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Original Article

aEEG as an early predictor of brain injury and prognosis in neonates with hypoxic-ischemic encephalopathy

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Abstract: Objective: This study aims to evaluate the independent risk factors associated with neonatal hypoxic-ischemic encephalopathy (HIE) using amplitude-integrated electroencephalography (aEEG), specifically exploring the relationship between aEEG scores, clinical manifestations, neurodevelopmental assessments, and neuron-specific enolase (NSE) levels with adverse outcomes in HIE. Methods: A retrospective analysis was performed on clinical data from 224 neonates diagnosed with HIE who were admitted between January 2022 and May 2024. Infants were grouped by HIE severity: mild, moderate, and severe. A control group of 100 healthy neonates was also included. All infants underwent aEEG monitoring, and clinical data (including Apgar and Neonatal Behavioral Neurological Assessment (NBNA) scores), as well as NSE levels, were collected. The correlations of aEEG scores, Apgar score, NBNA score, and NSE level, with HIE severity were analyzed using Pearson or Spearman correlation analyses. The independent risk factors for adverse outcomes within six months in the neonates with HIE were identified using univariate and multivariate Cox regression analysis. Results: HIE infants had significantly lower aEEG scores compared to the control group ($P < 0.001$). As the severity of HIE increased, aEEG scores and NBNA scores decreased notably ($P < 0.001$), while NSE levels increased ($P < 0.001$). aEEG scores were negatively correlated with HIE severity and NSE level, positively correlated with Apgar and NBNA scores. Both univariate and multivariate Cox regression analyses identified the severe HIE condition, amniotic fluid contamination, low aEEG scores, low Apgar scores, and high NSE levels as independent risk factors for adverse prognosis. Conclusion: aEEG is a valuable tool in early diagnosis, severity assessment, and prognosis prediction of neonatal HIE. The integration of aEEG with other biomarkers such as Apgar scores, NBNA scores, and NSE levels could further improve diagnostic accuracy and enhance clinical management.

Keywords: Amplitude-integrated electroencephalography, hypoxic-ischemic encephalopathy, NSE, prognostic evaluation, neurodevelopment

Introduction

Hypoxic-ischemic encephalopathy (HIE) is a common condition among term and near-term neonates, often resulting from acute hypoxia-ischemia during the perinatal period due to multiple factors [1, 2]. HIE primarily manifests as central nervous system damage and is a leading causes of neonatal death and disability [3]. Its incidence in China is notably higher than in developed countries (approximately 1/1000). Furthermore, with the increasing survival rate of neonates, the incidence of HIE in premature and high-risk infants continues to rise annually [4, 5]. Therefore, early diagnosis and intervention for HIE remain critical challenges in clinical medicine.

HIE primarily arises from brain injury induced by hypoxia. Following hypoxia, cerebral hemodynamic changes lead to insufficient oxygen supply to brain tissue, triggering neuronal edema, necrosis, degeneration, and even apoptosis [6]. Given that neonates have a high cerebral metabolic rate and poor tolerance to hypoxia, prolonged hypoxia exacerbates brain damage, making it increasingly difficult to reverse [7]. Therefore, early diagnosis and prompt intervention are essential for improving prognosis.

The diagnosis of HIE traditionally relies on clinical presentation and auxiliary examinations. Imaging techniques such as cranial ultrasound, MRI, and CT scans can identify the types of brain damage and assess severity. However,

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these methods typically reveal significant changes only after injury has occurred and are less effective at detecting subtle, early-stage damage [8, 9]. Moreover, neonatal brain injury often presents subtle and nonspecific symptoms, complicating early diagnosis using conventional clinical methods [10]. Thus, accurately identifying hypoxic-ischemic brain injury in the early stages remains a key area of ongoing research.

In recent years, amplitude-integrated electroencephalography (aEEG) has emerged as a promising tool for brain electrophysiological monitoring [11]. Unlike traditional EEG, aEEG simplifies waveform presentation by filtering, integrating, and compressing cerebral electrical signals, making it more accessible for clinical use. Additionally, aEEG offers real-time monitoring of brain function, which is especially useful for bedside care in neonatal intensive care units (NICUs) [12]. Due to its simplicity, non-invasive nature, and ability for long-term monitoring, aEEG has become an essential tool in neonatal neurological assessments [13]. By monitoring background activity, sleep-wake cycles (SWC), and epileptic-like electrical activity, aEEG reflects the degree of brain injury [14]. Furthermore, aEEG provides real-time feedback on brain function, enabling clinicians to make timely and informed decisions [15].

