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***Original Research***

# PROGNOSTIC VALUE OF ELECTROENCEPHALOGRAPHY IN HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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**Abstract**: *Background:* Hypoxic-ischemic encephalopathy (HIE) is one of the main causes of neurodevelopmental disorders. We developed a model that has diagnostic and prognostic value in predicting the neurodevelopmental outcomes in newborns with HIE. HIE staging allows us to start therapeutic interventions early in newborns with suspected encephalopathy.
*Methods:* This was a retrospective study in a cohort of 58 full-term neonates with clinical suspicion of HIE. We assessed electroclinical variables at birth [etiology of hypoxia, neonatal seizures, HIE stages based on Sarnat criteria, use of therapeutic hypothermia, neuroimaging tests and electroencephalography (EEG) findings] and two years of follow up (EEG findings, development of epilepsy, the presence of cognitive deficits, behavioral issues, language problems, visual or hearing disturbances, and cerebral palsy).
*Results:* There was a high electro-clinical correlation to severe HIE (88.8%) and moderate HIE (50%). There was a considerable proportion of patients affected by mild HIE, based on clinical examination, who presented with an abnormal EEG (32.3%). There is a relationship between the onset of neonatal seizures, epilepsy, and severe HIE diagnosed with EEG (88.9%). A higher percentage of patients with moderate and severe HIE, based on EEG findings, present abnormal results in cranial ultrasound and cerebral magnetic resonance imaging (62.5%). At two years of age, functional neurodevelopment disturbances were observed most frequently in patients affected with severe and moderate HIE based on EEG.
*Conclusions*: This study shows a model with diagnostic and prognostic value in predicting newborns' neurodevelopmental outcomes with suspected HIE. This knowledge allows us to assess the role of performing serial EEG in patients with suspected HIE and the relevance of EEG findings in the prognosis of neurodevelopmental disorders.

**Keywords** Clinical neurophysiology; Electroencephalography; Encephalopathy; Neonatology; Neurodevelopment

**INTRODUCTION** Hypoxic-ischemic encephalopathy (HIE) is one of the leading causes of neurodevelopmental disorders. This condition affects 3-5/1000 term neonates (TN) and causes 23% of neonatal deaths [1–3]. Electroencephalography (EEG) in newborns with suspected hypoxia is essential to monitor cerebral function and determine the severity of the damage. This potential injury, with subsequent damage due to an increase of reactive metabolites and synaptogenesis, cause disturbances in brain functioning and may result in seizures [1–4].

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If HIE is suspected, neuroimaging tests such as magnetic resonance imaging (MRI) and cranial ultrasound (CU), offer relevant information about the extent of the structural injury [5], but not to the depth of functional impairment. EEG is the primary tool for measuring HIE levels with prognostic value concerning neonates' neurological conditions, as Jadas *et al*. described in one study in 30 TN. This report underlined the importance of MRI and EEG in the prognosis of patients with clinical suspicion of perinatal asphyxia [6]. In 38 TN, Temko *et al*., analyzed the impact of one clinical criterion (Apgar score), two cardiac criteria, and nine electroencephalographic criteria as a predictor of neurological evolution [7]. A systematic review of neurophysiological tests by van Laerhoven *et al.* demonstrated an important role for EEG as a prognostic test in TN with HIE (sensitivity 0.92 [0.66, 0.99]; specificity 0.83 [0.64, 0.93]) [8]. Review of Walsh *et al.* highlighted the different neonatal EEG analysis schemes that currently exist and they advocated for consensus among neurophysiologists to aid in the universal implementation of EEG in neonatal intensive care units to identify the neonates who could benefit most from neuroprotective therapies [9].

Objective

To validate the prognostic value of EEG in HIE, a predictive model was developed based on diagnostic, clinical, and electroencephalographic variables to determine the longterm outcome according to injury stratification, based on EEG, with the implementation of best measures.

