochemical, microbiological and neurosonogram finding in NS. **Result:** NS occurred more commonly in full term babies (74.21%) and in males (58.98%). Subtle seizures (61.32%) were the commonest clinical type of seizure. Most of the neonates developed seizure within 72 hours of life (73.04%). Commonest aetiology of NS was hypoxic ischemic encephalopathy (HIE) (29.68%) followed by metabolic abnormalities in which hypoglycaemia was the commonest type (31.73%). Meningitis was seen in 13.67% of cases and most common organism isolated from CSF was Escherechia coli (37.14%). Neurosonogram abnormalities found in 19.14% of cases and diffuse parenchymal echoes were the commonest finding (55.10%). The mortality of study was 7.03% and commonest cause of mortality was HIE (59.6%). **Conclusion:** Biochemical abnormalities may be a major cause of seizure activity, and it's possible that correcting these abnormalities may have a big impact on seizure management. For all instances of NS, biochemical workup is required. Appropriate treatment with antibiotics is essential. Examination of CSF is essential work up in cases of NS. The neurosonogram should be used in the regular examination of seizures since it has high potential for predicting neurological outcomes.

KEYWORDS

Neonatal seizures (NS), Neurosonogram, Biochemical, Microbiological, Hypoxic ischemic encephalopathy (HIE), Hypoglycaemia, Escherechia coli

INTRODUCTION

Neonatal seizures (NS) are common neurological finding in neonatal period occurred in 0.95 to 3.5/1000 live birth [1]. The highest incidence of NS occurs during first 24 hours of life [2] whereas NS 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 [3]. Although NS can be divided into epileptic and nonepileptic seizures; NS of epileptic origin are generated by hypersynchronous cortical neuronal discharges. Nonepileptic seizures occur in the absence of electrical seizure activity [4]. Volpe classified seizures into five clinical types, namely subtle, multifocal clonic, focal clonic, generalized tonic, and myoclonic [5].

However, hypoxic-ischemic encephalopathy (HIE) is the commonest cause of NS, occurring in approximately 1 to 2 per 1000 live births [6]. Other causes of NS include cerebral infarction, vascular stroke, intracranial bleed, subarachnoid haemorrhage, intracranial infections, congenital malformation, metabolic and biochemical disturbances [7]. If seizures are not controlled, the electrical activity may continue to circulate, a phenomenon called kindling [8]. Though EEG provides a useful non-invasive test to diagnose NS and evaluate degree of 2 perinatal damage to brain and long-term prognosis, yet its interpretation is influenced by variations in normal maturation process of brain. It is well recognized that not all seizures can be picked by surface recorded EEG and many clinically silent electrographic seizures have been reported [9].

NS represent non-specific responses of the immature nervous system to varied insults and result in considerable neonatal mortality and long-term morbidity including motor and cognitive disabilities in the childhood [10]. The clinical diagnosis, classification of NS and appropriate management are critical for the neonate's care. As NS not only have short term but also long-term effects on morbidity and mortality in these neonates. Clinico-etiological profile of neonatal seizure has been found to be varied across different populations. Recognition of etiology is often helpful in prognosis and treatment. However, these NS are often under-recognized, and difficult to treat. Early recognition and treatment of etiological factors are essential for satisfactory long-term outcome. Hence the present study was planned to estimate the prevalence and assess the biochemical and microbiological parameters and neurosonogram abnormalities in newborn with neonatal seizures which would help in timely recognition of the cause and thus implementing early treatment and preventing morbidity and mortality.

MATERIALAND METHOD

After obtaining Institutional Ethical Committee approval and written informed consent from all the parents/guardian, this cross-sectional study was carried out in the Department of Pediatrics, at Tertiary Care Centre in central India during a period of 1 year from January 2021 to December 2021. A total 256 neonates (first 28 days of life) admitted in NICU with at least one of the clinical types of seizure (Subtle seizure, multifocal clonic seizure, focal clonic seizure, Myoclonic seizure, and tonic seizure) and patient's parents willing to give informed written consent were included in the study. Neonates with isolated subtle phenomenon, apnoea or paroxysmal autonomic changes that is only subtle motor movements or apnoea without tachycardia, jitteriness in neonates, tetanic spasm in neonates, those neonates with congenital anomalies were excluded from the study.