Neuron-specific enolase (NSE), a biomarker for brain injury detection, has been used to assist in the early diagnosis of neonatal HIE [16]. NSE levels rise significantly during brain injury, and its concentration in peripheral blood correlates with the severity of the injury, offering valuable diagnostic information [17]. However, unlike aEEG, NSE, as a single biochemical marker, does not capture dynamic changes in brain function. Therefore, it is often used in conjunction with aEEG to enhance diagnostic accuracy and sensitivity.

This study aims to investigate the independent risk factors for adverse outcomes in neonatal HIE, focusing on the relationship between aEEG scores, clinical manifestations, neurodevelopmental assessments, and NSE levels with HIE prognosis. By combining aEEG scores with clinical manifestations and auxiliary examination results, this research seeks to support early identification, timely intervention, and prognosis assessment for HIE. Ultimately, we intend to provide evidence-based recommendations to advance the application of aEEG in neonatal critical care and improve clinical diagnostic and treatment standards.

Methods and materials

Study subjects

This retrospective study included 224 neonates diagnosed with HIE who were admitted in our hospital between January 2022 and May 2024. The severity of HIE in these infants was classified according to the Sarnat 3-level grading system: 92 cases (41%) were classified as mild, 54 cases (24%) as moderate, and 78 cases (35%) as severe [18]. A control group of 100 healthy neonates born during the same period was also included for comparison. The study was approved by the Medical Ethics Committee of Baoji Maternal and Child Health Hospital.

Inclusion and exclusion criteria

Inclusion criteria: Neonates diagnosed with HIE within 24 hours of birth, meeting the established diagnostic criteria for hypoxic-ischemic encephalopathy [19]; Infants who underwent aEEG monitoring within the 24 hours after birth; Infants with complete clinical records available, including birth history, clinical manifestations, and treatment processes, as well as follow-up data for at least six months.

Exclusion criteria: Infants with congenital respiratory system diseases, circulatory system diseases, or heart disease; Infants with central nervous system diseases; Infants with inherited metabolic disorders; or Infants with hypocalcemia or hypoglycemia.

Data collection

Clinical data: Clinical data from both the HIE and control groups were collected, including general information (gender, gestational age, birth weight, length, and head circumference), maternal delivery-related data (gravidity, parity, delivery mode, amniotic fluid condition), postnatal assessment indicators (5-minute Apgar score, Neonatal Behavioral Neurological Assessment (NBNA) score), amplitude-integrated electroencephalogram evaluation (aEEG score), and neurobiochemical markers (NSE). Neonates were classified into mild, moderate, and severe groups based on the severity of HIE as evaluated using Sarnat 3-level grading.

Follow-up data: Clinical outcomes, including survival and adverse prognosis, were tracked over a six-month follow-up period. Adverse prognosis is defined as any adverse neurological or developmental outcome, primarily severe neurological impairment. Neurological development is assessed periodically through follow-up visits in the areas of brain function, motor skills, and language development, with particular attention to recognizing any signs of cerebral palsy, developmental delay, or cognitive impairment. Based on the definition of poor prognosis, patients were categorized into two groups: a poor prognosis group (61 cases) and a good prognosis group (163 cases).

Detection methods

aEEG monitoring: aEEG scores assess neonatal brain function by reflecting changes in brain electrical activity, such as sleep-wake cycles, continuity, and amplitude. The scores range from 0 to 12 points, with higher scores indicating more mature brain function and normal background brain activity [20]. In this study, aEEG was performed using the Brainz B3 model by Natus Medical Incorporated (USA). This portable neonatal electroencephalogram monitor allows continuous recording and analysis of neonatal brain activity. It offers long-term, non-invasive monitoring, making it particularly suitable for NICU settings.

NSE levels: NSE levels in peripheral blood were measured within the first 24 hours of birth using electrochemiluminescence immunoassay (ECLIA) method with the Elecsys NSE model from Roche Diagnostics (Germany). This method had high sensitivity and specificity, aiding in the early diagnosis of HIE.

Apgar scoring: The 5-minute Apgar score was recorded to assess the neonate's vital signs, including heart rate, respiration, muscle tone, reflex response, and skin coloration. The score ranges from 0 to 10, with higher scores indicating more stable vital signs and better overall health. A score above 7 indicates good vital signs, while a score below 3 suggests severe asphyxia requiring immediate intervention [21].

NBNA scoring: The NBNA score, reflecting neurological development, involving neurobehavioral responses, muscle tone, reflexes, and other neurological functions, was evaluated within the first 72 hours of life. The score ranges from 0 to 60 points, with higher scores indicating more mature neurological development and normal neurobehavioral responses. Lower scores may indicate neurological abnormalities linked to brain injury or other conditions [22].

Outcome measures

Primary outcome measures: Univariate and multivariate analyses were performed to identify factors influencing adverse prognosis within six months for neonates with HIE.