**METHODS**

This study was a retrospective, analytical, and descriptive study in a cohort of 58 neonates with clinical suspicion of HIE by intensive care doctors from the pediatric intensive care unit. Patients were born between 2009 and 2012 at the Materno-Infantil Hospital of Malaga. We performed EEGs in neonates with suspected clinical HIE based on neurological examination from pediatricians responsible for the patients. We had no ethical conflicts because of the observational and retrospective nature of the study and the anonymity of the subjects.

We assessed electroclinical variables at birth and longterm outcomes (2 years of follow-up). The clinical variables are shown in Table 1.

EEGs were performed with an Xltek portable EEG machine (EEG 32U, Natus©, San Carlos, CA, United States), with a modified 10-20 system, in circular and longitudinal montages. As active electrodes, we used metal disc electrodes (Silver Cup EEG electrodes, Ambu©, Ballerup, Denmark), applied at Fp1, Fp2, F7, F8, T3, T4, Cz, C3, C4, O1 and O2 locations (Figure 1). We set the low-frequency filter at 1 Hz and the high-frequency filter at 30 Hz. The EEG recordings lasted 20-30 minutes. We distinguished HIE in three stages based on EEG findings: mild HIE (minimal electroencephalographic changes, brain immaturity), moderate HIE (low-voltage activity or epileptic abnormalities), and severe HIE (burst-suppression or isoelectric EEG) [10]. The EEGs were read by a clinical neurophysiologist who specialized in pediatric electroencephalography.

We also made electrocardiograms with patch electrodes and monitored respiration with an abdominal band (Piezo Crystal Effort Sensor-Velcro Tab, Natus©, San Carlos, CA, United Sates).

We evaluated the neurodevelopmental outcomes through clinical examination at two years of life at consultations. We performed EEG in all the patients recruited (58 patients). Also, neuroimaging was performed on 44 patients at the request of doctors. Seven patients died during the two years of study.

Statistical analysis

We performed two analyses. The first was a descriptive analysis of all variables where we calculated the rate of etiology of hypoxia, stages of HIE based on clinical examination, and EEG in cases of initial suspicion of HIE, the onset of neonatal seizures, use of hypothermia, findings in neuroimaging tests, EEG findings at birth, and longterm variables related to neurodevelopment (cognitive deficit, behavioral issues, language problems, visual or hearing disturbances, and cerebral palsy), assessed using the Bayley Scales of infant and toddler development, and the presence of epilepsy.

We also conducted a univariable correlational analysis to evaluate the relationship between HIE stages based on clinical observations and EEG at the time of diagnosis. We differentiated encephalopathy stages based on clinical criteria, according to Sarnat and Sarnat criteria [11].

| **Sarnat clinical criteria category** | **HIE staging** | | |
|---|---|---|---|
| | ***Mild*** | ***Moderate*** | ***Severe*** |
| **Consciousness level** | Hyper alert | Lethargic | Stuporous/Coma |
| **Muscular tone** | Normal | Mild hypotonic | Flaccid |
| **Posture** | Mild distal flexion | Strong distal flexion | Intermittent decerebration |
| **Stretch reflexes** | Overactive | Overactive | Decreased/Absent |
| **Segmental myoclonus** | Present | Present | Absent |
| **Suck reflex** | Weak | Weak/Absent | Absent |
| **Moro reflex** | Strong, low threshold | Weak, incomplete, high threshold | Absent |
| **Oculovestibular reflex** | Normal | Overactive | Weak/Absent |
| **Tonic neck reflex** | Slight | Strong | Absent |
| **Autonomic function** | Generalized sympathetic | Generalized parasympathetic | Both systems depressed |
| **Pupils** | Mydriasis | Miosis | Variable, often unequal, poor light reflex |
| **Heart rate** | Tachycardia | Bradycardia | Variable |
| **Bronchial and salivary secretions** | Sparse | Profuse | Variable |
| **Gastrointestinal motility** | Normal or decreased | Increased, diarrhea | Variable |
| **Seizures** | None | Common | Uncommon (excluding decerebration) |
| **EEG findings** | Normal (awake) | Early: low voltage, continuous delta and theta.<br>Later: periodic pattern (awake) | Early: periodic pattern with isopotential phases<br>Later: totally isopotential |
| **Duration** | Less than 24 hours | 2-14 days | Hours to weeks |
| **EEG criteria** | **HIE staging** | | |
| | ***Mild (Stage I)*** | ***Moderate (Stage II)*** | ***Severe (Stage III)*** |
| | Normal/Minimal changes<br>Amplitude and frequency decreased | Low voltage<br>Periods with attenuation of voltage<br>Paroxysmal abnormalities (focal,multifocal) | Burst-suppression<br>Flat pattern |

