Section: Paediatrics

Original Research Article

A STUDY OF CLINICAL AND BIOCHEMICAL PROFILE IN NEONATAL SEIZURES IN A TERTIARY CARE CENTRE

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Abstract

Background: Seizures in neonates can result in a high incidence of mortality and long term morbidity if emergency timely treatment is not started. Identifying the etiology of seizure is an essential for adequate treatment. The study aims to identify and correlate the clinico-biochemical abnormalities in neonates with seizures. **Materials and Methods:** This observational study was conducted at the NICU of Government Kilpauk Medical College and Hospital, Chennai, for 6 months in which,70 neonates (from day one of birth to 28 days) admitted for neonatal seizures were included. Before initiating the treatment, biochemical parameters were evaluated by quantitative and qualitative methods, using various statistical analyses. **Result:** The incidence of neonatal seizure was high in males (55.71%), with subtle (61.43%), tonic (25.71%), and clonic (12.86%) being common types. Incidence of biochemical abnormalities reported were hypoglycemia (24.29%), hypocalcemia (20.00%), hyponatremia (8.57%), hypomagnesemia (4.29%), and hypernatremia (4.2%) respectively. This study finds a higher incidence of seizures in pre-term neonates and low birth weight (<2.5 kg) at 44.29%, respectively, with presentation of seizure in the first three days after birth . **Conclusion:** Neonatal seizures in one of the most prevalent neurological conditions which results in severe complications if left untreated. A quick and thorough examination, prompt diagnosis, and emergency treatment are required to prevent severe neurological damage to the neonate . The use of biochemical abnormalities can be a secondary link to identify the etiology of seizures. Hence, a battery of simple test workup should be able to detect patients with altered biochemical states.

INTRODUCTION

One of the most prevalent and characteristic clinical signs of a neurological system abnormality is neonatal seizures. Neonatal seizures cause significant neonatal mortality and long-term morbidity, including motor and cognitive deficits in infancy.[1,[2] They are non-specific responses of the developing nervous system to many stressors. Seizures appear more common in the neonatal era than at any other point in life, suggesting that the undeveloped brain is more prone to them. This may be due to excitatory synapses developing earlier than inhibitory ones during the early stages of growth.[1] Neonatal seizures frequently indicate a dangerous neurological disease, most frequently hypoxia-ischemia. Stroke, intraventricular haemorrhage, intraparenchymal haemorrhage, meningitis, sepsis, and metabolic abnormalities are some of the more frequent causes of neonatal seizures.[3]

Understanding the cause is frequently beneficial for prognosis and treatment. However, in clinical practice at neonatal intensive care units (ICU) in developing countries where synchronized video-EEG monitoring is nonexistent, clinical observation becomes the key to the diagnosis. Studies suggest that neonatal seizures and their etiology significantly impact the developing brain.[4] Due to a condition known as electroclinical dissociation, where there are frequently no clinical correlations of the electrographic seizures, neonatal seizures can be challenging to detect. Due to inadequate myelination of white matter pathways, regional interconnectedness, including interhemispheric and

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corticospinal, tract is not fully developed, resulting in only subtle symptoms of these seizures.[5]
The study aims to identify neonatal seizures using clinical criteria and determine the biochemical abnormalities related to these clinical convulsions, we conducted this study in our centre where continuous video-EEG monitoring is not available

MATERIALS AND METHODS

This observational study included all neonates admitted to the Neonatal Intensive Care Unit of the Department of Paediatrics, Government Kilpauk Medical College and Hospital, Chennai, India, between birth and 28 days of age, who met the inclusion and exclusion criteria. From April 2017 to September 2017, six months were spent doing this investigation. Seventy neonates who met the inclusion criteria were enrolled in the research. Given that 67 is the minimum number of subjects needed for the study and that the power of the study is 80%.

Inclusion Criteria

All Term and pre-term babies presenting with seizures, including both intramural and extramural neonates, were enrolled in the study.