Secondary outcome measures: Baseline data and aEEG scores were compared between the HIE and control groups. Besides, aEEG scores, clinical scores, and NSE levels were compared among HIE infants with varying severities. Correlation analyses were performed to observe the relationships between aEEG scores, Apgar scores, NBNA scores, NSE levels and HIE severity.

Statistical analysis

Data were analyzed using SPSS 26.0 software. Continuous variables were compared using independent sample t-tests (for normally distributed data) or rank-sum tests (for non-normally distributed data). Categorical variables were compared using chi-square tests. Pearson or Spearman correlation analyses were performed based on data distribution. One-way analysis of variance (ANOVA) was employed for comparisons among groups of varying severity, with post hoc comparisons made using the Bonferroni correction. Univariate and multivariate Cox regression analyses were conducted to identify independent factors affecting prognosis, with Kaplan-Meier survival curves and Log-rank tests used to compare survival differences among groups. Statistical significance was set at $P < 0.05$. Data visualization was performed using R software.

Results

Comparison of baseline data between HIE and control groups

No significant differences were observed between the two groups in terms of gender distribution, gestational age, birth weight, length, head circumference, maternal parity and gravida, or delivery mode ($P > 0.05$). Additionally, the proportions of clean versus contaminated amniotic fluid did not differ significantly between

Table 1. Comparison of baseline characteristics between the HIE and control groups

Variable	HIE Group (n = 224)	Control Group (n = 100)	Statistical Value	*P*-value
Gender			1.023	0.312
Male	182 (56.17%)	52 (52%)		
Female	142 (43.83%)	48 (48%)		
Gestational Age (weeks)	39.00 [39.00, 40.00]	39.00 [39.00, 40.00]	0.497	0.619
Birth Weight (kg)	3.21 [2.87, 3.42]	3.24 [3.00, 3.50]	1.613	0.107
Height (cm)	49.55 ± 2.09	49.60 ± 1.63	-0.239	0.811
Head Circumference (cm)	33.873 ± 1.149	33.761 ± 1.147	0.813	0.417
Maternal Gravida	2.00 [1.00, 3.00]	2.00 [2.00, 3.00]	1.842	0.065
Maternal Parity	1.50 [1.00, 2.00]	2.00 [1.00, 2.00]	-1.078	0.225
Mode of Delivery			0.236	0.627
Vaginal Delivery	149 (45.99%)	48 (48%)		
Cesarean Section	175 (54.01%)	52 (52%)		
Amniotic Fluid Condition			1.734	0.188
Clean	237 (73.15%)	78 (78%)		
Contaminated	87 (26.85%)	22 (22%)		

Note: HIE: hypoxic-ischemic encephalopathy.

Table 2. Comparison of aEEG scores between the HIE and control groups

Variable	HIE Group (n = 224)	Control Group (n = 100)
aEEG Score	6.00 [4.00, 8.00]	11.00 [10.00, 12.00]
Statistical Value	14.443	
P-value	< 0.001	

Note: aEEG: amplitude-integrated electroencephalography, HIE: hypoxic-ischemic encephalopathy.

the groups (P = 0.188). These results suggest that the baseline characteristics of the neonates in the HIE and control groups were generally comparable (**Table 1**).

Comparison of aEEG scores between HIE and control groups

A significant difference was observed in aEEG scores between the HIE and control groups (P < 0.001). The neonates in the HIE group exhibited significantly lower aEEG scores compared to the control group, indicating that lower amplitude levels in brain electrical activity correlate with the degree of neurological impairment (**Table 2**).

Comparison of aEEG scores, clinical scores, and NSE levels among HIE infants of different severities

As HIE severity increased, aEEG scores progressively decreased (P < 0.001), while NBNA scores (P < 0.001) and NSE levels (P < 0.001) significantly increased. However, the differences in Apgar scores among different severity groups did not reach statistical significance (P = 0.001). These results reflect the impact of HIE severity on both neurological function and biochemical markers (**Figure 1**).

Correlation analysis of aEEG score, Apgar score, NBNA score, and NSE level with HIE severity

A correlation analysis was conducted between aEEG score, Apgar score, NBNA score, NSE level, and the severity of HIE, revealing significant correlations for all four indicators with HIE severity. Specifically, aEEG score, Apgar score, and NBNA score were all negatively correlated with HIE severity (all P < 0.001). Conversely, NSE level significantly increased with the worsening of HIE severity (P < 0.001) (**Figure 2**).