Table 1. HIE staging based on Sarnat clinical criteria [11] and HIE staging based on EEG criteria [10].

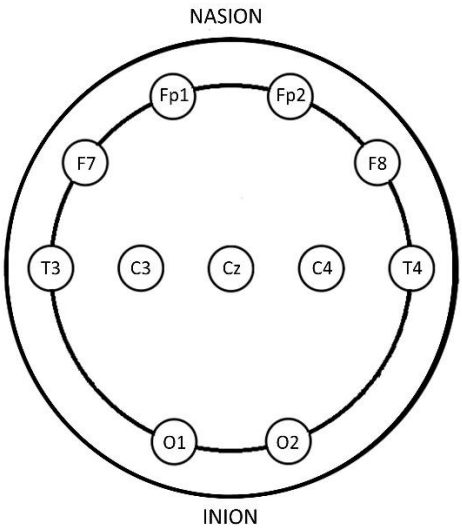


Figure 1: Metal disc electrodes were applied at locations Fp1, F7, F8, T3, T4, Cz, C3, C4, O1, and O2.

Correlations between different HIE stages were based on EEG and the following categorical variables: neonatal seizures, epilepsy, findings in neuroimaging tests (MRI and CU), and variables related to neurodevelopment (cognitive deficit, behavioral issues, language problems, visual or hearing disturbances, and cerebral palsy). Because of the limited sample size in some correlations, non-parametric tests were used (Fisher exact test). A *p*-value < 0.05 was considered to be statistically significant.

Furthermore, we performed a forward logistic regression multivariable analysis to estimate odds ratio (OR) and 95% confidence interval (CI), including in a model of the significant variables in the previous univariable analysis as independent variables, and the status of various types of neurodevelopmental deficits (cognitive deficit, behavioral issues, language problems, visual/hearing disturbances, or cerebral palsy) as the dependent variable. Wald test and inclusion $p < 0.05$ and exclusion $p > 0.10$ were used.

We performed the statistical analysis using Stata, version 14 and the S.P.S.S. statistical package, version 23 for Windows (S.P.S.S. Inc., Chicago, IL, U.S.A.).

**RESULTS**

Descriptive analysis at diagnosis

We studied 58 neonates (31 males and 27 females) born in Andalusia and Melilla. The first variable analysed was hypoxia's etiology, highlighting a high rate of meconium aspiration as the leading cause of hypoxia in TN (12 patients), followed by cardiorespiratory arrest (Table 2).

Before the performance of EEG, physicians staged HIE based on initial clinical examination, and found a high proportion of patients affected by mild HIE (56.9%). HIE staging, based on EEG at diagnosis, produced a high percentage of normal EEG recordings (41.3%).

Onset of neonatal seizures were observed in 33 patients (56.9%). Therapeutic hypothermia was applied to 7 TN (12.1%) (4 severe HIE, two moderate HIE, and one mild HIE). Abnormal findings in neuroimaging tests were present in 80% of patients with pathological CU (eight patients from the group had a CU performed) and 61.5% had a pathological MRI (Table 2).

