

ORIGINAL RESEARCH

Etiology and Determinants of Neonatal Seizures: A cross-sectional study

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ABSTRACT

Background: Neonatal seizures are the most prevalent and recognisable clinical symptom of neurological dysfunction in the newborn baby. Neonatal seizures manifests as abnormal muscular activity or an autonomic changes. Neonatal brain is immature and is more prone for seizures. **Objective:** to find the details about neonatal seizures and its early diagnosis, better treatment and prognosis. **Methods:** Our study was carried out upon patients admitted in NICU with complaints of abnormal body movement at Rohilkhand Medical College and Hospital, Bareilly (U.P.). There were total 50 study participants. **Result:** Neonatal seizures were occurring more in term gestation, males, outborn deliveries, vaginal deliveries. 42% seizures occurred within 1st 24 hours of life. Subtle seizure was most common followed by multifocal-clonic seizure. HIE was the commonest etiology of seizures followed by meningitis. Most of the cases were hospitalized within a week of onset of neonatal seizures. Most of the cases got discharged from the hospital. Maximum APGAR score of at 5 minutes was 5. Maximum APGAR score of at 10 minutes was 6. **Conclusion:** There was no statistical association of etiology with type of seizures or day of onset of seizures (p-value was more than 0.05). There was no statistical association of type of seizures with gestational age or day of onset of seizures (p-value was more than 0.05).

Keywords: Etiology, Determinants, Neonatal Seizures

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INTRODUCTION

Neonates who have risks factors has increased rate of Neonatal seizures & risks further increases if gestational age at time of birth is also less, whereas preterm with low birth weight (LBW) and extremely LBW have a greater incidence.¹

Epidemiological research indicates that the largest incidence of seizures occurs during the 1st year of life, suggesting that the growing brain is very vulnerable to seizures. Infants having neonatal seizures are predisposed to neurological damage, epileptic issues later in life and neonatal death. Seizures occur in 1% to 5% of infants during the 1st month of life (the neonatal phase), which is one of the very dangerous periods for seizures in human life.²

The most common etiology of neonatal seizures among 1 to 2 out of every 1000 live infants is HIE (hypoxic-ischemic encephalopathy). Other illnesses that frequently present clinically with seizures include cerebrovascular disease like arterial and venous stroke, intracerebral haemorrhage, and subarachnoid haemorrhage. Other etiological issues, such as hypoglycaemia, hypocalcaemia, and ICH may coexist with prenatal asphyxia and should always be ruled

out. Recurrent seizures can lead to permanent neuronal damage and has increased danger of developing epilepsy in future and long term cognitive disabilities.

Mainly there are four types of seizures³ Subtle, clonic, tonic and myoclonic. Each seizure can focal, multifocal and generalised. Clinically new born seizures are difficult to identify and distinguish from normal behaviours or abnormal movements of non-epileptic origin.

As a result, it is hard to diagnose and treat seizures as soon as possible, as failure to do so may result in brain damage. The seizures onset is related to the aetiology & prognosis can be made on basis of it. Birth asphyxia, example: frequently occurs within the 1st 3 days of life, however meningitis appears after the first week. If the neonate convulses within hours of birth, it indicates a dismal prognosis and brain damage.⁴ Neonatal seizures differ significantly from seizures seen in older children, owing to the young brain's limited ability to propagate generalised or structured electrical discharges.

The importance of this study is to understand that neonatal seizures could be the initial and possibly

only, clinical symptom of a central nervous system problem in a newborn. Seizures in neonates might show the presence of a possibly curable aetiology, necessitating a rapid evaluation to ascertain the cause and initiate early etiology-specific therapy. As a result, clinical diagnosis, neonatal seizure classification, and appropriate management are crucial for the neonate's care.

The purpose of this study is to find out most common etiology of neonatal seizure in the neonates presenting with complaint of abnormal body movement and admitted in NICU at Rohilkhand medical college and hospital. In the literature there are very few studies on this topic in this part of Uttar Pradesh, hence the present study is being carried out to find the details about neonatal seizures and its early diagnosis, better treatment and prognosis.