Correlation analysis of Apgar score, NBNA score, and NSE level with aEEG scores

Correlation analysis revealed that Apgar score and NBNA score were positively correlated with aEEG scores (P < 0.001), indicating that higher aEEG score was associated with better brain function and neurological development. In con-

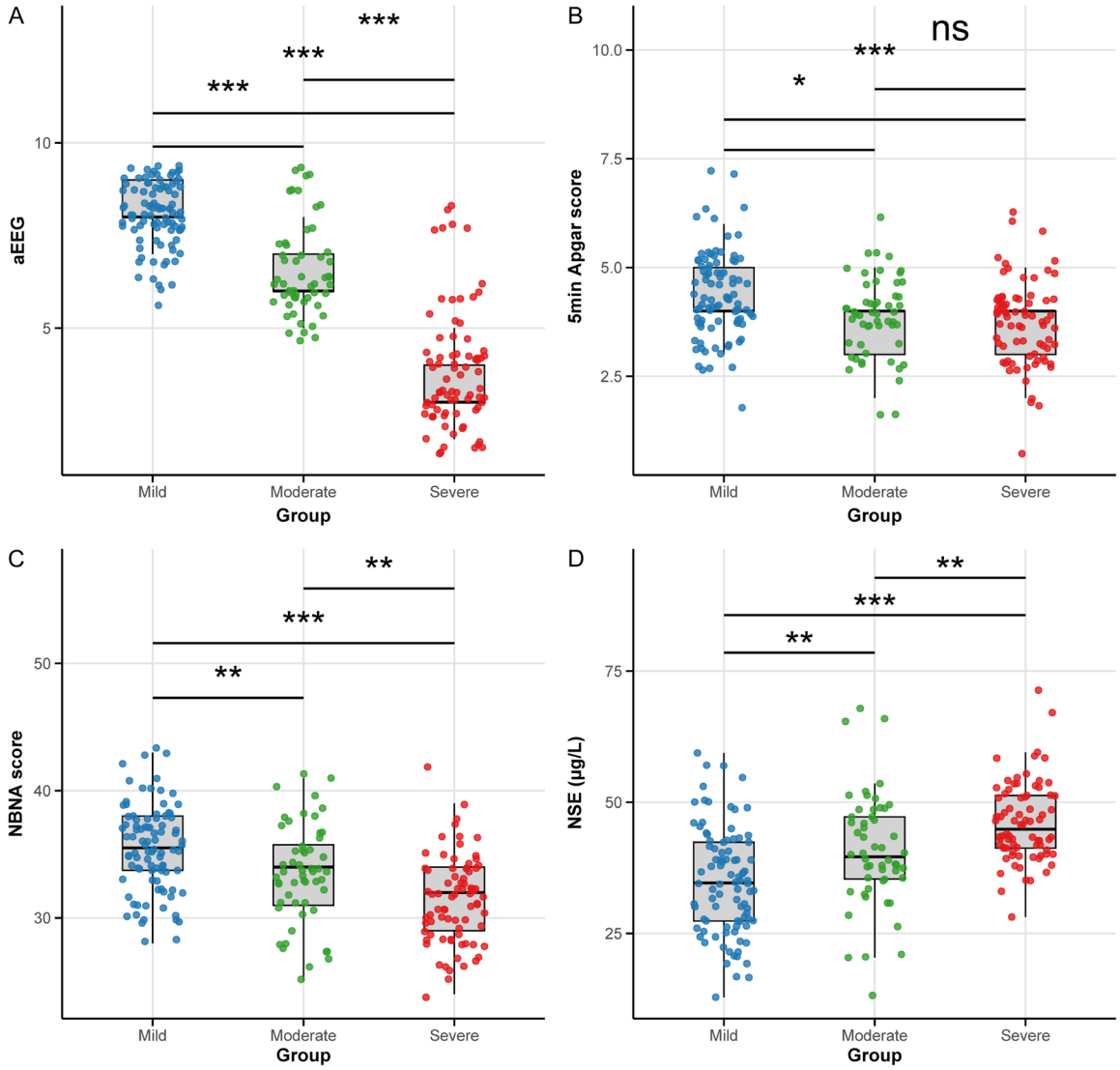

Figure 1. Comparison of aEEG scores, clinical scores, and NSE levels among HIE patients with different severities. A. aEEG scores of HIE patients with different severities. B. 5-min Apgar scores of HIE patients with different severities. C. NBNA scores of HIE patients with different severities. D. NSE levels of HIE patients with different severities. Note: aEEG: amplitude-integrated electroencephalography, HIE: hypoxic-ischemic encephalopathy, NBNA: Neonatal Behavioral Neurological Assessment, NSE: Neuron-specific enolase. ***P < 0.001.

trast, NSE levels were negatively correlated with aEEG scores (P < 0.001), indicating that lower aEEG scores reflect more severe brain injury (**Figure 3**).