EEGs at initial diagnosis of HIE (24-48 hours) displayed a high frequency of normal patterns (41.3%, 24 patients), followed by focal paroxysmal abnormalities (18.9%, 11 patients), low voltage tracings (17.2%, 10 patients), burst-suppression (13.8%, 8 patients), generalized slowing (5.2%, 3 patients), and generalized slowing with focal paroxysmal abnormalities (3.4%, 2 patients).

Longterm EEG findings (2 years) were available from 16 patients. They represented the most severe cases of HIE with suspected seizures or epilepsy. Focal paroxysmal abnormalities with generalized slowing was found in 7 patients (43.7%) and paroxysmal abnormalities without slowing was observed in 5 patients (31.2%). Two patients had a normal pattern (12.5%) and one showed a low voltage tracing (6.2%). A burst-suppression pattern was observed in the final case (6.2%).

We observed a cognitive deficit in 35.3% (18 patients), behavioral issues in 35.3% (18 patients), and language delay in 37.2% (19 patients). A high rate of developing epilepsy was noted, with a prevalence of 34.7% (17 patients). Cerebral palsy was observed in 21.5% (11 patients). Finally, 7.8% (4 patients) suffered hearing injury and 5.9% (3 patients) displayed visual injury (Table 2). Seven patients died during the follow-up period.

Correlational analysis

HIE stages based on clinical examination and EEG at diagnosis showed a statistically significant correlation (Fisher exact test, $p<0.001$). There was a high electro-clinical correlation to severe HIE (88.8%), as we observed eight patients with EEG suggestive of severe HIE from nine

| | *Patients* | *p-Value* |
|---|---|---|
| **Etiology of hypoxia** | | |
| Meconium aspiration | 12 | |
| Metabol**ic disease** | 5 | |
| Cardiological pathology | 5 | |
| Dystocia | 5 | |
| Infection | 4 | |
| Apnea | 3 | |
| Cardiorespiratory arrest | 10 | |
| Pulmonary hypertension | 5 | |
| Others | 9 | |
| **HIE staging based on clinical examination** | | |
| Mild | 33 (56.90%) | p=0.018 |
| Moderate | 16 (27.59%) | |
| Severe | 9 (15.52%) | |
| **HIE staging based on EEG findings** | | |
| Normal | 24 (41.38%) | |
| Mild | 7 (12.07%) | p=0.002 |
| Moderate | 12 (20.68%) | |
| Severe | 15 (25.86%) | |
| **Neonatal seizures** | | |
| No | 25 (43.10%) | p=0.253 |
| Yes | 33 (56.90%) | |
| **Hypothermia*** | | |
| No | 51 (87.93%) | p=0.51 |
| Yes | 7 (12.07%) | |
| **Abnormal Cranial Ultrasound** | | |
| No | 2 (20%) | p=0.485 |
| Yes | 8 (80%) | |
| **Abnormal MRI** | | |
| No | 10 (38.46%) | p=0.142 |
| Yes | 16 (61.54%) | |
| **Neurodevelopmental impairment** | | |
| **Cognitive deficit** | | |
| No | 33 (64.7%) | p=0.035 |
| Yes | 18 (35.3%) | |
| **Behavioural problems** | | |
| No | 33 (64.7%) | p=0.064 |
| Yes | 18 (35.3%) | |
| **Language delay** | | |
| No | 32 (62.7%) | p=0.088 |
| Yes | 19 (37.2%) | |
| **Hearing/visual disturbances** | | |
| No | 44 (86.3%) | p=0.797 |
| Yes | 7 (13.7%) | |
| **Cerebral palsy** | | |
| No | 40 (78.5%) | p=0.055 |
| Yes | 11 (21.5%) | |
| **Epilepsy** | | |
| No | 34 (65.3%) | p=0.277 |
| Yes | 17 (33.7%) | |