Exclusion Criteria

Neonates who had already received anticonvulsant therapy were not included in the trial, and mothers or other caretakers that refused to consent to the study

A thorough antenatal history was taken, including the mother's age, previous medical history, parity, gestational age, history of illness during pregnancy, medication taken during pregnancy, natal history, including signs of fetal distress, the Apgar score, type of delivery, and medication given to the mother during delivery, as well as perinatal history. Before enrolling a neonate in the study, the parent or carers provided their written informed permission. On the prescribed proforma, the fundamental characteristics of each infant were recorded, including name, age, sex, address, weight, length, head circumference, and gestational age, which was calculated from the mother's last menstrual period, an ultrasound examination of the fetus before birth, or the new-born's Ballard score. A comprehensive physical examination was performed, and clinical observation was used to identify seizures. Each seizure episode's clinical information was documented, such as age at seizure onset, seizure duration, number, and type. According to Volpe's criteria, seizure types include mild, focal clonic, multifocal clonic, tonic, and myoclonic.

Before beginning a particular course of treatment, tests such as blood glucose, total serum calcium levels, serum sodium levels, and serum magnesium levels should be performed. Therefore, 3ml of blood will be collected by sterile technique in a sterile test tube for the following investigations. Random blood glucose measurements were made by using a glucometer, and the results were validated by calculating plasma glucose levels using the glucose oxidase method. The ion-selective method was used to estimate serum sodium, potassium, total calcium, and magnesium levels. The ARSENAZO-3 method was used to measure the levels of serum calcium.

For quantitative variables, the mean and standard deviation were used in the descriptive analysis; for categorical variables, the number and proportion were used. The proper diagrams, such as box plots, pie charts, and bar charts, were also used to display the data. Cross-tabulation and percentage comparison were used to determine the relationship between explanatory variables and category outcomes. The odds ratio and 95% confidence interval are shown. The statistical significance was examined using the Chi-Square test. Statistical significance was defined as a P value of 0.05. The statistical evaluation was performed using IBM SPSS version 22.

Quantitative outcome: The relationship between categorical explanatory variables and the quantitative outcome was evaluated by contrasting the mean values. The mean differences and their 95% confidence intervals were shown. Paired t-tests, ANOVA, and independent sample t-tests were performed to determine statistical significance. Data was depicted in a scatter plot, and the association between quantitative explanatory and outcome variables was evaluated by computing the person correlation coefficient. In addition, there was a linear regression analysis. The regression coefficient is shown together with its 95% confidence interval and p values.

RESULTS

During the study's six-month period from April 2017 to September 2017, 70 new-borns who had seizures and were hospitalized in the neonatal unit were examined. In the study population, the percentage of delivery by FORCEPS was 2.86%, LSCS was 48.57%, and normal vaginal delivery was 48.57% [Table 1].

Table 1: Descriptive analysis of the mode of delivery in study population (N=70)

Mode of delivery	Number	Percentages
FORCEPS	2	2.86%
LSCS	34	48.57%
NVD	34	48.57%

A total of 58 (82.86%) infants were born inside the study population, while 12 (17.14%) were referred from outside. Male participants in the research made up 39 (55.71%), while female participants made up 31 (44.29%) [Figure 1].

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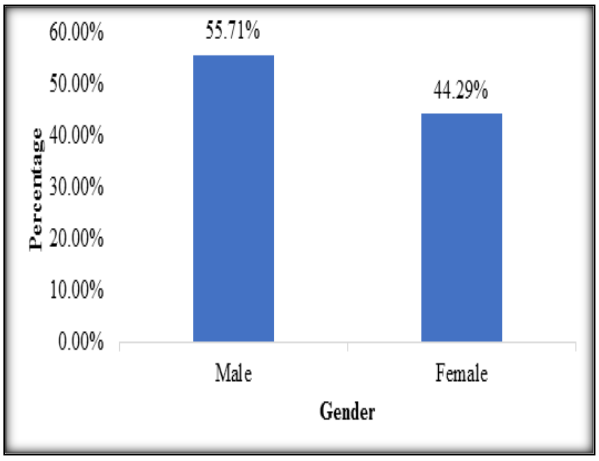

Figure 1: Bar chart of Gender distribution in the study population (N=70)

There were 19 pre-term births (27.14%), 51 term births (72.86%), and no post-term births within the study population [Figure 2].