Univariate analysis of factors affecting adverse prognosis within six months in HIE infants

Univariate analysis (**Table 3**) indicated that the severity of HIE, gestational age, aEEG scores, 5-minute Apgar scores, NBNA scores, and NSE levels were significantly associated with adverse prognosis (P < 0.001). Specifically, neonates with more severe conditions (HR = 4.260, P < 0.001), amniotic fluid contamination (HR = 2.108, P = 0.004), lower aEEG scores (HR = 0.380, P < 0.001), lower Apgar scores (HR = 0.324, P < 0.001), lower gestational age (HR = 0.459, P < 0.001), and higher NSE levels (HR = 1.113, P < 0.001) were more likely to have poorer prognoses.

Survival analysis (Kaplan-Meier analysis) of factors affecting adverse prognosis within six months

K-M survival analysis (**Figure 4**) was performed to assess the impact of different factors on the

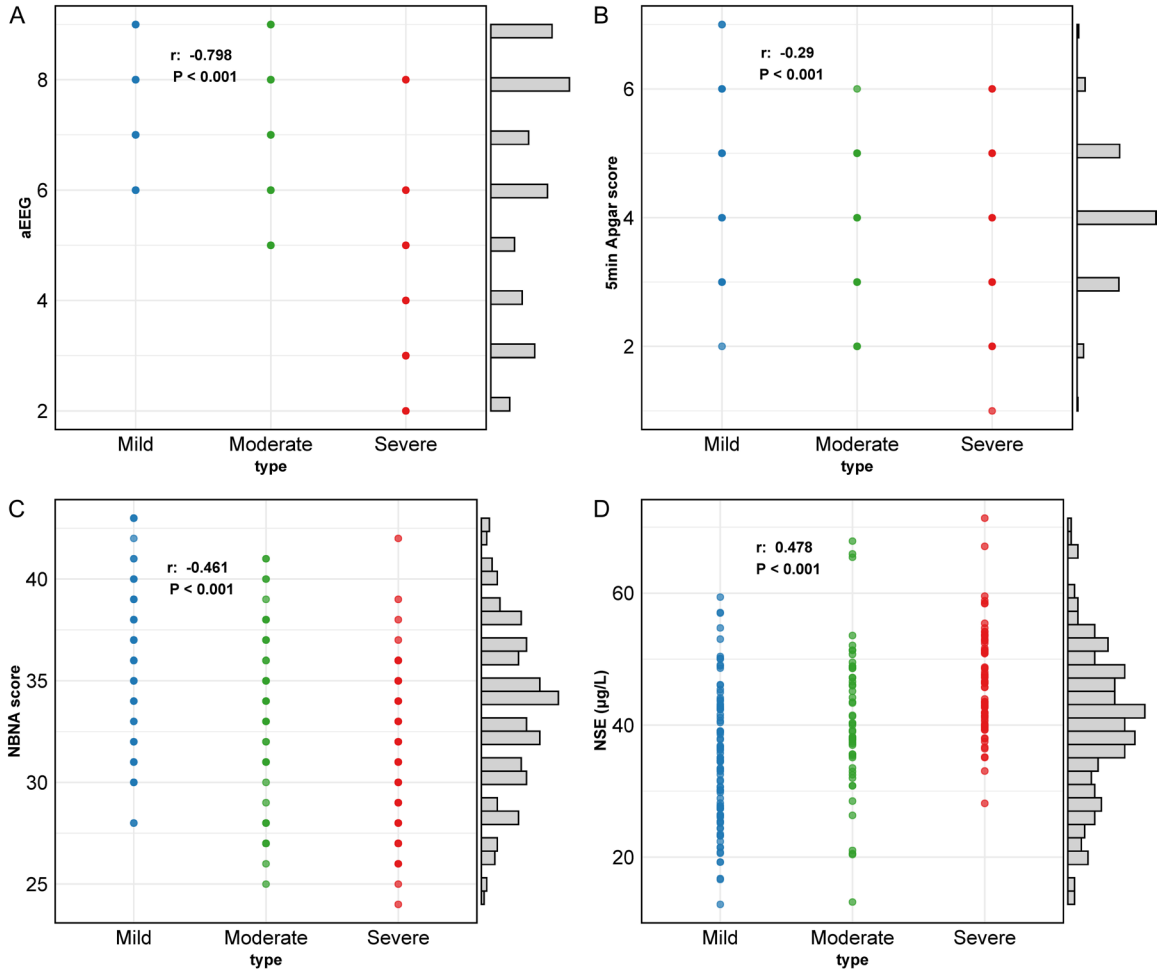

Figure 2. Correlation analysis of aEEG scores, Apgar scores, NBNA scores, and NSE levels with HIE severity. A. Correlation analysis between aEEG scores and HIE severity. B. Correlation analysis between Apgar scores and HIE severity. C. Correlation analysis between NBNA scores and HIE severity. D. Correlation analysis between NSE levels and HIE severity. Note: aEEG: amplitude-integrated electroencephalography, HIE: hypoxic-ischemic encephalopathy, NBNA: Neonatal Behavioral Neurological Assessment, NSE: Neuron-specific enolase.

