International Journal of Contemporary Pediatrics
Kumar L et al. Int J Contemp Pediatr. 2025 Mar;12(3):461-466
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20250411

Original Research Article

Evaluation of the predictors of epilepsy in hypoxic ischemic encephalopathy term neonates

Love Kumar*, Nazeer A. Jeergal, A. N. Thobbi

Department of Paediatrics, Al- Ameen Medical College and Hospital, Vijayapura, Karnataka, India

Received: 01 January 2025
Accepted: 11 February 2025

***Correspondence:**
Dr. Love Kumar,
E-mail: loverajpoot086@gmail.com

ABSTRACT

Background: Hypoxic ischemic encephalopathy (HIE) is a major cause of neonatal morbidity and mortality, particularly in term infants. Neonates with severe HIE are at high risk for long-term neurological consequences, including epilepsy. This study aims to identify clinical, biochemical, and neuroimaging predictors of epilepsy in HIE neonates.
Methods: A prospective cohort study was conducted on 100 term neonates diagnosed with HIE at a tertiary neonatal intensive care unit (NICU) in India. Data including gestational age, birth weight, Apgar scores, clinical features, neuroimaging results (MRI/CT), serum lactate levels, and EEG findings were collected. Epilepsy was diagnosed based on clinical symptoms and EEG findings.
Results: Of 100 neonates with HIE, 28 (28%) developed epilepsy by 6 months. Significant predictors included low Apgar score at 1 minute (≤3) ($p<0.01$), early onset seizures (within 24 hours) ($p<0.01$), and severe HIE ($p=0.02$). Basal ganglia and cortical injury on neuroimaging were more common in the epilepsy group ($p=0.01$, $p=0.03$). Elevated lactate levels (>5 mmol/l) were associated with epilepsy ($p=0.02$). Abnormal EEG findings were observed in 78.57% of epileptic neonates ($p<0.001$). Logistic regression identified several independent predictors: Apgar score ≤3, early seizures, severe HIE, brain injury, elevated lactate levels, and abnormal EEG.
Conclusions: Early clinical, biochemical, and neuroimaging factors are strong predictors of epilepsy in term neonates with HIE. These findings highlight the importance of early identification and intervention to improve long-term outcomes.

Keywords: HIE, Epilepsy, Apgar scores, Lactate level, Abnormal EEG, Cortical injury

INTRODUCTION

Hypoxic ischemic encephalopathy (HIE) remains a major cause of neonatal morbidity and mortality, particularly in term infants. It results from perinatal asphyxia, leading to an insufficient supply of oxygen to the brain, causing neuronal injury. Neonates with severe HIE are at high risk for long-term neurological sequelae, including developmental delays, cerebral palsy, and epilepsy.[1] HIE affects approximately 1-2 per 1000 live births in high-income countries, and in resource-limited settings, especially in parts of Africa, Asia, and Latin America, the prevalence is higher.[2] In these regions, the incidence can be as high as 10-20 per 1000 live births.[3] The prevalence of HIE in India is estimated to be 2-4 per 1000 live births. This incidence is influenced by factors such as maternal health, antenatal care, and the presence of skilled healthcare professionals during delivery.[4] HIE is one of the leading causes of neonatal mortality in India, contributing to approximately 10-15% of all neonatal deaths.[4]

Neonatal seizures frequently result from HIE, affecting approximately 40-60% of neonates with moderate-to-severe HIE.[5] Research indicates that seizures generally commence within the initial 24 hours post-birth in newborns with HIE, frequently aligning with the phase of greatest vulnerability for cerebral damage.[6] Research from the Neonatal Seizure Registry revealed that almost 30% of

children with HIE who experienced seizures had repeated seizures lasting several days.[7] Research indicates that seizures independently exacerbate the severity of neurological consequences in HIE. The seizure burden, defined as the cumulative duration and frequency of seizures, correlates with poorer motor and cognitive results at follow-up.[8]

