

Original Research Article

Neonatal seizures-clinical profile and evaluation of associated biochemical abnormalities in a tertiary newborn intensive care unit

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ABSTRACT

Background: Seizure is the most common sign of neurological dysfunction in a neonate. Seizures increase the risk of impaired neurologic development and also the risk of death. Neonatal seizures per se are not a disease entity but rather a symptom commonly related to significant underlying disorders.

Methods: It is a non-randomized prospective observational study conducted in the NICU at Ranees hospital, government Pudukkottai medical college, Pudukkottai from December 2023 to June 2024. Both intramural and extramural neonates with seizures were included in the study as per protocol and evaluated.

Results: Out of the 152 neonates included in the study, 64% had onset of seizure in the first day of life. A slight male preponderance in seizure incidence is noted. Hypoxic ischaemic encephalopathy is the commonest aetiology followed by biochemical abnormalities. Subtle seizures are the commonest single type of seizures and subtle + multifocal combined are the commonest combination type seen. Hypoglycaemia, hypocalcaemia and hypomagnesaemia are the common biochemical abnormalities noted.

Conclusions: Early recognition of seizures and early correction of the Biochemical abnormalities is crucial to prevent neonatal morbidity and mortality.

Keywords: Neonatal, Seizures, Subtle, Biochemical, Hypoglycaemia, Hypocalcaemia

INTRODUCTION

Seizure is the most common sign of neurological dysfunction in a neonate.¹ Seizures occur more frequently during the neonatal period than other periods of life.²

The incidence of seizures varies from 2.3/1000 to 5/1000 live births in live term neonates. The incidence in preterm neonates may be as high as 20%.³ Data from India suggests an incidence of 1.3% of all live births.⁴ The underlying aetiology in a seizure may be either neurological or metabolic.³ Neonatal seizures increase the risk of impaired neurologic development and also the risk of death.⁵

Volpe notes that “seizures are defined clinically as a paroxysmal alteration in neurological function, i.e. behaviour, motor and autonomic function. Seizures result when an excessive synchronous discharge of neurons within the central nervous system occurs (i.e. depolarization).⁶ Neonatal seizures are not a disease entity but rather a symptom commonly related to significant underlying disorders, which may require specific treatment.⁷ Finally, there are experimental data suggesting that seizures themselves may result in brain injury.⁸

Seizures in a neonate may or may not be accompanied by abnormalities of the surface EEG.⁶ Clinical presentation

of seizures is considerably different in the new born period when compared with the well-organized seizure activity seen in older children and adults. The precise reason must be related to the development state of the nervous system in the prenatal period. The most common neuroanatomical processes in this period are organizational events. These events are characterised by proper orientation, alignment and laying of cortical neurons, elaboration of axonal and dendritic ramifications and establishment of synaptic connections.⁹

Rhythmic activities such as sucking, respiration, cycling and walking movements are controlled by brain stem in an infant. These may suddenly appear as seizures. Changes in respiratory pattern, sudden assumption of a fixed posture or sudden bout of rapid sucking, blinking and cycling movement all indicate brain damage in a neonate and may be suggestive of seizure.¹⁰

Hill and Volpe classified neonatal seizures into the following types¹¹: Subtle, tonic (generalised, focal), clonic (multifocal, focal) and myoclonic (generalised, focal, multifocal).

Subtle seizure is the most frequently observed category of neonatal seizures and includes repetitive bucco-lingual movements, orbital-ocular movements, unusual bicycling or pedalling, swimming and autonomic findings.¹²

Neonatal seizures due to biochemical abnormalities are treatable. Delay in initiation of correction of biochemical abnormalities will increase the risk of neonatal mortality, morbidity, and long-term sequelae. Early recognition of seizures and early correction of the biochemical abnormalities is important.

Hence study in this topic may bring out a decision tree which will be useful in early diagnosis and appropriate management.

Objective

Objectives were to study the clinical profile and various biochemical abnormalities in newborn presenting with seizures in a tertiary neonatal intensive care unit.

METHODS

Approval was obtained from the institutional ethics committee, government Pudukkottai medical college, Pudukkottai. This non-randomized prospective observational study was conducted in the neonatal intensive care unit of Ranees hospital, government Pudukkottai medical college, Pudukkottai from December 2023 to June 2024.