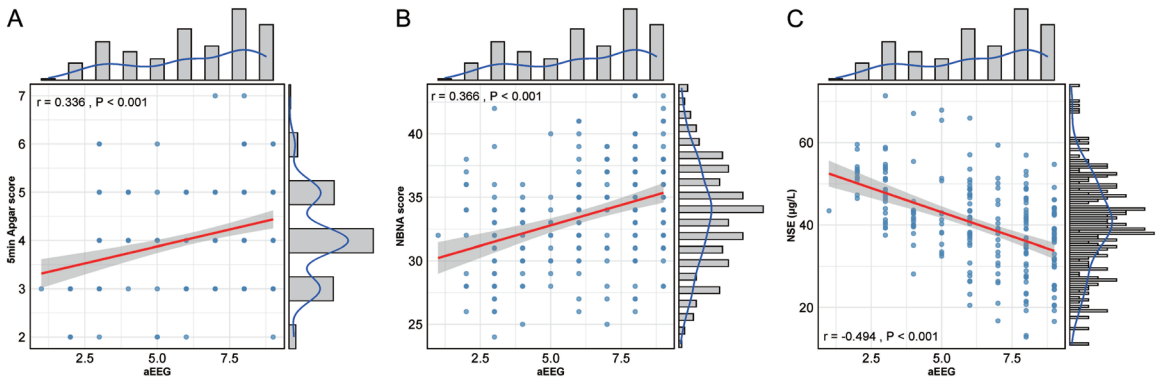

Figure 3. Correlation analysis of Apgar scores, NBNA scores, and NSE levels with aEEG scores. A. Correlation analysis between Apgar scores and aEEG scores. B. Correlation analysis between NBNA scores and aEEG scores. C. Correlation analysis between NSE levels and aEEG scores. Note: aEEG: amplitude-integrated electroencephalography, NBNA: Neonatal Behavioral Neurological Assessment, NSE: Neuron-specific enolase.

Table 3. Univariate cox regression analysis of adverse prognosis within six months in HIE infants

Factor	Beta	SE	*P*-value	HR	Lower	Upper
Disease Severity	1.449	0.218	< 0.001	4.26	2.78	6.527
Gestational Age	-0.779	0.132	< 0.001	0.459	0.354	0.594
Birth Weight	0.155	0.346	0.655	1.167	0.592	2.3
Height	-0.076	0.06	0.208	0.927	0.824	1.043
Head Circumference	0.03	0.115	0.794	1.03	0.823	1.29
Maternal Gravida	0	0.125	0.997	1	0.783	1.276
Maternal Parity	-0.401	0.26	0.124	0.67	0.402	1.116
Gender	0.114	0.258	0.657	1.121	0.676	1.858
Mode of Delivery	-0.104	0.256	0.685	0.901	0.545	1.49
Amniotic Fluid Condition	0.746	0.261	0.004	2.108	1.265	3.513
aEEG Score	-0.967	0.109	< 0.001	0.38	0.307	0.471
5-min Apgar Score	-1.128	0.166	< 0.001	0.324	0.234	0.448
NBNA Score	-0.131	0.034	< 0.001	0.878	0.822	0.937
NSE (μg/L)	0.107	0.011	< 0.001	1.113	1.088	1.138

Note: aEEG: amplitude-integrated electroencephalography, NBNA: Neonatal Behavioral Neurological Assessment, NSE: Neuron-specific enolase.