Epilepsy in HIE neonates may occur as a direct result of the brain injury or as a secondary complication of metabolic disturbances. The pathophysiology of neonatal seizures, particularly in the context of HIE, is complex and multifactorial, involving ischemic damage to cortical and subcortical regions of the brain, disruption of neuronal excitability, and alterations in neurotransmitter systems.[9] Given the high risk of poor outcomes associated with epilepsy in neonates, early identification of neonates who are at increased risk for developing epilepsy is crucial for timely intervention.[5] While previous studies have identified various clinical, biochemical, and neuroimaging factors associated with poor outcomes in HIE, few studies have specifically focused on the predictors of epilepsy in neonates with this condition.[10] The goal of this study is to evaluate the clinical, biochemical, and neuroimaging predictors of epilepsy in term neonates diagnosed with HIE. By identifying key factors associated with epilepsy, this study aims to enhance the understanding of how early brain injury and systemic disturbances may influence the development of seizures in this vulnerable population.

METHODS

Study design

This study was a prospective cohort study conducted on 100 term neonates at a tertiary care neonatal intensive care unit (NICU) in India over a period of one year from May 2023 to May 2024 at the Department of Paediatrics, Al-Ameen Medical College, Vijayapura, and Karnataka, India. The study was approved by the Institutional Ethical Review Board (IRB). Written informed consent was obtained from the parents or guardians of all participating neonates.

Inclusion criteria

Neonates born at term (≥37 weeks gestation), diagnosed with HIE based on clinical and neuroimaging criteria, with complete clinical, biochemical, and neuroimaging data, and neonates with at least 6 months of follow-up were included.

Exclusion criteria

Neonates with congenital genetic disorders or chromosomal abnormalities, pre-existing neurological conditions (e.g., cerebral palsy, genetic syndromes), incomplete follow-up data (i.e., lost to follow-up before 6 months), and neonates with birth defects unrelated to HIE were excluded.

Study procedure

The study was conducted on 100 term neonates and the gestational age, birth weight, gender, Apgar scores at 1 and 5 minutes were recorded. The presence of clinical features of HIE such as lethargy, hypotonia, abnormal movements, seizures (timing of onset), feeding difficulties, and respiratory distress were also observed.

Severity of HIE

Neonates were categorized into three severity grades (mild, moderate, and severe) based on clinical presentation and according to the Sarnat & Sarnat classification (1976) for HIE.[11]

Grade 1 (mild) included some lethargy, but no abnormal movements or tone; grade 2 (moderate) included marked lethargy, hypotonia, abnormal reflexes, and seizures; and grade 3 (severe) included severe hypotonia, absent reflexes, and prolonged seizures or coma.

MRI or CT scans of the brain were obtained for all neonates within the first 72 hours after birth, depending on the clinical condition. Brain imaging was used to assess the extent and location of brain injury, including - basal ganglia injury: injury to the deep nuclei, typically associated with severe HIE; cortical injury: injury to the cerebral cortex, typically seen in moderate to severe cases; and no brain injury: cases with normal brain imaging findings.

Biochemical analysis

Blood samples were taken within the first 24 hours after birth to measure lactate levels (normal range: 0.5-2.0 mmol/l). Elevated lactate levels were defined as >5 mmol/l. Electroencephalogram (EEG) was performed on neonates suspected of having seizures within 24-48 hours of birth. The EEG was used to identify abnormal patterns such as generalized spike-and-wave or focal spikes, which could indicate a predisposition to seizures. Epilepsy was diagnosed based on clinical symptoms (e.g., recurrent seizures) and EEG findings.

Statistical analysis

Statistical analysis was performed using statistical package for the social sciences (SPSS) version 25, IBM Corp. The continuous variables were expressed as mean±SD and the categorical variables were expressed as frequencies (n) and percentages (%). The comparison of variables neonates who developed epilepsy and those who did not were performed using the Chi-square test and students' t test. A logistic regression analysis was used to identify independent predictors of epilepsy in neonates with HIE, adjusting for potential confounders such as severity of HIE, lactate levels, and neuroimaging findings. A p value <0.05 was considered as statistically significant.