Sample size was estimated using the OpenEpi software and was calculated based on the incidence from previous studies with a confidence level of 95% and was found to be 145 cases.

Statistical analysis was performed with IBM SPSS version 27.0 statistics software package. Data were tabulated and evaluated.

The following definitions and diagnostic criteria were used according to specifications in standard text books.

Seizure

Seizure is defined as a paroxysmal involuntary disturbance of brain function that may manifest as an impairment or loss of consciousness, abnormal motor activity, behavioural abnormality, sensory disturbance or autonomic dysfunction.⁶

Neonatal seizures

Seizures occurring during the neonatal period (birth to 28 days of life) are classified as neonatal seizures. These are classified according to classification given by Hill and Volpe.¹¹

A detailed history was recorded in each case in a pretested proforma. Importance was laid on the age of occurrence of first seizure, duration, number and type of seizure, ante natal, natal and post-natal risk factors which includes maternal diabetes, drug addiction / withdrawal, prolonged rupture of membranes, perinatal asphyxia, traumatic delivery, preterm, small for date, low birth weight, septicaemia, meningitis, intracranial bleed and hyperbilirubinemia.

Biochemical abnormalities

The criteria for diagnosing various biochemical disturbances were: Hypoglycaemia-glu-<40 mg/dl, hyperglycaemia-glu->125 mg/dl, hyponatremia-Na²⁺<130 meq/l, hypernatremia-Na²⁺>150 meq/l, hypokalaemia-K⁺<3.5 meq/l, hyperkalaemia-K⁺>5.5 meq/l, hypocalcaemia-Ca²⁺<7.0 mg/dl, hypercalcemia-Ca²⁺>11 mg/dl, hypomagnesaemia-Mg²⁺<1.5 mg/dl, hypermagnesaemia -Mg²⁺>2.5 mg/dl, hypophosphatemia-P>8.0 mg/dl and hyperphosphatemia-P<3.5 mg/dl.

All the cases were subjected to the following investigations: blood glucose estimation by glucose oxidase-peroxidase method, serum sodium and potassium estimation by flame photometry, serum calcium estimation by o-cresol-phthalein complexone (OCPC) method, serum phosphorus estimation by ammonium molybdate method (UV end point technique), serum magnesium by arsenazo dye binding method, haemoglobin estimation by cyanmethaemoglobin method, total leucocyte count by automated coulter counter and differential leucocyte count by automated count analyser.

Following specific investigations were done as per requirement: Blood culture and sensitivity, cerebrospinal

fluid analysis: Cytology-cell type and count, biochemistry-glucose and protein, microbiology-gram staining and culture. CT brain: EEG (Electroencephalography).

Inclusion criteria

All neonates with seizures admitted to the neonatal intensive care unit, Ranees hospital, government Pudukkottai medical college, are included in the study.

Exclusion criteria

Neonates whose parents did not give consent for the study were excluded.

RESULTS

All neonates with seizures admitted to the NICU in the department of paediatrics were included in this study.

Table 1: Incidence of neonatal seizures in inborn neonates.

No. of live birth at Ranees hospital	No. of neonatal seizures	Incidence in intramural neonates
7447	50	6.7 / 1000

Out of the total 7447 live births within the hospital during the study period, 50 intramural neonates had seizures. The incidence is 6.7/1000.

A total of 102 neonates delivered outside were admitted to Ranees hospital with seizures during the study period and they were also included in the study. So, a total of 152 neonates with seizures were included in this study.

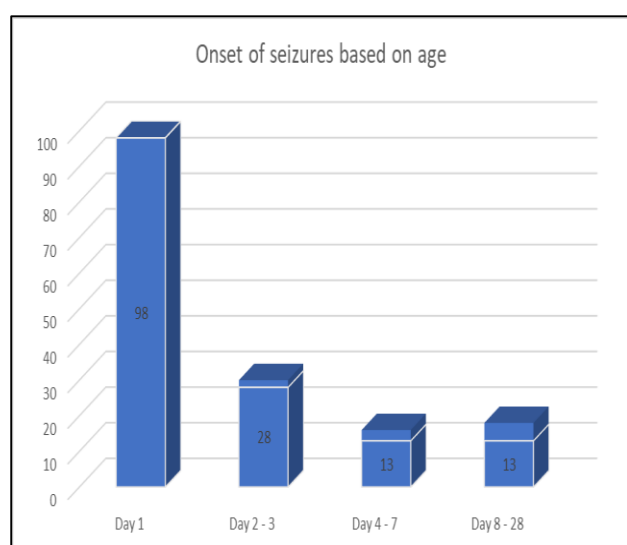


Figure 1: Onset of seizures based on age.