MATERIAL AND METHODS

This cross-sectional study was done on patients admitted in NICU with complaints of abnormal body movement Department of Pediatrics at Rohilkhand Medical College and Hospital, Bareilly (U.P.). The study was done for total duration of 12 months. (August 2023 to July 2024).

Inclusion Criteria

- All patients admitted in NICU at Rohilkhand medical college and hospital and had complaints of abnormal body movement.
- Clinically diagnosed and investigation proven neonatal seizures.

Exclusion Criteria

- Patient's having abnormal body movements other than neonatal seizures (Eg: Jitteriness, benign myoclonus of infancy, etc.)
- Patient's attendant who did not give informed consent.

Sample Size

P =anticipated proportion of neonatal seizures because of meningitis⁵

Q =100- p

L =absolute error (5%)

$N=4pq/l^2$

$=(4 \times 3.2 \times 96.8)/25$

$=49.56$

≈ 50

Thus, the sample size planned for this study was 50.

METHODOLOGY

After taking clearance from Institutional Ethics Committee, Rohilkhand Medical College and Hospital, Bareilly, the study was conducted.

Written informed consent was taken from

parents/guardians of all the patients participating in the study in a language they could understand. Anonymity was proposed as optional and confidentiality was guaranteed.

A detailed clinical history and examination was done of the patient with seizures. Appropriate investigations according to history and clinical presentation (for example, RBS, CSF Analysis, S. electrolytes, ABG, CBC, Blood cultures, EEG, MRI Brain, USG Cranium etc.) was done. Heart rate, respiration, capillary refill time, blood pressure, and temperature were recorded in all cases. Gestation, birth weight, weight for age were recorded. The neonate were examined for malformation, dysmorphic features and anterior fontanel. Detailed neurological examination was done including the assessment of consciousness, tone, and fundus examination. Systemic examination was done to rule out hepatosplenomegaly, abnormal urine odor, neuro-cutaneous markers, hypopigmented macules on skin etc. All essential investigations were conducted as multiple etiologies can coexist. Patient with seizures onset had undergone lumbar puncture under all aseptic precautions to confirm the diagnosis like meningitis. All the patients were also planned to undergo contrast enhanced MRI brain under proper protocol but most of them were hemodynamically unstable hence MRI brain was planned for follow up. USG cranium was also done in participants of study in order to rule out intracranial hemorrhages and malformations. EEG was also planned for all participants. Also, additional investigations were done in neonates who didn't respond to combination of drugs i.e. phenobarbitone & phenytoin in or earlier in newborns with specific features.

From all the patients who gave consent to participate in study, detailed maternal medical and obstetric history was obtained and recorded in predesigned proforma. Details of gestation including complications during pregnancy, gestational age at time of delivery, mode of delivery and birth weight were noted. The types of seizure and its causes were collected for the study and data was analysed.

STATISTICAL ANALYSIS

The data was imported into SPSS (statistical package for Social Sciences); licensed version 23.0. Data was analysed by applying frequency, percentage, mean, standard deviation. Appropriate statistical tests were applied depending upon the type and distribution of data. P value <0.05 is considered significant.

RESULTS

In our study, majority of the study subjects had term gestation. 58 % study subjects had term gestational age whereas 42 % study subjects had preterm gestational age.

Table 1: Distribution of neonatal seizures according to gender

TYPE OF SEIZURES	GENDER		TOTAL	P-VALUE
	MALE	FEMALE		
SUBTLE	12	6	18	
MULTIFOCAL CLONIC	9	5	14	0.498
FOCAL CLONIC	9	1	10	
TONIC	6	1	7	
MYOCLONIC	1	0	1	
Total	37	13	50	

In our study, majority of the study subjects of both genders had subtle seizures followed by multifocal-clonic seizures. Out of 50 study subjects, 37 were males and 13 were females. There is no statistical association of types of neonatal seizures with gender as p-value is more than 0.05.

In our study, majority of the study subjects were outborn. 84 % study subjects had outborn delivery whereas 16 % study subjects had inborn delivery. In our study, majority of the study subjects were delivered vaginally. 78 % study subjects had vaginal delivery whereas 22 % study subjects had c-section delivery.

