

Evaluation of clinical profile of neonatal seizures and outcome interventions

¹Dr Chippy Haridas, ²Dr Chandra Prakash Meena, ³Dr. Shintu Thomas, ³Dr. Chander Mohan,
⁴Dr. Rajendra Kumar Gupta.

¹Senior Resident, Department of Paediatrics, Jhalawar Medical College, Jhalawar (Rajasthan), India

²Senior Resident, Department of Paediatrics, NIMS Medical College, Jaipur (Rajasthan), India

³Junior Resident, Department of Paediatrics, Jhalawar Medical College, Jhalawar (Rajasthan), India

⁴Senior Professor and Head, Department of Paediatrics, Jhalawar Medical College, Jhalawar (Rajasthan), India

Corresponding Author

Dr Chandra Prakash Meena

Senior Resident, Department of
Paediatrics, NIMS Medical College,
Jaipur (Rajasthan), India

Article Received: 24-06-2024

Article Accepted: 27-11-2024

©2024 Biomedical and
Biopharmaceutical Research. This is an
open access article under the terms of
the Creative Commons Attribution 4.0
International License.

ABSTRACT

Background: Seizures are most likely to occur in the neonatal period than at any other point in life. A prompt diagnosis and aggressive management is critical in developing short- or long-term adverse neuro-developmental outcome including cerebral palsy, post-neonatal epilepsy and intellectual disability. Therefore, we evaluated the different causes, clinical characteristics, types and immediate outcome of neonatal seizures. Material and methods: Present study was carried out among 191 neonates (age 0 to 28 days) who presented to the hospital with history of seizures or who developed seizures during hospital stay. Male babies were more than females. Results: Onset of seizures on first day of life was seen among 73 neonates, 81 (42.41%) neonates had subtle seizures. Gestational age of neonates was 86 (46.03%) were full term babies and 105 (54.97%) were preterm babies. 54.45% (104 cases) had normal vaginal delivery and 39.27% (75 cases) by LSCS and 6.28% (12 cases) were born with the assistance of forceps. Birth weight of neonates was 102 (53.40%) babies were under weight (<2.5kg) and 89 (46.06%) babies were weighing >2.5 kg. The etiology of seizures was 107 (56.02%) had birth asphyxia, 34 (17.08%) had septicemia, 29 (15.18%) had hypoglycaemia, 11 (5.78%) had hypocalcaemia, 2 (1.05%) had bilirubin encephalopathy and 8 (4.19%) had unknown reason for experiencing seizures. 163 neonates (85.34%) were successfully discharged and 28 neonates (14.66%) were expired. Conclusion: Neonatal seizures typically showed underlying unidentified neurological disease and it presented non-specific response of the immature neural system to varied degrees of insults.

Keywords: Neonatal Seizures, hypoxic-ischemic encephalopathy, neurological events

INTRODUCTION

The most common threat is seizures that occur in both term and preterm neonates, however, The International League against Epilepsy Task Force on neonatal seizures has projected various pre, peri and postnatal neurological events of the central nervous system (CNS) to be the

etiopathological causes.¹Seizures are among the most critical and frequent signs of significant neurological dysfunction during the neonatal period, a time when their occurrence is more common than at any other stage of life. The incidence rate is 57.5 per 1,000 in infants weighing less than 1,500 g and 2.8 per 1,000 in those weighing between 2,500 and 3,999 g. The underlying causes of neonatal seizures vary depending on the age of onset, as well as EEG patterns and clinical characteristics. The neonatal brain is uniquely prone to seizures due to its immature state, which differs significantly from the mature brain. Evidence from animal studies highlights factors such as delayed maturation of Na⁺/K⁺ ATPase and elevated densities of NMDA and AMPA receptors, particularly calcium-permeable GLUR2 AMPA receptors. These features contribute to heightened excitability and the lasting effects of seizures, especially those associated with perinatal hypoxia. Drugs that inhibit AMPA receptors, like topiramate, could therefore play a beneficial role in managing this condition.²The main aim of the study was to evaluate the different causes, clinical characteristics, types and immediate outcome of neonatal seizures.

METHODOLOGY

Source of data: Neonates who were admitted in neonatal intensive care unit of Shrimati Heera Kunwar Baa Mahila Hospital, Jhalawar Medical College

Type of the study: Observational study.