Out of the 152 cases, 64% had seizures on day 1, 18% had seizures between day 2 and 3 and 9% between day 4-7 and another 9% between day 8-28.

Table 2: Distribution of cases according to gender.

Sex	Intramural	Extramural	Total
Male	29 (58%)	56 (55%)	85 (56%)
Female	21 (42%)	46 (45%)	67 (44%)
Total	50 (33%)	102 (67%)	152 (100%)

Among intramural neonates, 58% (29 cases) were male and 42% (21 cases) were female. In extramural cases 55% (56 cases) were male and 45% (46 cases) were female.

Table 3: Distribution of cases according to gestational age.

Gestational age	Term	Preterm	Total
Intramural	31	19	50
Extramural	94	8	102
Total	125	27	152

Seizures were predominantly seen in term neonates in both intramural and extramural admissions. Among the 50 intramural cases, 31 were term and 19 were preterm. Similarly in extramural 94 were term and 8 were preterm.

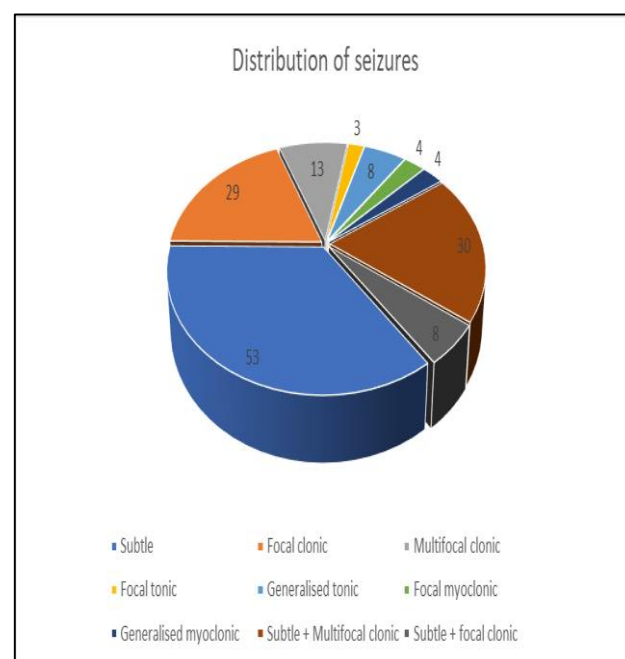


Figure 2: Distribution of different types of seizures.

Subtle seizures were the most common type with 35% incidence, focal clonic were the next common type with 19% incidence. Among the combined types, subtle + multifocal clonic were the commonest with 19.7% incidence.

Table 4: Biochemical profile of neonates with seizures related to gestational age.

Biochemical abnormality	Hypoglycaemia	Hyponatremia	Hypocalcaemia	Hypomagnesaemia	Hyperphosphatemia
Term	38	27	27	24	8
Preterm	11	5	6	6	2

Overall, hypoglycaemia was commonest biochemical abnormality 32.2% (49) followed by the hypocalcaemia

21.7% (33), hyponatremia 21% (32), hypomagnesaemia 19.7% (30) and hyperphosphatemia 6.5% (10).

Table 5: Biochemical abnormalities in neonates with seizures as per aetiology.

Aetiology	Hypoglycaemia	Hypocalcaemia	Hyperphosphatemia	Hypomagnesaemia	Hyponatremia
Metabolic	15	17	2	16	11
HIE	23	4	3	6	13
Septicaemia	8	11	4	7	6
IC bleed	1	1	2	1	2

Hypocalcaemia was the commonest metabolic cause of seizures and was found in 17 cases followed by hypomagnesaemia (16) and hypoglycaemia (15). In HIE, hypoglycaemia was the commonest biochemical abnormality noted and was found in 23 cases followed by hyponatremia in 13 cases. In sepsis, hypoglycaemia was the commonest abnormality noted and was found in cases followed by hypomagnesaemia. Hyperphosphatemia was more commonly seen in IC bleed.