A detailed history including antenatal, natal, and post-natal risk factors, clinical features, onset of first seizure with its duration, number and type of seizure were recorded in pre structured case record form. Thorough clinical examination was done including general and systemic examination with special reference to central nervous system.

Under aseptic precaution 5 ml venous blood was collected from all neonates and send for basic/ first line investigations such as complete blood count (CBC), C-Reactive Protein (CRP), blood culture sensitivity (BCS), blood glucose, sr. electrolyte (Sodium, Potassium and Calcium) and USG cranium. Also, all neonates had relevant biochemical and microbiological investigations like serum calcium, magnesium, blood for culture and sensitivity, cerebrospinal fluid analysis for proteins, sugar, cell count and type, cerebrospinal fluid for culture and sensitivity.

Criteria for diagnosing various biochemical disturbances and hematological parameter are as follows [8]

- Hypoglycemia- Glucose < 40 mg/dl
- Hypocalcemia- Ca<7.0 mg/dl
- Hyponatremia- Na < 130 mEg/L
- Hypernatremia- Na> 150 mEg/L
- Hypokalemia- K<3.5mEq/L
- Hyperkalemia- K<5.5mEq/L
- Polycythemia - Hematocrit>65

Statistical Analysis

The results were analyzed by using SPSS software version 20. For the comparison of qualitative data, Chi-square or Fishers exact test was used. The confidence limit for significance was fixed at 95% level with p value <0.05. For qualitative data chi square test was used and for quantitative data unpaired t test was used. P value <0.05 was considered as statistically significant.

OBSERVATION AND RESULTS

Total number of neonates admitted to NICU during the study period from January 2021 to December 2021 was 1851, out of which 256 neonates had one or more episodes of NS, comprising 13.83% of all NICU admission. Out of 256, 165 (64.45%) babies were born by normal vaginal delivery, 88 (34.37%) babies by cesarean section and 3 (1.17%) were by forceps delivery. The number of babies born within the institution was 216 (84.37%) and referred from outside was 40 (15.62%). However, the majority of neonates were male (58.98%), full-term babies 190 (74.21%). The mean birth weight of study population was 2.58 kg, ranged from 0.98 to 4.13 kg. The maximum babies (129; 50.39%) had APGAR score of < 7 at 5 min as shown in table 1.

Table 1: Demographic data and clinical profile of neonatal seizures

Variables		No. of patients	Percentages
Gender	Male	151	58.98
	Female	105	41.01
Gestation	Full term(>37week)	190	74.21
	Preterm (<37 week)	66	25.78
Birth weight for gestational age	SGA	69	26.95
	AGA	179	69.92
	LGA	08	3.12
Birth weight (kg)	Low birth weight (<2.5kg)	117	45.70
	Normal Birth weight (≥2.5kg)	139	54.29
APGAR score (5 min)	<7	129	50.39
	>7	127	49.60

Onset of seizure mostly occurs within 24 to 72 hours (44.53%) followed by in 24 hours (28.51%) as shown in figure 1. Subtle seizures (157; 61.32%) were most common type of seizure followed by clonic seizure (65; 25.39%), tonic (32; 12.50%) and myoclonic seizure (2; 0.78%).