RESULTS

The study included 100 neonates diagnosed with HIE, of which 28 (28%) developed epilepsy by 6 months of age, and 72 (72%) did not. Below are the clinical characteristics, neuroimaging findings, biochemical results, and EEG findings of these neonates.

The demographics and clinical characteristics of the study participants were shown in Table 1. Gestational age and birth weight showed no significant differences between the epilepsy and non-epilepsy groups. However, neonates who developed epilepsy had lower Apgar scores at 1 minute ($p<0.01$) and a significantly higher occurrence of seizures within the first 24 hours (78.57% versus 25%; $p<0.01$). Severe HIE was more common in the epilepsy group (60.71% versus 44.44%), though this difference was not statistically significant ($p=0.02$).

Table 1: Demographics and clinical characteristics of the HIE neonates.

Variables	Epilepsy (n=28) (%)	No epilepsy (n=72) (%)	P value
Gestational age (weeks)	39.5±1.1	39.7±1.2	0.57[aNS]
Birth weight (grams)	2800±400	2950±300	0.07[a]*
Apgar score (1 min)	3.8±1.1	4.9±1.0	<0.01[a]*
Seizures (first 24 hours)	22 (78.57)	18 (25)	<0.01[a]*
Grading of HIE (Sarnat classification)			
Mild (stage I)	3 (10.71)	17 (23.61)	0.01[b]*
Moderate (stage II)	8 (28.57)	22 (30.56)	0.56[bNS]
Severe (stage III)	17 (60.71)	32 (44.44)	0.02[b]*

The data is shown as mean (SD) and frequency (%), *denotes significant, $p<0.05$; NS – non significant, a – unpaired students' t test, and b – Chi square test

The neuroimaging findings among the HIE neonates was shown in Table 2. In the present study, basal ganglia injury and cerebral cortical injury were significantly more common in the epilepsy group (71.43% versus 40.28% and 64.29% vs. 34.72%, respectively, $p<0.05$). In contrast, no brain injury was more frequently observed in non-epileptic neonates (29.17% versus 10.71%, $p=0.04$), indicating a stronger association between brain injury and the development of epilepsy.

In the present study, among the HIE neonates elevated lactate levels (>5 mmol/l) were significantly associated with epilepsy, with 60.71% of epileptic neonates having elevated lactate levels compared to 29.17% in the non-epilepsy group ($p=0.02$). The results were shown in Table 3.

Table 2: Neuroimaging findings in HIE neonates.

MRI findings	Epilepsy (n=28) (%)	No epilepsy (n=72) (%)	P value
Basal ganglia injury (N, %)	20 (71.43)	29 (40.28)	0.01*
Cerebral cortical injury	18 (64.29)	25 (34.72)	0.03*
No brain injury	3 (10.71)	21 (29.17)	0.04*

The data is shown as frequency (%), *denotes significant, $p<0.05$; Chi square test

Table 3: Association between lactate levels and the development of epilepsy in HIE neonates.

Lactate level (mmol/l)	Epilepsy (n=28) (%)	No epilepsy (n=72) (%)	P value
>5	17 (60.71)	21 (29.17)	0.02*
≤5	11 (39.29)	51 (70.83)	0.01*

The data is shown as frequency (%), *denotes significant, $p<0.05$; Chi square test

EEG was performed on neonates suspected of having seizures, and abnormal EEG patterns were analyzed to determine their relationship with the development of epilepsy in HIE neonates. In this study, 78.57% of neonates who developed epilepsy had abnormal EEG findings, compared to only 25% in the non-epileptic group ($p<0.001$). The results were shown in Table 4.

Table 4: EEG abnormalities and seizure prediction among the HIE neonates.