Table 2. Descriptive Analysis * Therapeutic hypothermia was not widely used in the pediatric intensive care unit at the time of recruitment of study subjects. Also, when mild encephalopathy was suspected, they did not use hypothermia.

patients with the suspicion of severe HIE based on clinical examination. With moderate HIE, there was consistency observed between clinical staging and EEG staging in half of the patients (50%), showing eight patients with EEG suggestive of moderate HIE from 16 patients with the suspicion of moderate HIE based on clinical examination. However, a considerable proportion of patients with clinically moderate HIE presented with EEG signs suggestive of severe HIE (37.5%, six patients based on EEG and 16 patients based on initial clinical examination). Also, a considerable proportion of patients were affected by mild HIE based on clinical examination who had presented with a normal EEG (69.7%, 23 patients with normal EEG among 33 patients who sustained mild clinical HIE) (Figure 2).

(88.9%, 8 patients, p=0.111). To a lesser degree, there was a direct
relationship between the absence of neonatal seizures and epilepsy and lack of abnormalities on the EEG (50.0%, 11 patients, p=0.214).

Regarding structural alterations detected on neuroimaging tests, a higher percentage of patients with moderate and severe HIE, based on EEG findings, presented with abnormal findings in CU and MRI. In cases with pathological findings using ultrasonography, we observed 37.5% (3 patients) with moderate HIE and 25% (2 patients) with severe HIE, according to EEG findings. In cases with visible injuries on MRI, 18.7% (3 patients) presented with moderate HIE and 43.7% (7 patients) presented with severe HIE based on EEG findings.

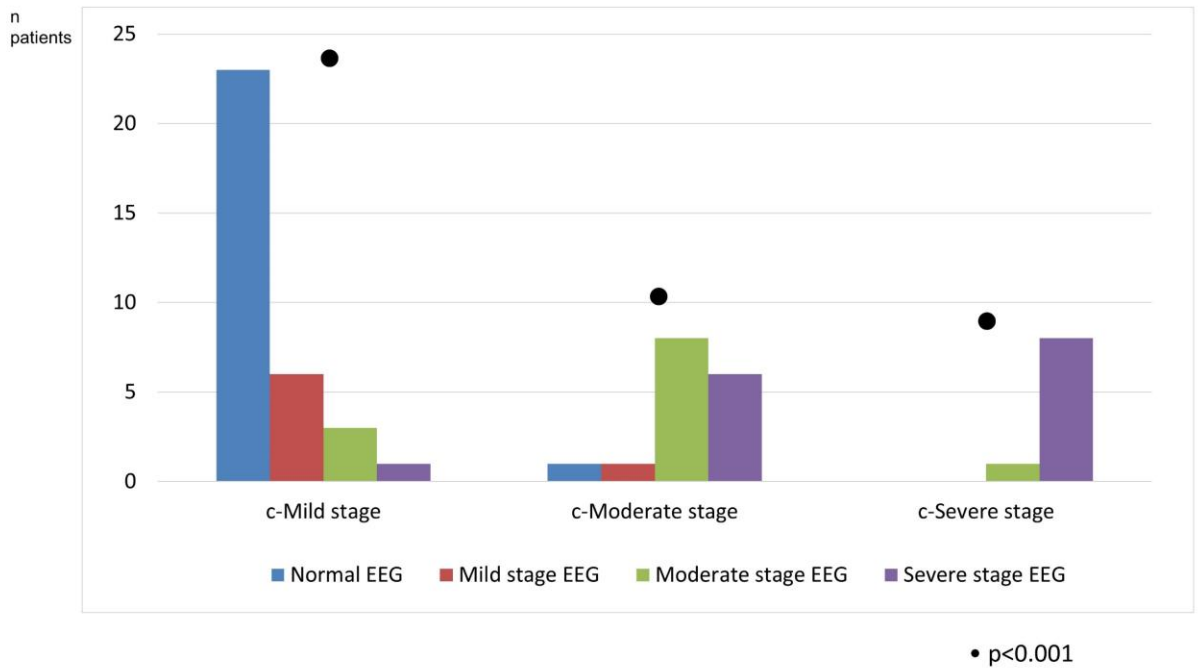


Figure 2. Electro-clinical correlation in HIE staging (c = clinical staging).