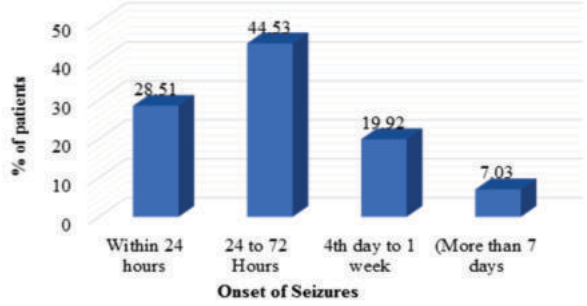

Figure 1: Distribution of cases according to onset of seizures

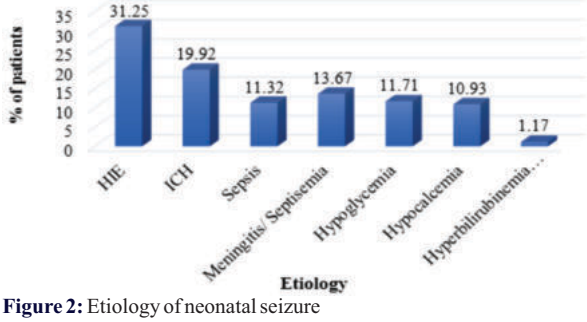

Figure 2: Etiology of neonatal seizure

Figure 2 show that the hypoxic ischemic encephalopathy (HIE) was the most common cause of neonatal seizures (31.25%) followed by ICH (19.92%) and sepsis (9.76%). Among metabolic causes hypoglycemia was the most common cause (11.71%) followed by hypocalcemia (10.93%). (Figure 2).

Hypoglycemia was the most common biochemical abnormalities (31.73%) followed by hypocalcemia (29.80%) and 2 (0.78%) neonates were reported to had combine hypoglycemia and hypocalcemia as shown in table 2.

Table 2: Various biochemical abnormalities in study population

Biochemical Abnormalities	No. of patients	Percentage
Hypoglycemia (mg/dL)	33	31.73
Hypocalcemia (mg/dL)	31	29.80
Hyponatremia (mmol/l)	26	25.0
Hypernatremia (mEq/L)	14	13.46
Hypoglycemia + Hypocalcemia.	02	0.78

The most common organism causing meningitis was E. coli (37.14%) followed by Klebsiella (31.42%) and Staphylococcus aureus (23%) as depicted in figure 3.

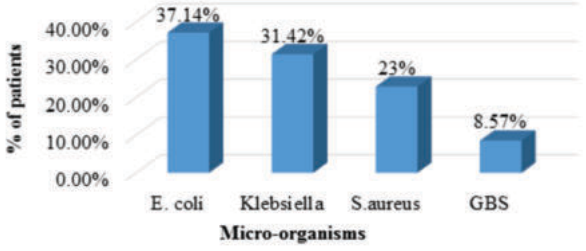

Figure 3: Distribution of various microorganisms implicated in neonatal seizures

Group B Streptococci (GBS)

Neurosonogram was done in all the cases of which 49 (19.14%) cases had abnormalities and rest had normal neurosonogram (80.86%). Diffuse parenchymal echoes were the most common finding (55.10%) as shown in table 3.

Most of the neonates around 70.70% (181) were responded to single AED Phenobarbitone whereas 19.53% responded to Phenobarbitone + Phenytoin and only fewer (09, 3.51%) required more than two AED's (Phenobarbitone + Phenytoin + Levetiracetam). Dextrose and calcium given to 8 cases each.

Table 3: Study of neurosonogram abnormality in neonates with HIE

Neurosonogram findings	No. of patients	Percentage
Diffuse parenchymal echoes	27	55.10
Slit like ventricles	10	20.40
Focal parenchymal echoes	04	8.16
Periventricular echoes	08	16.32

The mortality of study was 7.03% (Figure 4), among these patients, the causes of seizures were HIE, meningitis, and IC bleed in 59.6%, 26.03%, and 13.47% of the patients, respectively. Most of the patients around 47.26% neonates had to stay in the hospital for >15 days followed by 6 to 10 days (21.09%), 11 to 15 days (16.79%) and a smaller number of cases had to stay in the hospital for 1 to 5 days (14.84%). The mean value of hospital stay was 13.85±6.57 days.