Sample size: $n = (t)^2 p (1-p) / e^2$

Where,

t = 95% confidence interval (t = 1.96)

p = proportion of neonates with seizures (132) in total admission (978) during last 4 months

Hence $p = 132/978 = 0.1349$

e = allowed error 5% (e = 0.05)

Hence $n = \frac{1.96 \times 1.96 \times (0.14)(1-0.14)}{0.05 \times 0.05}$

= 180.63 = 181

Now with effect of error

$n = n + 5\% \text{ of } n = 181 + 9.05$

$n = 190.05$

n = 191

Inclusion Criteria:

All neonates (age 0 to 28 days) who presented to the hospital with history of seizures or who develop seizures during hospital stay were taken into study.

Exclusion Criteria:

1. Babies > 28 days of life.
2. Seizure like activity like jitteriness, titanic spasm.
3. Subtle activity without autonomic features of apnoea.

Method of Data Collection

All neonates admitted in the NICU during the study period, who fulfil the inclusion criteria was included in the study.

The eligible babies were registered for the study and the following particulars collected

- Perinatal details
- Indication for NICU admission
- Baby details on admission (indication, vitals, anthropometry)

- Details during hospital stay
 1. Time of Onset of seizures
 2. Type and duration of seizures
 3. Investigations done during the period

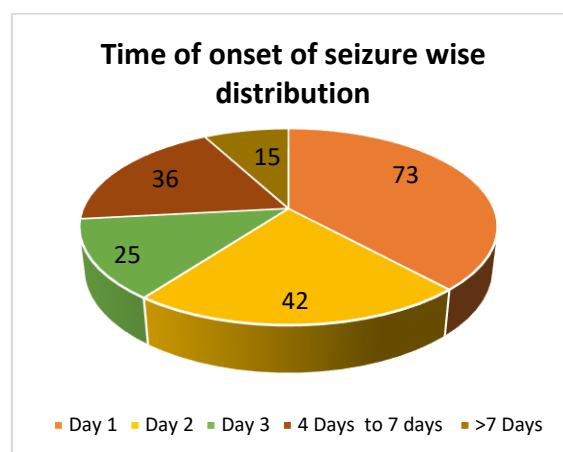
Methods of Data Analysis and Interpretation:

Data was analysed according to the objectives of the study using descriptive and inferential statistics and was presented in the form of tables, graphs, and diagram. Qualitative and categorical data were expressed in the forms of percentage to analyse further.

Duration of The Study: 1 year (as approved by Ethical Committee).

RESULTS

In our study, 112 (58.64%) were males and 79 (41.36%) were female babies with male to female ratio of 1.41:1. The onset of seizures on first day of life was seen in 73 neonates (38.22%). On second day of life 42 neonates developed seizures (21.99%), on third day of life 25 (13.09%) babies developed convulsions. From fourth to seventh day 36 neonates have developed seizures (18.85%). The first three days of life together constituted 74% of neonatal seizures.

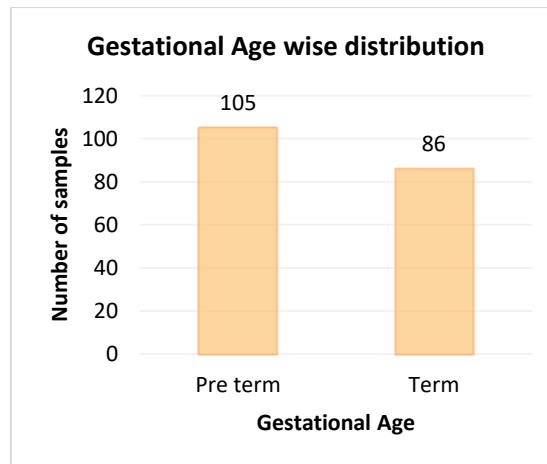


Out of 191 neonatal seizures, 81 (42.41%) neonates had subtle seizures, 68 (35.60%) neonates had multifocal seizures, 30 (15.71%) had focal clonic seizures, 11 (5.76%) neonates had tonic seizures and 1 (0.52%) neonate had myoclonic type of seizures.