Conversely, the correlation between HIE-staging based on EEG at diagnosis and the onset of neonatal seizures was analyzed along with the further development of epilepsy (Figure 3). No statistically significant trend existed between the onset of neonatal seizures and epilepsydevelopment and severe HIE diagnosed with EEG

Functional neurodevelopment sequelae presenting at two years of follow-up were observed most frequently in patients affected with severe and moderate HIE based on perinatal EEG changes (Figure 4). We also found that 27.8% (5 patients) with moderate HIE and 50.0% (9

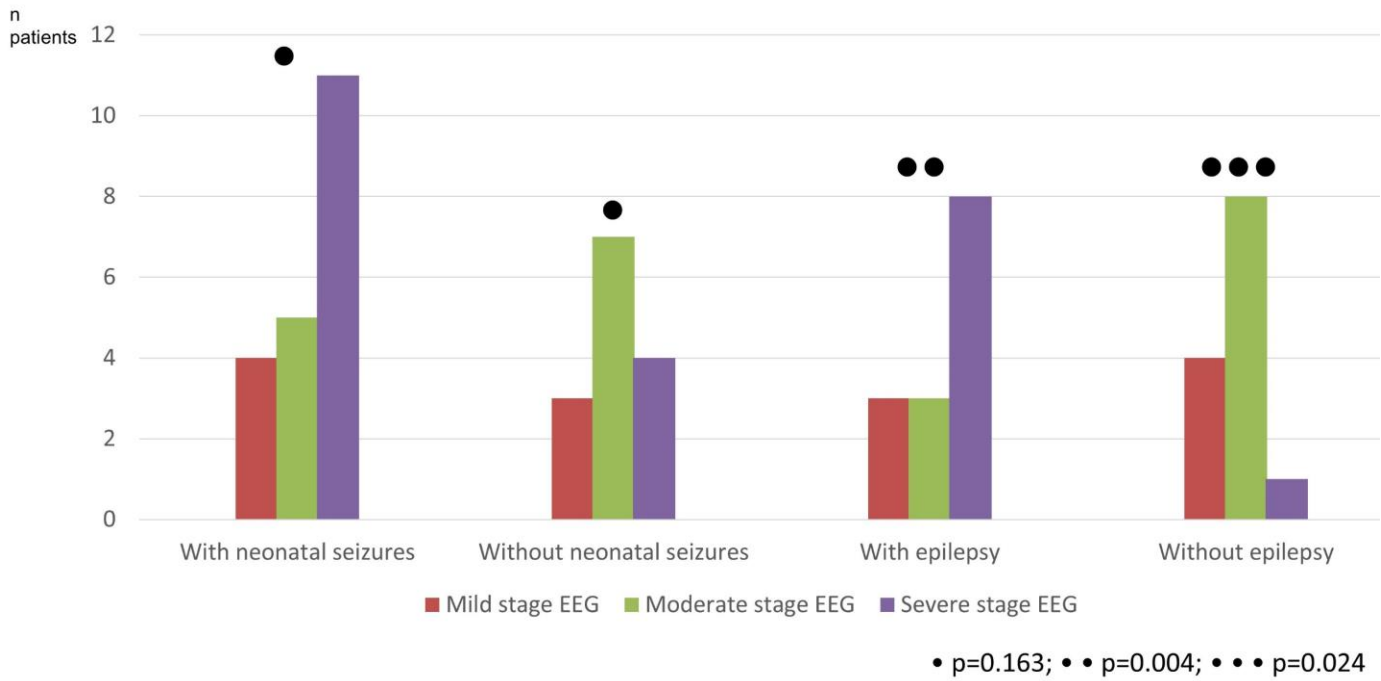


Figure 3. Correlation between HIE staging based on EEG - neonatal seizures and development of epilepsy.