EEG abnormality	Epilepsy (n=28) (%)	No epilepsy (n=72) (%)	P value
Abnormal	22 (78.57)	18 (25)	<0.001*
Normal	6 (21.43)	54 (75)	<0.001*

The data is shown as frequency (%), *denotes significant, $p<0.05$; Chi square test

In addition, logistic regression analysis performed to identify independent predictors of epilepsy in neonates diagnosed with HIE. The results were shown in Table 5. Neonates with an Apgar score ≤3 at 1 minute were 3.15 times more likely to develop epilepsy than those with higher Apgar scores (OR=3.15, 95% CI=1.60-6.20; $p=0.002$). Neonates who presented with seizures within the first 24 hours of life had a 4.80 times higher risk of developing epilepsy (OR=4.80, 95% CI=2.30-9.50; $p<0.001$). Severe cases of HIE had a 2.50 times higher risk of developing epilepsy compared to mild or moderate cases (OR=2.50, 95% CI=1.10-5.60; $p=0.03$). The presence of basal ganglia injury on neuroimaging increased the odds of epilepsy by 3.25 times (OR=3.25, 95% CI=1.50-7.00; $p=0.01$). Neonates with cortical brain injury were 2.75 times more likely to develop epilepsy (OR=2.75, 95% CI=1.30-6.00; $p=0.02$). Elevated serum lactate levels (>5 mmol/l) were associated with a 3.10 times higher risk of developing epilepsy (OR=3.10, 95% CI=1.40-6.80; $p=0.004$). Abnormal EEG findings were a

strong predictor of epilepsy, with neonates who had abnormal EEG patterns being 5.20 times more likely to develop epilepsy (OR=5.20, 95% CI=2.40-10.80; p<0.001). The results were shown in Table 5.

Table 5: Logistic regression analysis for predictors of epilepsy in neonates with HIE.

Predictor	Odds ratio (OR)	95% CI	P value
Apgar score (1 min ≤3)	3.15	1.60-6.20	0.002*
Seizures (first 24 hours)	4.80	2.30-9.50	<0.001*
Severe HIE	2.50	1.10-5.60	0.03*
Basal ganglia injury	3.25	1.50-7.00	0.01*
Cerebral cortical injury	2.75	1.30-6.00	0.02*
Serum lactate >5 mmol/l	3.10	1.40-6.80	0.004*
Abnormal EEG	5.20	2.40-10.80	<0.001*

*Denotes significant, p<0.05

DISCUSSION

This study aimed to identify clinical, biochemical, and neuroimaging predictors of epilepsy in term neonates diagnosed with HIE. The results underscore several key factors that are significantly associated with the development of epilepsy in these neonates. Our findings reveal that Apgar score, early onset seizures, severity of HIE, neuroimaging abnormalities, elevated serum lactate levels, and abnormal EEG findings are strong predictors of epilepsy.

In this study, gestational age and birth weight did not show significant differences between the HIE neonates who developed epilepsy and those who did not. This suggests that these factors may not be the primary determinants for the development of epilepsy in neonates with HIE. While prematurity and low birth weight established risk factors for many are well- neonatal complications, including neurological outcomes, their role in the specific development of epilepsy in HIE may not be as pronounced as other factors, such as severity of brain injury and early clinical features. However, a significant difference was observed in the Apgar scores at 1 minute between the two groups. Neonates who developed epilepsy had lower Apgar scores at 1 minute (3.8±1.1 versus 4.9±1.0), which was statistically significant (p<0.01). This is consistent with previous research that has shown a strong correlation between low Apgar scores and poor neurological outcomes, including seizures and epilepsy. HIE. In a study done by Murray et al, Apgar score of <5 at 5 minutes had a positive predictive value of 18% in the development seizures in HIE neonates.[12] In another study done by Pavel et al, the median 1 minute (1 versus 2) and 5 minutes (3 versus 4) Apgar scores was lower in seizure when compared to non-seizure HIE babies.[10] Furthermore, the occurrence of seizures within the first 24 hours was significantly higher in the epilepsy group (78.57% versus 25%, p<0.01). Neonates who experience seizures within the first 24 hours of life are at a much higher risk of developing recurrent seizures and epilepsy. In severe HIE was more prevalent in the epilepsy group (60.71% versus 44.44%) and it was significant, though this difference was not statistically significant (p=0.02). Studies indicate that the severe HIE (characterized by deep coma, absent reflexes, and prolonged seizures) is strongly associated with worse neurological outcomes, including epilepsy. The severity of brain injury, as determined by the Sarnat and Sarnat classification, is one of the most reliable predictors of long-term neurological impairment in HIE. Neonates with severe HIE tend to experience more widespread brain injury, making them more susceptible to developing epilepsy.[13]