Table 2: Distribution of cases according to day of onset of seizures

DAY OF ONSET OF SEIZURES	FREQUENCY	PERCENT
1	21	42.0
2	12	24.0
3	3	6.0
4	3	6.0
5	2	4.0
6	1	2.0
7 to 28	8	16.0
Total	50	100.0

In our study, majority of the study subjects had onset of seizures on day one.

Table 3: Distribution of cases according to type of neonatal seizures

TYPE OF SEIZURES	FREQUENCY	PERCENT
SUBTLE	18	36.0
MULTIFOCAL CLONIC	14	28.0
FOCAL CLONIC	10	20.0
TONIC	7	14.0
MYOCLONIC	1	2.0
Total	50	100.0

In our study, majority of the study subjects had subtle seizure (36 %) followed by multifocal clonic seizure (28%) > focal clonic seizure (20%) > tonic seizure (14%) > myoclonic seizure (2%).

Table 4: Distribution of cases according to etiology of neonatal seizures

ETIOLOGY	FREQUENCY	PERCENT
HIE	21	42.0
MENINGITIS	19	38.0
HYPOGLYCEMIA	2	4.0
HYPOCALCEMIA	2	4.0
HYPONATREMIA	1	2.0
IVH	5	10.0
Total	50	100.0

In our study, etiology of majority of the study subjects was HIE (42%) followed by meningitis (38%) > IVH (10%) > hypoglycemia (4%) > hypocalcemia (4%) > hyponatremia (2%).

Table 5: Distribution of cases according to resuscitation needed at time of birth to babies with neonatal seizures

RESUSCITATION NEEDED AT TIME OF BIRTH	FREQUENCY	PERCENT
YES	29	58.0
NO	21	42.0

Total	50	100.0
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In our study, majority of the study subjects were those who needed resuscitation at time of birth with neonatal seizures. 58 % study subjects needed resuscitation whereas 42 % study subjects didn't needed resuscitation. There is strong statistical association of etiology of seizures with resuscitation needed at time of birth to babies with neonatal

seizures as p-value is 0.001 by applying chi square formula.

In our study, majority of the study subjects (12%) were hospitalised in first 7 days.

In our study, majority of the study subjects (50%) got discharged; 34% got LAMA/DOPR and mortality occurred in 16% of the study subjects.

Table 6: Distribution of study subjects according to APGAR score at 5 minutes

APGAR SCORE AT 5 MIN	FREQUENCY	PERCENT
4	3	6.0
5	18	36.0
6	10	20.0
7	5	10.0
8	13	26.0
9	1	2.0
Total	50	100.0

In our study, maximum study subjects i.e. 36% had APGAR score at 5 minutes = 5. There is strong statistical association of etiology of seizures with

APGAR score at 5 minutes of patients with neonatal seizures as p-value is 0.001 by applying chi square formula.

Table 7: Distribution of study subjects according to APGAR score at 10 minutes

APGAR SCORE AT 10 MIN	FREQUENCY	PERCENT
5	6	12.0
6	23	46.0
7	2	4.0
8	9	18.0
9	10	20.0
Total	50	100.0

In our study, maximum study subjects i.e. 46% had APGAR score at 10 minutes = 6. There is strong statistical association of etiology of seizures with

APGAR score at 10 minutes of patients with neonatal seizures as p-value is 0.001 by applying chi square formula.

Table 8: Association of etiology with type of neonatal seizures

ETIOLOGY	TYPE OF SEIZURES					TOTAL	P-VALUE
	SUBTLE	MULTIFOCAL CLONIC	FOCAL CLONIC	TONIC	MYOCLONIC		
HIE	7	7	5	1	1	21	0.210
MENINGITIS	9	3	4	3	0	19	
HYPOGLYCEMIA	1	0	0	1	0	2	
HYPOCALCEMIA	0	0	1	1	0	2	
HYPONATREMIA	0	0	0	1	0	1	
IVH	1	4	0	0	0	5	
Total	18	14	10	7	1	50	

There is no statistical association of etiology with type of neonatal seizures as p-value is 0.210 by applying chi square test.