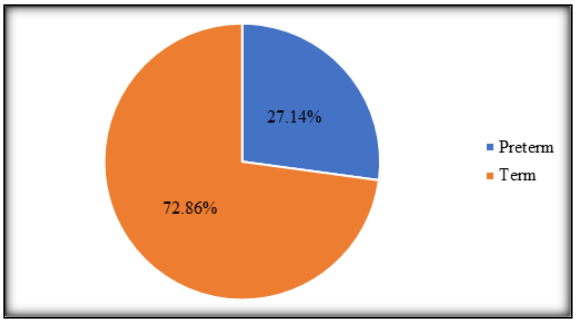

Figure 2: Pie chart of TERM/PRE-TERM/POST TERM distribution in the study population (N=70)

With a range of 0.99 kg to 4.16 kg, the average birth weight of the study group was 2.56 kg. (95% CI 2.40 to 2.72). In the study population, there were 31 new-borns with low birth weights (2.5 kg) and 39 neonates with normal birth weights (2.5 kg) [Figure 3].

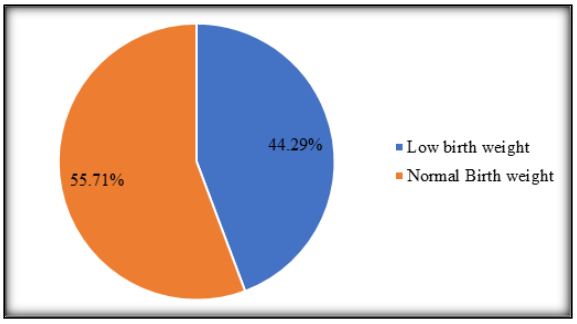

Figure 3: Pie chart of Birth weight category distribution in the study population (N=70)

In the research sample, the mean day when seizures started was 3.26, ranging from 1 to 17. (95% CI 2.40 to 2.72). In our study, the percentage of patients who experienced their first seizure within 24 hours was 20, followed by 24 to 72 hours (days 1 to 3), 4 days to 1 week (days 4 to 7), and more than 1 week (more than 7 days), with percentages of 31, 14, and 5 (7.14%), respectively. (Figure 4) The first three days of convulsions account for 72.86 percent. Tonic and clonic seizures affected 43 (61.43%), 18 (25.71%), and 9 (12.86%) infants in the study group, respectively [Figure 5].

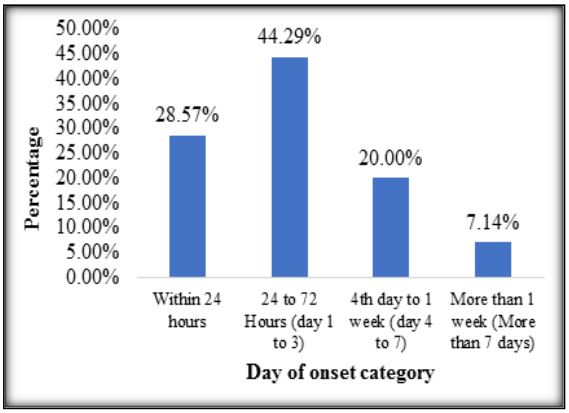

Figure 4: Bar chart of day of onset category distribution in the study population (N=70)

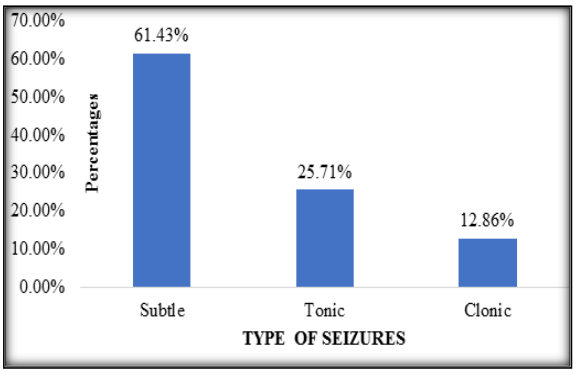

Figure 5: Bar chart of type of Seizures distribution in study population (N=70)

In this study, there were 70 participants, and 17 (24.29%) of them were found to have hypoglycemia. Fourteen neonates (20%) out of the study's 70 new-borns showed hypocalcemia. Out of 70 subjects, hyponatremia was reported in 6 neonates (8.57%). Three (4.29%) of the 70 new-borns exhibited hypomagnesemia. Out of 70 new-borns in my research, 3 (4.29%) had hypernatremia [Table 2].