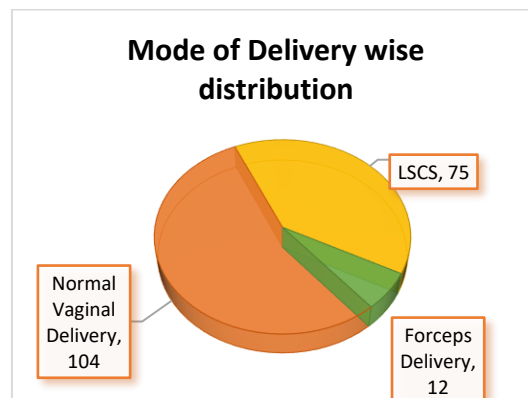
Table 1: Types of seizure wise distribution

Type of seizure	Studied Group	Percentage
Subtle	81	42.41%
Multifocal	68	35.60%
Focal Clonic	30	15.71%
Tonic	11	5.76%
Myoclonic	1	0.52%
Total	191	100%

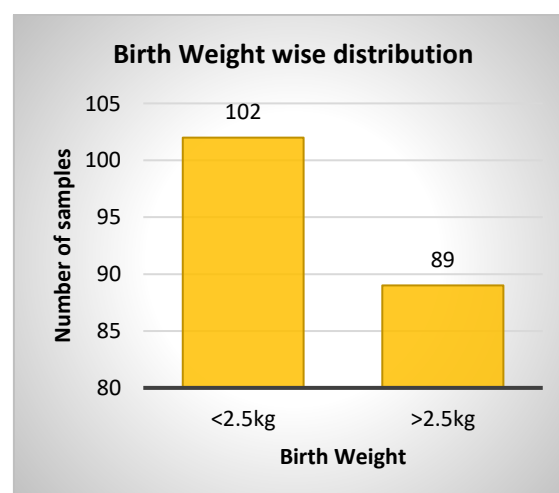
According to gestational age-wise distribution, out of 191 babies experienced seizure episodes, 86 (46.03%) were full term babies and there were 105 (54.97%) preterm babies.



With mode of delivery wise distribution, out of 191 cases, 54.45% (104 cases) were born from normal vaginal delivery and 39.27% (75 cases) by LSCS and 6.28% (12 cases) were born with the assistance of forceps.



When considering birth weight-wise distribution, out of 191 neonates suffered seizures, 102 babies were under weight (<2.5kg) (53.40%) and 89 babies were weighing >2.5 kg (46.06%).



When diagnosis was done for all the 191 neonates who suffered convulsions, 107 (56.02%) had birth asphyxia, 34 (17.08%) had septisaemia, 29 (15.18%) had hypoglycaemia, 11 (5.78%)

had hypocalcaemia, 2 (1.05%) had bilirubin encephalopathy and 8 (4.19%) had unknown reason for experiencing seizures.

Table 2: Diagnosis wise distribution

Diagnosis	Studied Group	Percentage
Birth Asphyxia	107	56.02%
Sepsis	34	17.80%
Hypoglycemia	29	15.18%
Hypocalcaemia	11	5.76%
Bilirubin Encephalopathy	2	1.05%
Unknown	8	4.19%
Total	191	100%

With outcome wise distribution, 163 neonates (85.34%) were successfully discharged and 28 neonates were expired (14.66%).

Table 3: outcome wise distribution

Outcome	Studied Group	Percentage
Discharged	163	85.34%
Expired	28	14.66%
Total	191	100%

DISCUSSION

In the present descriptive study, among 191 neonates, 112 (58.64%) were males and 79 (41.36%) were female babies with male to female ratio of 1.41:1. This male preponderance is consistence with most of the studies done by Chesti MS *et al.*³ and Devjibhai k *et al.*⁴ and Hannah C. Glass *et al.*⁵

S. No.	Name of the Author	Male predominance percentage
1	Chesti MS <i>et al.</i> ³	64% male
2	Devjibhai k <i>et al.</i> ⁴	60% male
3	Hannah C. Glass <i>et al.</i> ⁵	56% male
4	Present study	58.64% male