Table 9: Association of etiology of neonatal seizures with day of onset of seizures

ETIOLOGY	DAY OF ONSET OF SEIZURES							TOTAL	P-VALUE
	1.0	2.0	3.0	4.0	5.0	6.0	7.0		
HIE	14	4	0	0	1	1	1	21	0.122
MENINGITIS	3	4	3	3	0	0	6	19	
HYPOGLYCEMIA	1	1	0	0	0	0	0	2	
HYPOCALCEMIA	1	0	0	0	1	0	0	2	
HYPONATREMIA	0	1	0	0	0	0	0	1	
IVH	2	2	0	0	0	0	1	5	
Total	21	12	3	3	2	1	8	50	

There is no statistical association of etiology with day of onset of seizures as p-value is 0.122 by applying chi square test.

Table 10: Association of type of neonatal seizures with day of onset of seizures

TYPE OF SEIZURES	DAY OF ONSET OF SEIZURES							TOTAL	P-VALUE
	1.0	2.0	3.0	4.0	5.0	6.0	7.0		
SUBTLE	10	3	1	3	0	0	1	18	0.416
MULTIFOCAL CLONIC	5	5	1	0	0	1	2	14	
FOCAL CLONIC	4	1	0	0	1	0	4	10	
TONIC	1	3	1	0	1	0	1	7	
MYOCLONIC	1	0	0	0	0	0	0	1	
Total	21	12	3	3	2	1	8	50	

There is no statistical association of type of neonatal seizures with day of onset of seizures as p-value is 0.416 by applying chi square test.

There is no statistical association of types of neonatal seizures with gestational age as p-value is 0.409 by applying chi square test.

DISCUSSION

Neonatal seizures are most prevalent and recognisable clinical symptom of neurological dysfunction in any newborn baby. Neonatal seizures manifests as abnormal muscular activity or an autonomic changes. Neonatal brain is immature and is more prone for seizures. Neonates who have risks factors has increased rate of Neonatal seizures & risks further increases if gestational age at time of birth is also less, whereas preterm with low birth weight & extremely LBW have a greater incidence.

Most of the research participants in the study were delivered at term. Of the research participants, 42% had preterm gestational age and 58% had term gestational age. In contrast, Ajay *et al.* observed that the incidence was 0.69% for term newborns and 6.14% for preterm ones⁶. The incidence ranged from 0.1 to 0.5% in term and 10 to 22.7% in preterm, according to and Laroia *et al.*⁷. This variation is ascribed to the involvement of several factors, including maternal medical illness, socioeconomic status, & the availability of health facilities, among others. This can be also attributed to our centre being a tertiary healthcare centre and getting only critical referred cases.

Most of the research participants in index study, both male and female, experienced subtle seizures. 13 of the 50 research participants were female, and 37 were male. Since the p-value is greater than 0.05, there is

no statistical correlation between the kinds of newborn seizures and gender. Male preponderance was also seen by Shah GS *et al.*⁸ & Ajay *et al.*⁶ According to Sanjeev Kumar Digraet *et al.*⁹ (Jammu, India), the male to female ratio was 2.4:1, and they noted that this was because male sex received more care while female newborns were not given the medical attention they need.

Most of the research participants in index study were outborn. Outborn deliveries accounted for 84% of study participants, whereas inborn deliveries accounted for 16%. Most of the research participants in our study were delivered vaginally. While 22% of research participants underwent a c-section, 78% of study participants gave birth vaginally. Similarly, according to Sethy G, *et al.*¹⁰ 76% were born outside & Vaginal births accounted for 62.12% of all births.

The majority of study participants (42%) in our study were reported on the first day after their seizures began. According to Sanjeev *et al.*, seizures happen more frequently within 24 hours. Twelve percent of the research participants in index study were admitted to the hospital during the first seven days. However, seizures occurred in less than 3 days of life in 87.9% of instances. This is comparable to Shah GS *et al.*⁸ and Ajay *et al.*⁶ Subtle seizures were shown to be more prevalent in those aged 24 to 72 hours, but focal seizures were more common in those aged <24 hours. This difference is statistically significant.