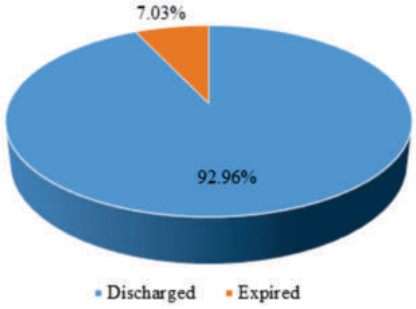

Figure 4: Outcome of the study

DISCUSSION

In the present study, the prevalence of neonatal seizures was 13.83% of all NICU admission. While the reported prevalence of neonatal seizures is approximately 1.5%. Padiyar S et al reported the prevalence of seizures varies according to gestational age ranging from 0.02% to 0.12% [11], which is much less than current study. In the current study, intramural prevalence of NS was more (11.66%) than extramural prevalence (2.16%) out of total admission (1851). In contrast to present study in previous studies intramural prevalence of NS was less as compared to extramural prevalence [12, 13]. Most of the babies (64.45%) were born by normal vaginal delivery which is comparable with the study done by Kumar R et al [12] and Sahay BP et al [14]. This higher percentage of vaginal deliveries may be due to higher contribution of birth asphyxia to total number of NS. Most of the neonates were male (58.98%). Likewise, several other series of NS show the male predominance [12, 15, 16]. This preponderance of males over females in present study could be due to social beliefs that male babies are cared better by their parents and are brought to the hospital even with minor complaints, but female babies are usually neglected and are managed at home even if they are very sick. The majority of neonates with seizures were full term appropriate for gestational age neonates. Similar observations were seen in study by Aziz et al [15, 17]. The mean birth weight of study population was 2.58 kgs, ranged from 0.98 to 4.13 kg which is comparable with the other studies [12, 15]. Among infants who had seizures, maximum (129; 50.39%) had APGAR score of < 7 at 5 min and 127 (49.60%) neonates had APGAR score of > 7 at 5 min. This result is consistent with the study conducted by Venkatesh G et al [18].

Most neonatal seizures occurred during the first 3 days of life (73.04%). Subtle seizures were the most common type of NS contributing to about 61.32% in about 157 neonates, followed by clonic seizure (65; 25.39%), tonic (32; 12.50%) and myoclonic seizure (2; 0.78%). Similar observations were made by Kulkarni SK et al [19], Das D et al [20] and Nawab et al [21]. In all these studies majority of NS cases had early onset of seizure (within 3 days) and all studies reported subtle seizures to be the most common type seizure.

The hypoxic ischemic encephalopathy (HIE) was the most common cause of NS (29.68%). ICH the second most common cause (18.35%) followed by meningitis/ septicemia (13.67%), sepsis (9.76%). Among metabolic causes hypoglycaemia was the most common cause of neonatal seizures (11.71%) followed by hypocalcemia (10.93%). These findings are in accordance with the study conducted by Venkatesh G et al [18], Kulkarni SK et al [19] and Abhishek et al [22].

Out of 256 neonates, 104 babies with seizures had one or more biochemical abnormalities contributing to about 40.62% in total. Similar observations were made by Nawab et al [21] and Madhusudan et al [23]. Among metabolic causes hypoglycaemia was the most common cause of NS (31.73%) followed by hypocalcemia (29.80%) which is comparable with the earlier studies [24, 25]. Further Das D et al in his study has added that hypoglycemia was more prevalent among preterm neonates [20] as suggested by current study. Thus, all these studies suggest the importance of doing biochemical work up in neonatal seizures especially blood glucose and calcium levels which are more prevalent, and correction of these transient biochemical abnormalities is associated with good prognosis and outcome.