There was general agreement between most of the studies that males have marginally higher incidence of provoked or unprovoked convulsions than in females.⁵ The difference was majorly because of higher exposure to risk factors like pre-term delivery, low birth weight, lesional epilepsy and acute symptomatic seizures. On the other hand, females have marginally low incidence of unprovoked seizures but high incidence of IGEs (Idiopathic Generalised Seizures) 15-20% of all other epilepsies. Over all to say the incidence of status epilepticus, sudden unexpected deaths, low prognosis and mortality are higher among male gender than in female genders.⁶

In the present study, most of the neonates (73 out of 191) (38.22%) had seizures on first day of life itself. On second day of life 42 neonates developed seizures (21.99%), on third day of life 25 (13.09%) babies developed convulsions. From fourth to seventh day 36 neonates have developed seizures (18.85%). The first three days of life together constituted 74% of neonatal seizures. About 7.85% of neonates had developed seizures after a week of birth.

Author	First day of life	Second day of life	3-7 day of life	>7 days of life
Chesti MS <i>et al.</i> ³	36.2% neonates had seizures	22.5% neonates had seizures	33.4% neonates had seizures	8.75% neonates had seizures
Devji bhai k <i>et al.</i> ⁴	40% neonates had seizures	30% neonates had seizures	19% neonates had seizures	11% neonates had seizures
Present study	38.22% neonates had seizures	21.99% neonates had seizures	32% neonates had seizures	7.85% neonates had seizures

Present study results regarding the onset of seizures were comparable and as similar as the studies done by Devjibhai k *et al.*⁴ and Chesti MS *et al.*³ These authors clearly stated that the actual reason for higher incidence of seizures on the first day of life was due to the immaturity of developing infant brain and low or varying levels of neurotransmitters. Neonatal seizures have unique pathophysiology and their EEG findings differ from older age groups. Most of the times the identification and evaluation of seizures will become difficult in infants and will be overlooked and missed out to treat.⁷

In our study most common type of neonatal seizure was subtle type (42.41%). 81 out of 191 babies had reported with subtle seizures. 68 (35.60%) neonates had multifocal seizures, 30(15.71%) had focal clonic seizures, 11 (5.76%) neonates had tonic seizures and 1 (0.52%) neonate had myoclonic type of seizures. These results were very similar and close with the results reported by other studies from developing and developed countries.

S.No.	Author	Most common seizure in their study
1	Manoel RR Holanda <i>et al.</i> ⁸	Clonic seizures in pre-term & subtle seizures in full term neonates.
2	Devjibhai k <i>et al.</i> ⁴	Subtle seizures
3	Chesti MS <i>et al.</i> ³	Subtle seizures
4	Acar DBet <i>et al.</i> ⁹	Subtle seizures
5	Present study	Subtle seizures

Many authors confirmed subtle (undefined) type of seizures which were common than many other convulsions in neonatal occurrence. Acar DBet *et al.*⁹ stated that neonatal brain has many immature neurons and a very high levels of N- methylD-aspartate and AMPA(Alpha amino hydroxy-5- Methyl-4-isoxazol Propionic Acid receptors but a very low GABA receptors (Gamma Amino Butyric Acid), which was one of the reason for low seizures threshold for neonates. More over in neonates GABA receptors acts as excitatory function through Na-k-Cl co transporter 1(NKCC 1) which was also a reason for very low threshold for getting

Convulsions. In case of hypoxia situations the effect would be double folded and even more decrease in threshold values. Study done by G.M Ronen, S. Penney *et al.*¹⁰ stated that Clinical neonatal seizures occurrence was 6 times more often in preterm infants than in full term infants.

In the present study, out of 191 babies experienced seizure episodes, 86 (46.03%) were full term babies and 105 (54.97%) were preterm babies. Our results showed that pre-term babies have suffered seizures more than full term babies. Our results were consistent with other studies done by GM Ronen, S penney *et al.*¹⁰ Our study results differed from the studies done by Malik BA, Butt MA *et al.*¹¹ Chesti MS *et al.*³, Devijbhai K Vadheret *et al.*⁴ and Manoel RR Holanda *et al.*⁸ in which they concluded that clinical neonatal convulsions occurred were more in full-term babies than pre-term. In a study done by Hanna C Glass *et al.*⁴⁵ about 88% of study group suffered seizures and were term babies.