In this study, basal ganglia injury and cerebral cortical injury were significantly more common in neonates who developed epilepsy (71.43% versus 40.28% and 64.29% versus 34.72%, respectively; p<0.05). These findings support the established relationship between severe brain injury, particularly in key regions like the basal ganglia and cortex, and the increased risk of developing epilepsy in neonates with HIE. The basal ganglia, involved in motor control, and the cerebral cortex, responsible for higher cognitive functions, are crucial areas whose damage can result in seizure activity. Conversely, no brain injury was more frequently observed in the non-epileptic group (29.17% versus 10.71%; p=0.04), indicating that milder forms of HIE without significant brain damage are less likely to lead to epilepsy. This underscores the critical role of neuroimaging in identifying neonates at higher risk for epilepsy based on the extent and location of brain injury. Likewise, in a study done by Glass et al in HIE neonates with severe seizure majority of the cases had basal nuclei pattern in 54.6% and watershed pattern in 36.4% babies respectively.[14]

In this study, elevated lactate levels (>5 mmol/l) were significantly associated with the development of epilepsy, with 60.71% of epileptic neonates having elevated lactate levels compared to 29.17% in the non-epilepsy group (p=0.02). Elevated lactate levels are indicative of metabolic acidosis and hypoxic-ischemic injury, reflecting the severity of brain damage.[15] Previous reports indicate that significant metabolic disturbances, exemplified by elevated lactate concentrations, correlate with poorer neurological outcomes, notably the onset of epilepsy in neonates diagnosed with HIE.[16] This underscores the significance of early metabolic monitoring in the prediction and management of epilepsy risk in neonates. In a study done by Murray et al sustained lactic acidosis is linked to significant encephalopathy as evidenced by EEG findings and demonstrates a correlation with the burden of seizures.[17]

In this study, abnormal EEG findings were strongly associated with the development of epilepsy, with 78.57% of epileptic neonates exhibiting abnormal EEG patterns compared to only 25% in the non-epileptic group ($p<0.001$). These findings emphasize the critical role of EEG in identifying neonates at high risk for epilepsy. Abnormal EEG patterns, such as spike-and-wave discharges, reflect underlying neurophysiological disturbances and serve as an early marker of epileptogenic brain injury in neonates with HIE.[18]

The logistic regression analysis identified several key independent predictors of epilepsy in neonates with HIE, underscoring the multifactorial nature of epilepsy development. Apgar score ≤3 at 1 minute was strongly associated with a 3.15 times higher likelihood of developing epilepsy. This highlights the importance of early resuscitation and the correlation between perinatal asphyxia and later neurological outcomes. Likewise, in a study done by Eun et al, 1 and 5 minute APGAR scores are associated with 1.5 times and 2.11 times increased risk in the development of epilepsy among the HIE neonates.[19]

Additionally, HIE neonates who presented with seizures within the first 24 hours had a 4.80 times higher risk of developing epilepsy, emphasizing the role of early brain injury in predisposing to epilepsy. In a study done by Glass et al, status epilepticus is a strong risk factor with the progression of epilepsy in HIE neonates with a hazard ratio of 17.3 and it was significant ($p=0.003$).[20]

The severity of HIE also played a significant role; neonates with severe HIE had a 2.50 times higher risk of epilepsy compared to those with mild or moderate HIE, aligning with existing literature that links brain injury severity with worse outcomes. In a study done by Yimenicioglu et al, HIE severity based on Sarnat staging showed significant association with development of seizure in HIE neonates.[21]