Table 2: Summary of various biochemical abnormalities in the study population

Various Biochemical Abnormalities	Number N=70	Percentage
Hypoglycemia	17	24.29%
Hypocalcemia	14	20.00%
Hyponatremia	6	8.57%
Hypomagnesemia	3	4.29%
Hypernatremia	3	4.29%

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Note: The total percentages may not match 100% as this table reported the frequency of various metabolic abnormalities, which are not mutually exclusive.

Out of 70 subjects, 2 (2.86%) neonates were reported to combine hypoglycemia and hypocalcemia. 1 (1.43%) subject was reported to have combined hypocalcemia and hypomagnesemia [Table 3].

Table 3: Summary of combined biochemical abnormalities in neonates

Combined biochemical abnormalities	Frequency		Percentage	
	Yes	No	Yes	No
Hypoglycemia and Hypocalcaemia	2	68	2.86%	97.14%
Hypocalcaemia and Hypomagnesemia	1	69	1.43%	98.57%

The neonates reported with hypoglycemia were 7 (36.84%) among the 19 pre-terms, whereas only 10 (19.61%) were found among 51 term neonates. The difference in the proportion of hypoglycemia between term and pre-term neonates was statistically insignificant (P-value 0.135). The association with hypocalcemia for 19 pre-term neonates was 6 (31.58%), and for 51 term neonates was only 8 (15.69%), respectively. There was no significant difference in the proportion of hypocalcemia between term and pre-term subjects. (P-value 0.139). Among 19 pre-term neonates, 2 (10.53%) had hyponatremia; among 51 term neonates, only 4 (7.84%) had hyponatremia. The difference in the proportion of hyponatremia between term and pre-term neonates was statistically insignificant (P-value 0.721). Among 51 term new-borns, only 1 (1.96%) exhibited hypomagnesemia, compared to 2 (10.53%) of the 19 pre-term infants. There was no statistically significant difference in the prevalence of hypomagnesemia between term and pre-term infants (P-value 0.116) [Table 4].

Table 4: Summary of association of TERM/PRE-TERM with various biochemical abnormalities

Various biochemical abnormalities	Term/Pre-term		P-value
	Pre-term (N=19)	Term(N=51)	
Hypoglycemia	7 (36.84%)	10 (19.61%)	0.135
Hypocalcemia	6 (31.58%)	8 (115.69%)	0.139
Hyponatremia	2 (10.53%)	4 (7.84%)	0.721
Hypomagnesemia	2 (10.53%)	1 (1.96%)	0.116

The combination of hypoglycemia and hypocalcemia was not reported in term neonates, but for the pre-term, only 2 (10.53%) among 19 neonates were reported. Among 19 pre-term babies, only 1 (5.26%) neonate had a combination of hypocalcemia and hypomagnesemia [Table 5].

Table 5: Association of TERM/PRE-TERM/POSTTERM with a combination of various biochemical abnormalities of the study population (N=70)

Combine biochemical abnormalities		TERM/PRE-TERM/POST TERM	
		Pre-term (N=19)	Term (N=51)
Hypoglycemia and Hypocalcemia	Yes	2 (10.53%)	0 (0%)
	No	17 (89.47%)	51 (100%)
Hypocalcemia and Hypomagnesemia	Yes	1 (5.26%)	0 (0%)
	No	18 (94.74%)	51 (100%)

12 (63.16%) of the 19 new-borns had mild seizures, 4 (21.05%) had tonic seizures, and 3 (15.79%) experienced clonic seizures. 31 (or 60.78%) of the 51 term neonates experienced mild, 14 (or 27.45%) tonic, and 6 (or 11.76%) clonic seizures. There was no statistically significant difference between term and pre-term neonates in the number of seizure types (P value 0.816) [Table 6].