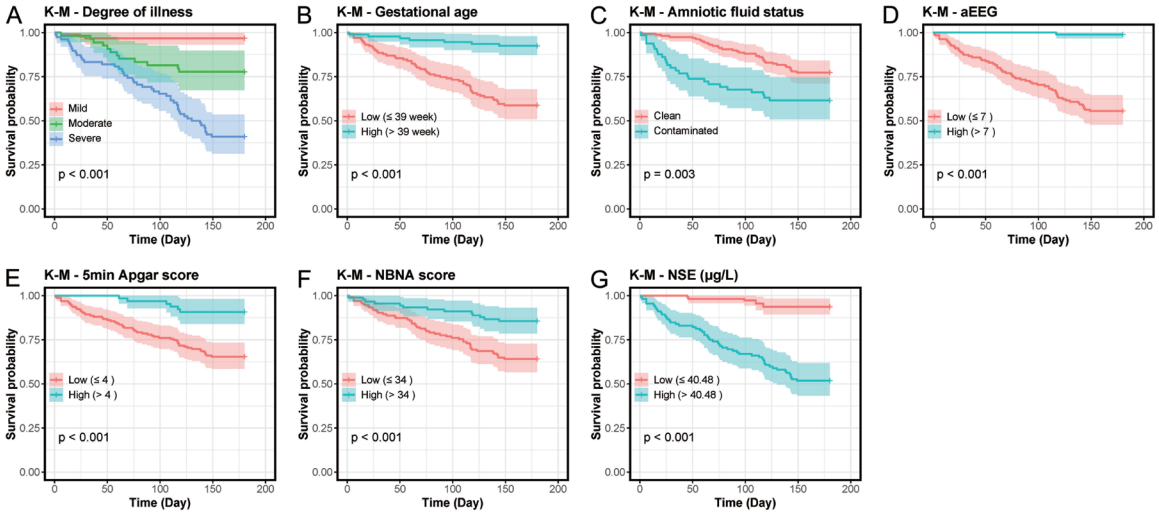

Figure 4. Survival curves for variables with significant differences in univariate analysis for adverse prognosis at 6 months. A. Six-month adverse prognosis survival curves for HIE patients with different disease severities. B. Six-month survival curves for HIE patients with different gestational ages. C. Six-month survival curves for HIE patients with different amniotic fluid conditions. D. Six-month survival curves for HIE patients with different aEEG scores. E. Six-month survival curves for HIE patients with different 5-min Apgar scores. F. Six-month survival curves for HIE patients with different NBNA scores. G. Six-month survival curves for HIE patients with different NSE levels. Note: aEEG: amplitude-integrated electroencephalography, NBNA: Neonatal Behavioral Neurological Assessment, NSE: Neuron-specific enolase.

survival and prognosis of HIE infants over the six-month follow-up period. The results indicated significant differences in survival between groups based on the severity of HIE, gestational age, aEEG scores, 5-minute Apgar scores, NBNA scores, and NSE levels ($P < 0.001$). Specifically, infants with more severe HIE, lower aEEG scores, and higher NSE levels showed significantly poorer survival outcomes, consistent with the findings from the univariate analysis.

Multivariate analysis of factors affecting adverse prognosis within six months in HIE infants

In the multivariate Cox regression analysis (**Table 4**), the severity of HIE, amniotic fluid con-

Table 4. Multivariate cox regression analysis of adverse prognosis within six months in HIE infants

Factor	Beta	SE	*P*-value	HR	Lower	Upper
Disease Severity	-1.367	0.571	0.017	0.255	0.083	0.781
Gestational Age	-0.278	0.175	0.113	0.757	0.537	1.068
Amniotic Fluid Condition	1.103	0.318	0.001	3.013	1.615	5.62
aEEG Score	-1.175	0.223	< 0.001	0.309	0.199	0.478
5-min Apgar Score	-0.586	0.212	0.006	0.556	0.367	0.843
NBNA Score	-0.018	0.04	0.646	0.982	0.907	1.062
NSE (μg/L)	0.058	0.016	< 0.001	1.06	1.028	1.093

Note: aEEG: amplitude-integrated electroencephalography, NBNA: Neonatal Behavioral Neurological Assessment, NSE: Neuron-specific enolase.

tamination, aEEG scores, 5-minute Apgar scores, and NSE levels remained significant independent prognostic factors. Specifically, neonates with more severe conditions (HR = 0.255, P = 0.017) and lower aEEG scores (HR = 0.309, P < 0.001) continued to have significant risk factors for adverse prognosis. Additionally, amniotic fluid contamination (HR = 3.013, P = 0.001) increased the risk of poor outcomes. Lower 5-minute Apgar scores (HR = 0.556, P = 0.006) and higher NSE levels (HR = 1.060, P < 0.001) were also associated with worse prognoses.

Discussion

Hypoxic-ischemic encephalopathy (HIE) is one of the most common neurological disorders in neonates, particularly affecting preterm infants, low birth weight infants, and other high-risk neonates [23]. It is characterized by acute brain function impairment that may result in permanent brain damage or death [24]. Despite advances in neonatal intensive care, early diagnosis and intervention remain vital for improving the prognosis. Therefore, identifying effective diagnostic tools for assessing brain injury and predicting outcomes is of great clinical importance.

A key finding in this study is the significant correlation between aEEG scores and the severity of HIE. We found a negative correlation between aEEG scores and the severity of HIE, with lower aEEG scores corresponding to more severe clinical manifestations of HIE. This suggests that aEEG is a valuable tool for the early assessment of HIE. Previous studies have demonstrated the predictive value of aEEG for the early diagnosis and prognosis of HIE, with aEEG results strongly correlating with NBNA scores [25]. Additionally, Unoke Meder et al. [11] emphasized that longitudinal analysis of aEEG background patterns improves the accuracy of long-term neurodevelopmental prognosis in HIE infants. Del Río et al. [26] also found that aEEG within 72 hours after birth, regardless of therapeutic hypothermia, offers high predictive value for prognosis, consistent with our findings that aEEG scores are associated with clinical outcomes. Furthermore, Caramelo et al. [27] showed that neuron-specific enolase (NSE), a biomarker for brain injury, is closely related to HIE severity and negatively correlated with aEEG scores, suggesting that combining aEEG and NSE improves diagnostic sensitivity and accuracy. Huang et al. [28] also found that combining NSE with aEEG and MRI enhances prognosis prediction accuracy for HIE. Thus, combining aEEG with NSE can significantly improve both diagnostic sensitivity and prognostic accuracy for HIE.