S.No.	Author	Inference
1	Manoel RR <i>et al.</i> ⁸	Among 104 neonates (study group) had seizures, 74 are full term babies and 30 are pre-term babies.
2	G M Ronen, S penney <i>et al.</i> ¹⁰	Seizure incidence rate was 2 per term babies and 11.1 for pre-term neonates.
3	Hanna. C. Glass <i>et al.</i> ⁵	Among 426 consecutive neonates having seizures 88% were term babies
4	Malik BA, Butt MA <i>et al.</i> ¹¹	Full term babies have higher seizures rate than in pre-term babies.
5	Devjibhai k <i>et al.</i> ⁴	Among 100 babies, 94 were full term and only 5 were pre-term babies.
6	Chesti MS <i>et al.</i> ³	Among 80 study group, 71 were full term and 8 were pre-term babies.
7	Present study	Among 191 babies with seizures, 86 were full term and 105 were pre-term babies.

In our study, when it comes to mode of delivery, out of 191 cases, 54.45% (104 cases) were born from normal vaginal delivery and 39.27% (75 cases) by LSCS and 6.28% (12 cases) were born with the assistance of forceps. Our results were consistent with the studies done by Devjibhai k *et al.*⁴ and Chesti MS *et al.*³

S. No	Author	Normal vaginal delivery	LSCS	Forceps Delivery
1	Devjibhai k <i>et al.</i> ⁴	82%	15%	3%
2	Chesti MS <i>et al.</i> ⁵	53.7%	38.7%	7.5%
3	present study	54.45%	39.27%	6.28%

In the current study, we have also studied about birth weight wise distribution. Out of 191 total neonates suffered seizures, 102 babies were under weight (<2.5kg) (53.40%) and 89 babies were weighing >2.5 kg (46.06%).

A study done by G M Ronen *et al.*¹⁰ stated that incidence rate of seizures was 13.5 for infants weighing less than 2500grs at birth in their total study group. Low birth weight and shorter gestational age were obvious risk factors for a neonate to get suffered by seizures. A cohort

study done in Japan by Yuelian Sun, Mogenset *al.*¹² on birth weight risk for epilepsy stated that incidence rates were increased consistently with decreased birth weight <2000 gms. They also stated that there was five-fold increased risk of epilepsy if the gestational period was less than 32 weeks. Our study results confirmed the correlation between low birth weight and incidence of seizures in neonates.

In the present study, when it comes to diagnosis wise distribution of seizures incidence, total of 191 neonates who suffered convulsions, out of them 107 (56.02%) had birth asphyxia, 34 (17.08%) had septicemia, 29 (15.18%) had hypoglycaemia, 11 (5.78%) had hypocalcaemia, 2 (1.05%) had bilirubin encephalopathy and 8 (4.19%) had unknown reason for experiencing seizures.

In the present study, most common etiology of neonatal seizures included asphyxia and septicemia, then followed by hypoglycaemia, hypocalcaemia, bilirubin encephalopathy and a very few idiopathic seizures. Our results were as similar as with the studies done by Chesti MS *et al*³ and Devjibhai k *et al.*⁴

Peri natal asphyxia is also called as hypoxic - ischaemic encephalopathy. When the oxygen supply to the brain is decreased, all the mental processes will be delayed resulting in excessive nerve impulses leading to seizures. Occurrence of seizures worsens the brain injury and therefore it is crucial for physicians to implement and start appropriate treatment measures to prevent or control the seizure activity. Perinatal asphyxia is consistently common in both developing and developed countries as reported by other studies. When it comes to septicemia, its being the second most common reason for developing infantile seizures across the globe causing many mortalities and morbidities in neonates. Aseptic precautions during delivery, following sterilisation regulations and appropriate antibiotic administration will prevent infection chances in NICU.