Neuroimaging findings were also crucial; basal ganglia injury and cortical injury were associated with significantly higher risks of epilepsy, with odds ratios of 3.25 and 2.75, respectively, reinforcing the importance of early neuroimaging in identifying at-risk neonates ($p=0.01$ and $p=0.02$). Likewise, in a study done by Glass et al, HIE neonates exhibiting a severe pattern of injury involving the basal ganglia and thalamus, along with cortical involvement, demonstrated the highest susceptibility to the development of epilepsy.[20]

Furthermore, elevated lactate levels (>5 mmol/l) were 3.10 times more likely to occur in HIE neonates who developed epilepsy, highlighting metabolic acidosis as a key indicator of severe injury. Likewise, in a prospective study conducted by Murray et al, on 50 babies with HIE indicated that an extended duration for serum lactate normalization correlated with the severity of encephalopathy observed on EEG and the burden of seizures.[22]

In addition, the strongest predictor of epilepsy was abnormal EEG findings, with a 5.20 times higher likelihood of developing epilepsy in neonates with abnormal EEG patterns (OR=5.20, 95% CI=2.40-10.80; $p<0.001$), confirming the critical role of early EEG monitoring in detecting neonates at high risk for seizures and long-term neurological impairments. Likewise, in a study done by Natarajan et al, the incidence of seizure was higher in HIE neonates with severely abnormal background as compared to HIE neonates with less abnormal background (50% versus 5%) with a relative risk of 9.5.[18]

Limitations

The study limitations were as follows, first, it was conducted at a single tertiary care NICU, which may limit the generalizability of the findings to other settings, particularly in resource-limited areas. Second, the sample size of 100 neonates may not be large enough to detect subtler differences or rarer predictors of epilepsy. Third, the study was conducted over a relatively short period (1 year), and a longer follow-up period could provide a more comprehensive understanding of the long-term outcomes of neonates with HIE.

CONCLUSION

This study highlights key clinical, biochemical, and neuroimaging predictors of epilepsy in neonates with HIE, including low Apgar scores, early seizures, severe HIE, brain injury, elevated lactate levels, and abnormal EEG findings. Identifying these factors early can help target interventions for neonates at higher risk of developing epilepsy, potentially improving long-term outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Glass HC, Wood TR, Comstock BA, Numis AL, Bonifacio SL, Cornet MC, et al. Predictors of Death or Severe Impairment in Neonates With Hypoxic-Ischemic Encephalopathy. JAMA Netw Open. 2024;7(12):e2449188.
2. Cornet MC, Kuzniewicz M, Scheffler A, Forquer H, Hamilton E, Newman TB, et al. Perinatal Hypoxic-Ischemic Encephalopathy: Incidence Over Time Within a Modern US Birth Cohort. Pediatr Neurol. 2023;149:145-50.
3. Thigha R, Alzoani A, Almazkary MM, Khormi A, Albar R. Magnitude, short-term outcomes and risk factors for hypoxic ischemic encephalopathy at abha maternity and children hospital, Abha City, Saudi Arabia and literature review. J Clin Neonatol. 2020;9(2):98-110.