Subtle seizures accounted for 36% of the research participants, followed by multifocal-clonic seizures (28%), focal clonic seizures (20%), tonic seizures (14%), and myoclonic seizures. This is comparable to Shah GS *et al.*⁸, who claimed that the most prevalent form of seizures, accounting for more than 50% seizures, are mild seizures. According to Ajay *et*

*al.*⁶, multifocal seizures are most prevalent kind. Preterm infants frequently experienced subtle seizures, whereas term infants frequently experienced multifocal seizures; both findings are statistically significant.

The majority of study participants in index study had HIE as their aetiology (42%), followed by meningitis (38%), IVH (10%), hypoglycemia (4%), hypocalcaemia (4%), and hyponatraemia (2%). Similar to earlier studies by Shah GS *et al.*⁸ Meningitis was the next most common cause of neonatal convulsions, following HIE in the our study as well as in the study of Shah GS *et al.*⁸. Increased sepsis is a result of protracted premature membrane rupture, frequent P/V exams, and inadequate cleanliness by the mother & family members. The metabolic abnormalities we found were hyponatraemia (2%) in our study were hypoglycemia (4%), hypocalcaemia (4%) & hyponatraemia (2%) and are comparable to those reported by Shah GS *et al.*⁸ & Ajay *et al.*⁶. In our study, around 10% of newborns experienced intracranial haemorrhage, which is fewer than the 10% described in Cloherty¹¹.

The bulk of the research participants in our research were newborns with seizures who required resuscitation at delivery. While 42% of research participants did not require resuscitation, 58% of them did. Similar findings were observed by Glass HC *et al.*¹² & van Rooij LG *et al.*¹³.

The majority of study participants (50%) were released, 34% had LAMA/DOPR, and 16% died during the research. According to Glass HC *et al.*¹² study reports, up to 20% of newborns die from convulsions.

The majority of study participants in our study, or 36%, had an APGAR score of 5 minutes = 5. The highest percentage of study participants in our study, or 46%, had an APGAR score of 6 at 10 minutes. There was strong statistical association of etiology of seizures with APGAR score at 5 minutes as well as 10 minutes of patients with seizures as p-value is 0.001 in both scenarios by applying chi square formula. Eun S *et al.*¹⁴ discovered that infantile seizures were significantly predicted by Apgar scores. Birth weight & gestational age have an impact on Apgar scores. Regardless of delivery method, researchers discovered a significant association (p-value < 0.001) between Apgar ratings & infantile seizures in both the full-term & normal-birth weight study groups (bodyweight ≥ 2.5 kg). Persson M *et al.*¹⁵ suggested that, while there were fewer obvious correlations between Apgar scores and seizures, newborns with a 5-minute Apgar score of seven or lower and a 10-minute Apgar score of eight or below had higher hazard ratios. Apgar score had a range of 277.7 (154.4 – 499.5) corresponding to an Apgar score of 0 to 1.9 (95% CI 1.6 – 2.2) given for Apgar score of 9. Newborns with a 5-minute Apgar score of 7-8 & a 10-minute Apgar score of 9-10 had greater hazard ratios of cerebral

palsy & epilepsy than newborns with an Apgar score of 9-10 at both five and ten minutes.

It was also found in index study that the chi square test yielded a p-value of 0.210, there has been no significant association between the type of newborn seizures and their aetiology. The chi square test yielded a p-value of 0.122, indicating that there is no significant association between the aetiology and the day on which seizures began. Given that the chi square test yielded a p-value of 0.416, there is no significant association between the type of newborn seizures and the day on which they began. Using the chi square test, the p-value is 0.409, indicating no association correlation between the kinds of newborn seizures and gestational age.

CONCLUSION

It was concluded that Maximum study subjects i.e. 36% had APGAR score of 5 at 5 minutes. Maximum study subjects i.e. 46% had APGAR score of 6 at 10 minutes. There was no statistical association of etiology with type of seizures (p-value = 0.210). There was no statistical association of etiology with day of onset of seizures (p-value = 0.122). There was no statistical association of types of neonatal seizures with gestational age (p-value = 0.409). There was no statistical association of types of neonatal seizures with day of onset of seizures (p-value = 0.416).

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