Of the 256 cases, meningitis accounts for 35 cases. Of these the most common organism causing meningitis is E. coli (37.14%) followed by Klebsiella (31.42%), Staphylococcus aureus (23%) and Group B Streptococci (GBS) (8.57%). These findings are consistent with the other studies conducted by Rao MS et al [16] and Ortibus EL et al [26].

Neurosonogram was done in all the cases of which 49 (19.14%) cases had abnormalities. The rest had normal neurosonogram (80.86%). Diffuse parenchymal echoes were the most common finding (55.10%) followed by slit like ventricles (20.40%), periventricular echoes (16.32%) and focal parenchymal echoes (8.16%). Similar finding reported in Kumar A et al [9] and Rao MS et al [16]. Most of the neonates around 70.70% (181) were responded to single AED Phenobarbitone, only fewer (09, 3.51%) required more than two AED's which is in accordance with the study done by Venkatesh G et al [18] .

The mortality of study was 7.03% and the mean hospital stay was 13.85± 6.57 days, this findings are correlated with the previous studies [16, 18, 19, 22]. More than half the survivors have considerable disability across a range of developmental domains, most frequently cerebral palsy, postneonatal epilepsy, and/or intellectual disability requiring lifelong therapies and social and financial support [27]. Early recognition and treatment of biochemical disturbances are essential for optimal management and satisfactory long-term outcome.

Limitations

First limitation is inherent in the study design, this is a single centre study. It included both inborn as well as out born neonates and details about the quality of antenatal and perinatal care as exact birth weight of most out born children was not known. EEG correlation with the seizures was not done and so it is likely that the true incidence of seizures couldn't be reported. We couldn't do long term follow up of these neonates. There is still a need for research with large sample size and longer duration to find out the association between various biochemical abnormalities in a conclusive manner.

CONCLUSION

Quick assessment, timely diagnosis, and aggressive management according to the etiology are necessary to prevent NS. Biochemical abnormalities may significantly contribute to seizure activity and timely recognition and possibly early correction of these abnormalities may play a significant role in seizure control. Hence biochemical work up should be done in all neonates with seizures and should be included as the first line of investigations in all cases. Early correction of these biochemical abnormalities helps in preventing the further occurrence of seizures and also helps in avoiding overuse of anticonvulsants which may be unnecessary in some cases. Further early correction of these metabolic disturbances improves the prognosis and outcome of the neonate and also prevent the long-term neurological sequelae associated with it. However, neurosonogram had good potential in predicting neurological outcome, hence neurosonogram should be incorporated in the routine evaluation of seizures.

Wherever possible continuous video EEG monitoring should be included in identifying the NS to know the real magnitude of the problem and to treat these seizures promptly.