4. Kumar C, Peruri G, Plakkal N, Oleti TP, Aradhya AS, Tandur B, et al. Short-term Outcome and Predictors of Survival Among Neonates With Moderate or Severe Hypoxic Ischemic Encephalopathy: Data From the Indian Neonatal Collaborative. Indian Pediatr. 2022;59(1):21-4.
5. Kharoshankaya L, Stevenson NJ, Livingstone V, Murray DM, Murphy BP, Ahearne CE, et al. Seizure burden and neurodevelopmental outcome in neonates with hypoxic–ischemic encephalopathy. Dev Med Child Neurol. 2016;58(12):1242-8.
6. Tekgul H, Gauvreau K, Soul J, Murphy L, Robertson R, Stewart J, et al. The current etiologic profile and neurodevelopmental outcome of seizures in term newborn infants. Pediatrics. 2006;117(4):1270-80.
7. Glass HC, Shellhaas RA. Acute Symptomatic Seizures in Neonates. Semin Pediatr Neurol. 2019;32:100768.
8. Pisani F, Spagnoli C, Falsaperla R, Nagarajan L, Ramantani G. Seizures in the neonate: A review of etiologies and outcomes. Seizure. 2021;85:48-56.
9. Shetty J. Neonatal seizures in hypoxic–ischaemic encephalopathy – risks and benefits of anticonvulsant therapy. Dev Med Child Neurol. 2015;57(S3):40-3.
10. Pavel AM, O'Toole JM, Proietti J, Livingstone V, Mitra S, Marnane WP, et al. Machine learning for the early prediction of infants with electrographic seizures in neonatal hypoxic-ischemic encephalopathy. Epilepsia. 2023;64(2):456-68.
11. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol. 1976;33(10):696-705.
12. Murray DM, Ryan CA, Boylan GB, Fitzgerald AP, Connolly S. Prediction of seizures in asphyxiated neonates: Correlation with continuous video-electroencephalographic monitoring. Pediatrics. 2006;118(1):41-6.
13. Nevalainen P, Metsäranta M, Toiviainen-Salo S, Marchi V, Mikkonen K, Vanhatalo S, et al. Neonatal neuroimaging and neurophysiology predict infantile onset epilepsy after perinatal hypoxic ischemic encephalopathy. Seizure. 2020;80:249-56.
14. Glass HC, Glidden D, Jeremy RJ, Barkovich AJ, Ferriero DM, Miller SP. Clinical Neonatal Seizures are Independently Associated with Outcome in Infants at Risk for Hypoxic-Ischemic Brain Injury. J Pediatr. 2009;155(3):318-23.
15. Lorain P, Bower A, Gottardi E, Dommergues M, Foix L'Helias L, Guellec I, et al. Risk factors for hypoxic–ischemic encephalopathy in cases of severe acidosis: A case–control study. Acta Obstet Gynecol Scand. 2022;101(4):471-8.
16. Hanrahan JD, Cox IJ, Edwards AD, Cowan FM, Sargentoni J, Bell JD, et al. Persistent increases in cerebral lactate concentration after birth asphyxia. Pediatr Res. 1998;44(3):304-11.
17. Murray DM, Boylan GB, Fitzgerald AP, Ryan CA, Murphy BP, Connolly S. Persistent lactic acidosis in neonatal hypoxic-ischaemic encephalopathy correlates with EEG grade and electrographic seizure burden. Arch Dis Child - Fetal Neonatal Ed. 2008;93(3):F183-6.
18. Natarajan N, Benedetti G, Perez FA, Wood TR, German KR, Lockrow JP, et al. Association Between Early EEG Background and Outcomes in Infants With Mild HIE Undergoing Therapeutic Hypothermia. Pediatr Neurol. 2022;134:52-8.
19. Eun S, Lee JM, Yi DY, Lee NM, Kim H, Yun SW, et al. Assessment of the association between Apgar scores and seizures in infants less than 1 year old. Seizure. 2016;37:48-54.
20. Glass HC, Hong KJ, Rogers EE, Jeremy RJ, Bonifacio SL, Sullivan JE, et al. Risk factors for epilepsy in children with neonatal encephalopathy. Pediatr Res. 2011;70(5):535-40.
21. Yimenicioglu S, Kaya TB, Yıldırım E, Arayıcı S, Bildirici Y, Ekici A. The factors affecting neurodevelopmental outcomes in HIE. Acta Neurol Belg. 2023;123(5):1903-9.
22. Murray DM, Boylan GB, Fitzgerald AP, Ryan CA, Murphy BP, Connolly S. Persistent lactic acidosis in neonatal hypoxic-ischaemic encephalopathy correlates with EEG grade and electrographic seizure burden. Arch Dis Child - Fetal Neonatal Ed. 2008;93(3):F183-6.

Cite this article as: Kumar L, Jeergal NA, Thobbi AN. Evaluation of the predictors of epilepsy in hypoxic ischemic encephalopathy term neonates. Int J Contemp Pediatr 2025;12: 461-6.