Table 6: Aetiological distribution of neonates with seizures.

Aetiology	No. of cases	Percentages of incidence (%)
HIE	59	38.8
Metabolic	39	25.7
Septicaemia	32	21.1
IC bleed	7	4.6
Meningitis	8	5.3
Unknown	7	4.6

HIE was the commonest aetiology for seizures and was found in 59 cases (38.8%) followed by metabolic in 39 cases (25.7%) and septicaemia in 32 cases (21.1%). The other causes were IC bleed in 7 cases and meningitis in 8 cases (5.3%).

DISCUSSION

Incidence

In our study, the incidence of seizures in intramural neonates is 6.7/1000. Various authors have reported the incidence of neonatal seizures from the 2/1000 to 14/1000.

For instance, Eriksson et al has reported 1.5/1000 whereas Sood et al has reported 13/1000.^{13,14}

Age

In the present study, 82% (126 cases) had onset of seizures within the first 3 days of life which is comparable to other studies such as Calciolari et al who had reported 74% of seizures within the first 2 days of life and Rose and Lombroso et al reported 78% of seizures within the first week of life.^{15,16}

Gender

The male to female ratio of incidence of neonatal seizures is 1.26:1 in this study which shows a slight preponderance of seizure activity in male neonates.

Clinical profile

In the present study, 35% (53 cases) had subtle seizures and it was the most common type encountered followed by focal clonic in 21% (32 cases). In combined type, subtle + multifocal clonic was the commonest and was seen in 19.7% (30 cases). This is comparable to other studies such as Singh et al from Nepal which showed subtle seizures at 42%, focal clonic at 32% and multifocal clonic at 11%.¹⁷

Aetiology

HIE was the commonest aetiology for neonatal seizure as per our study which is 38.8% (59 cases). Almost all the other studies referred such as Eriksson and Zetterstrom et al, Mizrahi and Calciolari had similar results. Metabolic causes constitute about 25.6% (39 cases) which is comparable with the studies of Kumar et al and Sood et al.^{13-15,19,18}

Biochemical abnormalities

In the present study, biochemical abnormalities were found in 107 cases out of the 152 cases with neonatal

seizures. Among these, hypoglycaemia was the commonest abnormality detected and was present in 32.2% (49 cases) followed by hypocalcaemia in 21.7% (33 cases), hyponatremia in 21% (32 cases) and hypomagnesaemia in 3.2% (5 cases).

These findings correlate with the study done by Kumar et al who studied neonatal seizures and found hypoglycaemia in 50% (11 cases), hypocalcaemia in 31.8% (7 cases), hyponatremia in 5.45% and hypomagnesaemia in 13.63% (3 cases).¹⁹

Sood et al studied 59 neonates with seizures with overall biochemical abnormalities in 49.15% (29 cases).¹⁴ In his study, hypocalcaemia was the commonest 51.72% (15 cases) followed by hypoglycaemia in 41.37% (12 cases).

In our study combined biochemical abnormalities were found in 64.10% cases. Most common combined biochemical abnormality was hypocalcaemia + hypomagnesaemia found in 36% followed by hypoglycaemia + hyponatremia in 16% cases.

Limitations

Being an observational study, randomization was not done in our study and hence it is difficult to rule out bias and confounding as possible alternative explanations for seizure association.

CONCLUSION

Seizures play a major role in mortality and morbidity during the neonatal period. In this study, seizures were found slightly more common in males than females. Hypoxic ischaemic encephalopathy was found to be the commonest aetiology of neonatal seizures followed by metabolic abnormalities. Hypoglycaemia, hypocalcaemia and hypomagnesaemia are the common biochemical abnormalities seen irrespective of the primary aetiology. Early identification and correction of these metabolic abnormalities would be helpful in control of the seizure thereby reducing the morbidity and mortality.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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