Table 6: Association of Term/Pre-Term with Type of Seizures of the study population (N=70)

Type Of Seizures	Term/Pre-Term/Post Term		P-Value
	Pre-Term (N=19)	Term (N=51)	
Subtle	12 (63.16%)	31 (60.78%)	0.816
Tonic	4 (21.05%)	14 (27.45%)	
Clonic	3 (15.79%)	6 (11.76%)	

DISCUSSION

Seizures are the most frequent neurological diseases in new-borns, and they are more common in pre-term neonates than in term neonates. In this study, 70 new-borns with seizures who have been hospitalized in the neonatal intensive care unit of the government Kilpauk medical college and met the inclusion and exclusion criteria were included.

Out of 70 new-borns, 49 were within normal ranges for gestational age, 19 were underweight for gestational age, and 2 were overweight, making up about 70%, 27.14%, and 2.86% of the total. Most of the neonates in this research who experienced seizures were full-term, gestationally-age-appropriate new-borns.[6,7] Compared to pre-term neonates, term new-borns had a much greater incidence. About 72.8% of the term, 27.1 in pre-term, had seizures.[6] Neonatal seizures showed male

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predominance. In this study, male neonates affected were about 55.71%, and female neonates were about 44.29%, with a male: female ratio of about 1.25:1. In other studies, (male 62.6%, females 37.4%) also showed that neonatal seizures are more common in males than females.[6] Also, other studies showed male: female ratio of 1.73:1, further supporting the study that seizures are common in males.[8] In this study, 2 new-borns delivered with forceps (2.86%), 34 new-borns delivered vaginally normally, and 34 newborns delivered through cesarean section. A study reported neonatal infants were born vaginally in 65.4% of cases, cesarean in 29.9%, and instrumentally in 4.7% of cases.[9] In my research, 31 new-borns (44.29%) and 39 neonates (55.71%) had birth weights under 2.5 kg and over 2.5 kg, respectively. Compared to neonates weighing more than 2500g, LBW babies had a greater prevalence of neonatal seizures.[9] 72.86% of the neonates in my research had seizures that mostly started within the first three days of life. In line with my findings, 73.6% of new-born seizures were documented within 3 days.[10] In our research, we discovered that subtle seizures, which accounted for roughly 61.43% of all new-born seizures in about 43 neonates, outnumbered tonic seizures (25.7%) and clonic seizures (12.86%), respectively. There were 8.2% tonic seizures, 27.2% clonic seizures, and 48.4% subtle seizures in pre-term neonates.[11] In a study, subtle seizures were reported to be the commonest type contributing about 42.6%, followed by tonic in 33.9% and clonic in 15.7% of neonates. [6].

Table 7: Comparison of overall metabolic abnormalities as reported by various authors

Overall biochemical abnormality	Kumar 1995 N=35	Aravind sood 1997 N=59	Madhu - Sudan 2016 N=120	Gayatri 2019 N=134	Present Study N=70
Present	22 (62.8 %)	29 (49.15 %)	52 (43.33 %)	85 (63.4 %)	34 (48.57 %)
Absent	13 (37.2 %)	30 (50.85 %)	68 (56.66 %)	49 (36.5 %)	36 (51.42 %)
Total	35 (100 %)	59 (100%)	120 (100%)	134 (100 %)	70 (100%)

A total of 48.57% of the 70 neonates in my study—34 of whom experienced seizures—had one or more metabolic abnormalities. According to the study by Sood et al overall biochemical abnormalities in 29 cases, constituting about 49.15%, were observed. [12] Compared to the Madhusudan et al 43.33%, Kumar et al discovered overall biochemical abnormalities in 62.8% of new-borns.[13,14] In study by Gayathri et al showed 63.4% overall abnormalities among 120 neonates.[15] Hypoglycemia was more common in pre-term infants—36.84% versus 19.61% in term infants. Pre-term new-borns reported hypocalcemia at 31.58%, which was greater than term babies' 15.69% rate. In other studies, hypoglycemia and hypocalcemia were the most common, with 39 (43.8%) and 28 (35.4%) cases, respectively.[16] Whereas another study found hypocalcemia followed by hypoglycemia to be the common biochemical abnormalities. Lastly, Pre-term new-borns were more likely to have hypoglycemia in a study that supports our study.[6] Thus, these studies point to the significance of performing a biochemical workup in new-born convulsions, particularly in light of the higher prevalence of blood glucose and calcium levels. Correcting these temporary biochemical abnormalities is related to a favourable prognosis and result. In our study, pre-term neonates showed 2 cases with a combination of hypoglycemia and hypocalcemia (5.88%) and one with hypocalcemia and hypomagnesemia (2.94%). A certain study showed hypoglycemia and hypocalcemia combination in 9% and hypocalcemia hypomagnesemia combination in 7.9% of cases.[8]