S.No	Author	Most common etiology for neonatal seizures
1	Manoel RR Holanda <i>et al.</i> ⁹	Peri-ventricular hemorrhage – in pre-term babies. Asphyxia – in full term babies
2	G.M Ronen, S penney <i>et al.</i> ¹¹	Hypoxic ischemic encephalopathy (Asphyxia)
3	Hannah. C Glass, Renee A Shellhass <i>et al.</i> ⁵	Hypoxic ischemic encephalopathy (Asphyxia)
4	E.M Mizrahi, P. Kellaway <i>et al.</i> ^{13, 14}	Hypoxic ischemic encephalopathy (Asphyxia)
5	Acar DBet <i>al.</i> ⁹	Hypoxic ischemic encephalopathy (Asphyxia)
6	Devjibhai k <i>et al.</i> ⁴	Hypoxic ischemic encephalopathy (Asphyxia)
7	Chesti MS <i>et al.</i> ³	Hypoxic ischemic encephalopathy (Asphyxia)
8	present study	Hypoxic ischemic encephalopathy (Asphyxia)

Our study results were as similar as the other studies done.

When we studied about metabolic disturbances like hypoglycaemia (5.78%) and hypocalcaemia (1.05%) of new borns, they had seizures on second day of birth and a week later respectively. A retrospective study done by Guang Yang, Li-ping Zou *et al.*¹⁵ on neonatal hypoglycemic brain injury leading to infantile seizures was studied. In their study they retrospectively analyzed infantile spasms of having neonatal hypoglycaemia on their first two days after birth. They found out that neonates who had low glucose <2.6 mmol/L developed

infantile spasms later in 2 to 10 months of life. They concluded that the neonatal hypoglycemic brain injury was associated with subsequent development of infantile spasm.¹⁵

Hypocalcemia on other hand was another cause of infantile seizures which was a treatable one of neonatal seizures. A study done by Matthew D. Thornton, Lei Chen *et al.*¹⁶ on hypocalcaemia effects on six days old neonate who developed seizure like episode. They found out the etiology behind this was due to maternal excessive usage of calcium carbonate during third trimester. Thus, educating about the dangers of taking excessive calcium during pregnancy will be an important anticipatory guidance.

Bilirubin encephalopathy is also called as kernicterus that is relatively rare but continues to occur despite global newborn screening.¹⁷ In our study, about 1.05% (2 cases) was reported with bilirubin encephalopathy induced seizures. Severe hyperbilirubinemia is considered when serum bilirubin level is more than 20mg/dl. It is always associated with other risk factors like low birth weight, short gestational period etc. appropriate treatments like phototherapy should be started as soon as possible to prevent further complications.

In the present study, outcome wise distribution had also been studied, out of 191 neonates, 163(85.34%) had been discharged with the improvement in their symptoms and about 28(14.66%) neonates unfortunately had been expired. Most of worst prognosis had been seen with the cases of asphyxia induced seizures. Neonates with septicemia were in the second position causing severe morbidity and mortality. A very few cases of hypoglycemia had been reported with worst prognosis resulting in death of the neonate.

S.no	Author	Death rate	Cause of death
1	Devjibhai k <i>et al.</i> ⁴	17.33%	Asphyxia
2	Chesti MS <i>et al.</i> ³	15%	Asphyxia, Sepsis and Hypoglycemia
3	present study	14.66%	Asphyxia, Sepsis and Hypoglycemia

Present study has the outcome as consistent with other studies from developed and developing counties.

CONCLUSION

This study conveys the occurrence of seizure was more on 1st day neonate and was less on later days, the subtle type of seizure was more with neonates compared with other types, the etiology was birth asphyxia, septicaemia and biochemical abnormalities. 85.34% babies had successful outcome and 14.66% were expired.

From the present study, we concluded that in most of the cases, neonatal convulsions cause was apparent, birth asphyxia was the main etiology identified in cases of neonatal seizures. However, identification of cause was helpful regarding treatment and prognosis in neonatal seizures.

On the other hand, transient metabolic abnormalities like hypoglycemia (particularly common in low-birth-weight babies) and hypocalcemia also has lead to neonatal seizures, on time and early intervention can prevent further brain damage in these conditions. Also, time of onset was also important thing to watch out in identifying etiology in neonatal seizures, generally with birth asphyxia which was commonly occurring in first three days of life, while CNS infections may start over after one week.

Subtle seizures were most common seizures in our present study. Neonatal seizure is generally associated with perinatal complications, therefore continued developments in neonatology may reduce incidence of seizures and thus it prevents cognitive, neurological, epileptic and cognitive consequences of neonatal seizures.