This study further investigated the independent risk factors for neonatal prognosis through multivariate Cox regression analysis. Disease severity emerged as one of the most important prognostic factors. More severe conditions are associated with higher mortality rates and poorer neurodevelopmental outcomes, as they directly correlate with the occurrence of hypoxic-ischemic brain injury [29]. Thus, accurately assessing disease severity is crucial for early intervention. The condition of amniotic fluid is another significant factor affecting neonatal prognosis. Contaminated or excessive amniotic fluid may indicate fetal distress during pregnancy, correlating with an increased risk of hypoxia and other complications. Research has demonstrated a significant association between amniotic fluid contamination and perinatal brain injury [30], highlighting its importance as a predictor of fetal health status. aEEG scores serve

as important prognostic markers for HIE; lower scores indicate restricted brain electrical activity, typically associated with brain injury and worse outcomes. A study found that aEEG scores have substantial predictive value for early neurodevelopmental outcomes in HIE neonates, particularly when monitored during therapeutic hypothermia [31]. Additionally, the 5-minute Apgar score is an essential indicator of neonatal health. Lower Apgar scores generally indicate severe hypoxia or asphyxia, increasing the risk of neurological damage and developmental delays [32]. Lastly, NSE levels, a biochemical marker of brain injury, are strongly correlated with HIE severity and provide valuable insight into early brain damage assessment. Studies show that elevated NSE levels are closely associated with severe HIE and poor neurodevelopmental outcomes, particularly in the acute phase [33].

One of the main advantages of aEEG is its ability to monitor brain electrical activity in real time, especially in intensive care settings, providing timely feedback to clinicians. Unlike traditional imaging techniques (e.g., MRI or CT), which often detect brain injury only after clinical symptoms are evident, aEEG offers continuous, non-invasive monitoring of brain function. This makes aEEG a vital tool for early diagnosis and prognosis evaluation of neonatal HIE. Chandrasekaran et al. [34] found that aEEG abnormalities, observed as early as 48 hours after birth in neonates undergoing therapeutic hypothermia, are predictive of long-term adverse outcomes. Similarly, Rondagh et al. [31] validated aEEG longitudinal analysis as an effective tool for predicting long-term outcomes in HIE infants, up to 2 to 5 years after birth. However, aEEG has limitations, notably its inability to provide detailed anatomical information, which imaging techniques can offer. Therefore, aEEG should be viewed as a complementary tool to imaging examinations, working synergistically for early assessment and treatment.

NSE levels, a biochemical marker of brain injury, significantly increase in response to neural injuries like hypoxia-ischemia. Higher NSE levels are associated with more severe brain injury and poorer prognostic outcomes. The results of this study further confirm that elevated NSE levels correlate with the severity of HIE and are indicative of adverse outcomes. NSE, therefore, serves as an auxiliary diagnostic indicator, helping clinicians assess the extent of damage and guide treatment. Previous studies have shown that NSE levels in cerebrospinal fluid (CSF) can predict severe brain injury and long-term neurodevelopmental outcomes in HIE infants receiving therapeutic hypothermia [33, 35]. Additionally, Lee et al. [36] found a positive correlation between the degree of EEG background suppression and elevated NSE levels, suggesting that combining aEEG and NSE enhances both brain injury assessment and prognosis prediction.

Despite its strengths, this study has limitations. The retrospective design may introduce selection bias, although strict inclusion and exclusion criteria were applied to minimize this risk. Additionally, the small sample size and single-center design may limit the generalizability of the results. Therefore, future multicenter, prospective studies are needed to validate these findings and enhance their applicability. Another potential limitation is the lack of a standardized aEEG scoring system and the possibility of technical variability, which may impact the reproducibility and clinical utility of aEEG. Refining and standardizing the aEEG scoring system is crucial for its broader application in clinical practice.

In conclusion, aEEG is a valuable tool in early diagnosis, severity assessment, and prognosis prediction for neonatal HIE. The integration of aEEG with other biomarkers such as Apgar scores, NBNA scores, and NSE levels could further improve diagnostic accuracy and enhance clinical management.

Disclosure of conflict of interest

None.

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