CONCLUSION

One of the most prevalent neurological conditions in new-borns is neonatal seizures. Thorough clinical examination, prompt diagnosis, and immediate timely care and diagnosing the etiology are required to prevent long term neurological damage to developing brain,. Additionally, biochemical anomalies could either be a secondary issue or be linked to other aetiologies. These transitory abnormalities are easily treated when detected early, with a good prognosis. Therefore, a biochemical workup should be performed on every new-born who exhibits seizure activity, and it should always be the initial line of investigation.. Early treatment of these metabolic imbalances aids in reducing the frequency of seizures and the overuse of anticonvulsants, which may not always be essential. To determine the true incidence of the problem and quickly treat these seizures, continuous video EEG monitoring should be used whenever it is practical to identify new-born seizures.

REFERENCES

1. Davis AS, Hintz SR, Van KP, LiL, Das A, Stoll BJ, et al. Seizures in extremely low birth weight infants are associated with adverse outcomes. J Pediatr 2010; 157:720-5.
2. MillerSP, WeissJ, BarnwallA, Ferriero DM, Latal HB, Ferrer RA, et al. Seizure-associated brain injury in a term new-born with perinatal asphyxia. Neurology 2002; 58:542-8.
3. Zupanc ML. Neonatal seizures. Pediatric Clinics. 2004; 51:961-78.
4. Holanda MRR, Melo AN. Comparative clinical study of pre-term and full-term new-born neonatal seizures. Arq Neuropsiquiatr 2006; 64:282–8.
5. Jensen FE. Neonatal seizures: an update on mechanisms and management. Clinics in perinatology. 2009; 36:881-900.
6. Das D, Debbarma SK. A study on the clinico-biochemical profile of neonatal seizure. J Neurol Res 2016; 6:95–101.
7. Park W, Kim DY, Jung CZ, Kim SD. Clinical study of neonatal seizure. Journal of the Korean Child Neurology Society 1998; 6:71–82.

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8. Sudia S, Berwal P, Nagaraj N, Jeavaji P, Swami S, Berwal A. Clinico-etiological profile and outcome of neonatal seizures. Int J Contemp Pediatr 2015; 2:389–94.
9. Taksande AM, Vilhekar K, Jain M, Lakra M. Clinico-Biochemical Profile of neonatal seizures. Pediatric Oncall Journal 2005; 2:68–68.
10. Nawab T, Lakshmipathy NS. Clinical profile of neonatal seizures with special reference to biochemical abnormalities. Int J ContempPediatr 2016; 3:183-8.
11. Ross AL, Lomorso C. Neonatal Seizures state: A study of clinical, Pathology and electrographic features in 137 full-term babies with a long term follow up. Pediatrics 1970; 45: 404-425.
12. Sood A, Grover N, Sharma R. Biochemical abnormalities in neonatal seizures. Indian Journal of Paed 2003; 70:221-4.
13. Kumar A, Gupta V, Kachhawaha JS, Singla PN. Biochemical Abnormalities in neonatal seizures. Indian Pediatr 1995; 32:424-428.
14. Madhusudhan K, Nadavapalli Suresh S, Babu TR, Rao JV, Kumar S B. Study of biochemical abnormalities in neonatal seizures with special reference to hyponatremia. Int J Contemp Pediatr 2016; 3:730-4.
15. Gayatri Bezboruah. A Study on Biochemical Abnormalities in Neonatal Seizures. IOSR J. Med. Dent. Sci 2019; 18:53-57.
16. Suganthi V, Vikneshwari K, Thivya G. Prevalence of hypomagnesemia in neonatal seizures in a tertiary care hospital in South India. Pediatr Rev Int J Pediatr Res 2017; 4:63–7.

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