Neonatal Seizures typically shows underlying unidentified neurological disease and it presents non-specific response of the immature neural system to varied degrees of insults. Neonatal seizures are difficult to identify and they are separate, unique & distinctive when compared to seizures in adults because of the immaturity of the nervous system and it may require separate classification.

LIMITATIONS

The main limitation of this study was small sample size, only clinically evident seizures were included, as a result of this only electrical seizures were included and very subtle seizures might have been missed. Also, non-availability of synchronized aEEG/ video EEG results in unnecessary unwanted inclusion of neonates with seizure mimics.

ACKNOWLEDGEMENT

The authors wish to thank all the neonates and their parents who participated in the study and made it possible. The authors also acknowledge Dr. Shailendra Vashistha (Assistant Professor, Deptt. of Transfusion Medicine, GMC, Kota) and VAssist Research Team (www.thevassist.com) for their contribution in manuscript editing and submission process.

REFERENCES

1. Kim EH, Shin J, Lee BK. Neonatal seizures: diagnostic updates based on new definition and classification. *Clin Exp Pediatr*. 2022;65(8):387-397.
2. Mikati MA, Lemmon ME. Neonatal seizures. In: Kliegman R, St Geme. Nelson textbook of paediatrics, Ed 21st. Place: Elsevier; 2019. p.
3. MohmadSaleemChesti, Naveed Shahzad et al. Clinical profile, etiology, type and outcome of neonatal seizures:a hospital-based study, *Int J ContempPediatr*. 2022 Jan;9(1):104-108.
4. Devjibhai K Vadher et al. A study of etiology, onset and clinical manifestations of neonatal seizures.volume-6 | issue-4 | april - 2017 • issn no 2277 - 8179 | if : 4.176 | icvalue : 78.46
5. Glass HC, Shellhaas RA, Wusthoff CJ, Chang T, Abend NS, Chu CJ, CilioMR,Glidden DV, Bonifacio SL, Massey S, Tsuchida TN. Contemporary profile of seizures in neonates: a prospective cohort study. *The Journal of pediatrics*. 2016 Jul1;174:98-103.
6. John.CMc Hugh, Norman Epidemiology and classification of epilepsy: gender comparisons *Int Rev Neurobiol* 2008;83:11-26.
7. Krawiec C, Muzio MR. Neonatal Seizure. [Updated 2023 Jan 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
8. Hesdorffer DC, Benn EK, Cascino GD, Hauser WA. Is a first acute symptomatic seizure epilepsy? Mortality and risk for recurrent seizure. *Epilepsia*. 2009 May;50(5):1102-8.
9. Acar DB, Bulbul A, Uslu S. Current Overview of Neonatal Convulsions. *Sisli Etfal Hastan Tip Bul*. 2019;53(1):1-6. Published 2019 Mar 22.
10. Ronen GM, Penney S, Andrews W. The epidemiology of clinical neonatal seizures in Newfoundland: a population-based study. *The Journal of pediatrics*. 1999 Jan1;134(1):71-5.

11. Malik BA, Butt MA et al. Seizure etiology in the new born period. J Coll physicians Surg Pak 2005;15:786-90
12. Yuelian sun, Mogensvestergaard et al. Gestational Age, Birth Weight, Intrauterine Growth and Risk for Epilepsy. Am J Epidemiol. 2008 Feb 1; 167(3): 262–270.
13. Mizrahi Eli M. Neonatal Seizures and neonatal epileptic syndromes. Neurologic clinics in epilepsy. 2001;19(2):427-56.
14. Mizrahi EM, Kellaway P. Characterization and classification of neonatal seizures. Neurology. 1987 Dec 1;37(12):1837-44.
15. Guang Yang, Li-Ping Zou et al. neonatal hypoglycemic brain injury is a cause of infantile spasms. Expther Med .2016 may;11(5)2066-2070
16. Thornton MD, Chen L, Langhan ML. Neonatal seizures: soothing a burning topic. *Pediatr Emerg Care*. 2013;29(10):1107-1110.
17. Sumit das, Frank K H et al. clinic pathological spectrum of bilirubin encephalopathy/kernicterus. Diagnostics (Basel)2019,mar;9(1):24