REFERENCES

1. De Plessis AJ. Neonatal seizures. In: Cloherty John P, Eichenwald EC and Stark AR. Manual of neonatal care, 6th edition Philadelphia: Lippincott Williams and Watkin Publication, 2008: p483-98.
2. Rennie JM. In: Rennie JM, editor. Roberton's Text Book of neonatology, 4th ed. Churchill Livingstone, Elsevier; 2005:1080-1087.
3. Singh M. Care of new born. Intracranial haemorrhage: 7 th edition. New Delhi: Sagar Publication, 2010: p335-342.
4. Nair BK, Sharma J, Chaudhary S. Clinicoetiological profile of neonatal seizure in a newborn care unit of a tertiary care teaching hospital in Northern India. J Clin Neonatol 2020;9:27-31.
5. Volpe J. Neonatal Seizures. N Engl J Med 1973;289:413-6.
6. Volpe JJ. Hypoxic-Ischemic Encephalopathy: Biochemical and Physiological Aspects. In: Neurology of the Newborn. 4th ed. Philadelphia: WB Saunders; 2000:217-276.
7. Singh M. Neurology disorders. In: Singh M, eds. Textbook of Care of Newborn. 2nd ed. Delhi: Sagar Publication; 1999: 340- 344.
8. MC Cabe BK, Silveira DC, Cilio MR. Reduced neurogenesis after neonatal seizures. J Neuroscience. 2001;6:2094-103.
9. Kumar A, Gupta A and Talukdar B. Clinico-etiological and EEG profile of neonatal seizures. [Indian J Pediatr 2007;74 (1):33-37.
10. Davis AS, Hintz SR, Van KP, LiL, Das A, Stoll BJ et al. Seizures in extremely low birth weight infants are associated with adverse outcome.JPediatr.2010;157(5):720-5.
11. Padiyar S et al. Neonatal seizures in the U.S. National Inpatient Population: Prevalence and outcomes. Pediatrics and Neonatology (2020) 61, 300e305.
12. Kumar R, Kumari N, Singh BK, Ansari MA. Clinico-etiological profile of neonatal seizures in a tertiary care hospital of Northern India: a prospective cohort study. International Journal of Health and Clinical Research, 2021;4(11):259-264.
13. Bhatt S, Raju N, Phanse S, Patel SV, Madan G, Mehta S, et al. Clinicoetiological and EEG profile of neonatal seizures. Ind J Clin Pract. 2013;24(1):69-75.
14. Sahay BP, & Irfan A. An observational study to assess the Clinicoetiological profile of term neonates presented with seizures. International Journal of Health and Clinical Research 2021;4(2), 277–279.
15. Wakil Paswan, Bankey Behari Singh. A study of clinico-biochemical profile of neonatal seizure: A tertiary care hospital study. IAIM, 2018; 5(4): 139-143.
16. Rao MS, Rao GC, Sultana A, Karthik PJ. Clinical, etiological, biochemical, microbiological and neurosonogram factors in related with neonatal seizures in Visakhapatnam, India. Int J Contemp Pediatr 2017;4:568-72.
17. Aziz A. Gattoo, M Aziz, G Rasool. Clinical and etiological profile of neonatal seizures: A tertiary care hospital-based study Int J Res Med Sci. 2015; 3(9): 2198-2203.
18. Venkatesh G, V Prakash, Sajjid M, Elango. Etiological and Clinical Profile of Seizures in Late Preterm and Term Neonates - A Retrospective Study in an Intramural Tertiary Care Centre. Asian J. Clin. Pediatr. Neonatol.2020;8(1):69-73.
19. Kulkarni SK, Shukla DA. Study of clinico-etiological profile of neonatal seizures in term neonates at a tertiary care hospital. MedPulse International Journal of Pediatrics. August 2021; 19(2): 38-41.
20. Das D and Debbarma SK. A Study on ClinicoBiochemical Profile of Neonatal Seizure. Journal of Neurology Research 2016;6:95-101.
21. Nawab T, Lakshmipathy NS. Clinical profile of neonatal seizures with special reference to biochemical abnormalities. Int J ContempPediatr2016;3:183-8.
22. Abhishek CK, Jha G, Singh BK, Kumar S. Profile, and short-term outcome of seizures in term neonates. International Journal of Contemporary Medical Research 2020;7(12):L1-L4.
23. Madhusudhan K, Nadavapalli Suresh S, Babu TR, Rao JV, Kumar S B. Study of

biochemical abnormalities in neonatalseizures with special reference to hyponatremia. Int J Contemp Pediatr2016;3:730-4.
24. Suganthi V, Vikneshwari K, Thivya G. Prevalence of hypomagnesemia in neonatal seizures in a tertiary care hospital inSouth India. J PediatrRes.2017;4(01):64-68.
25. Jain SK. Study of the clinical profile of neonatal seizuresJune 2015; 2(6): 336-338.
26. Ortibus EL, Sum JM, Hahn JS. Predictive value of EEG for outcome and epilepsy following neonatal seizures. Electroencephalogr Clin Neurophysiol. 1996;98:175-85.
27. Mizrahi EM, Kellaway P. Characterization and Classification of neonatal seizures. Neurology. 1987; 37:1837-44.