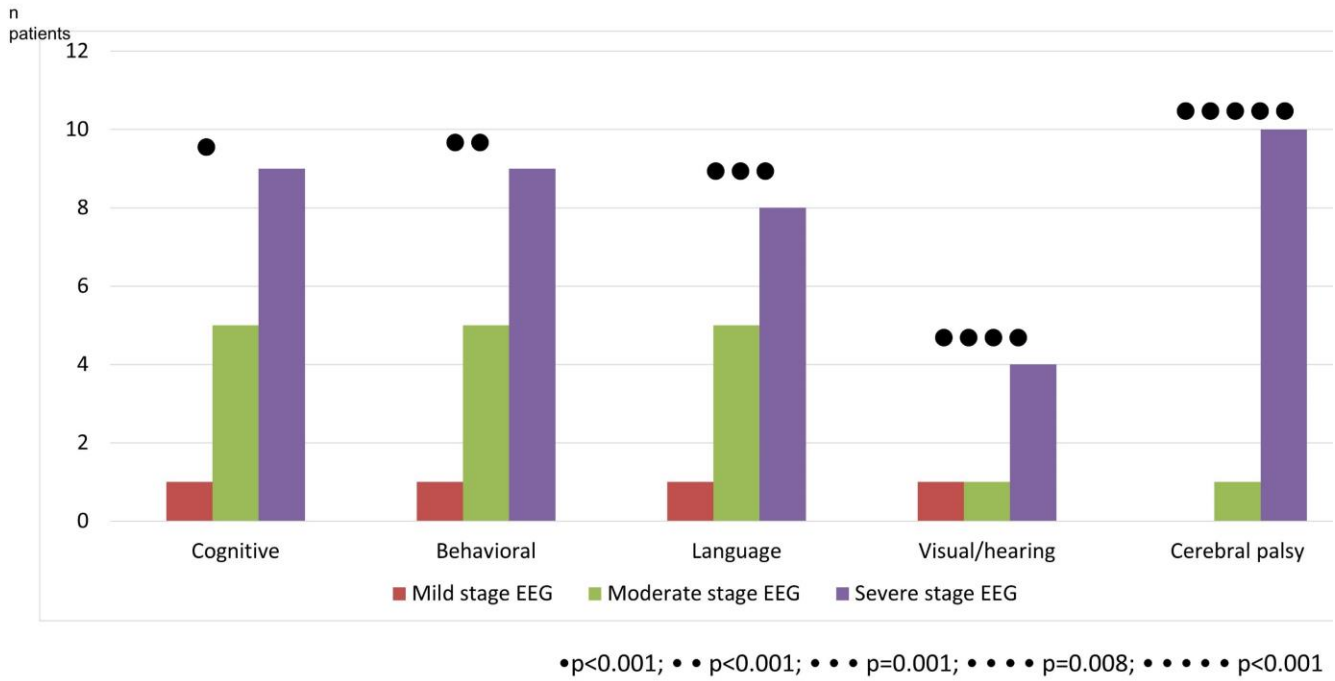


Figure 4. Correlation between HIE staging based on EEG – neurodevelopmental impairment.

patients) with severe HIE presented with cognitive deficits. There were similar findings in language difficulties, 26.3% of the TN (5 patients) with moderate HIE and 47.4% (9 patients) with severe HIE. Furthermore, we observed behavioral issues in these patients, with 27.8% (5 patients)

with moderate HIE and 50.0% (9 patients) with severe HIE. One patient (14.3%) had moderate HIE and hearing disturbances, and two patients (28.6%) had severe HIE. There were 2 cases of visual disorders (28.6%) in patients who presented with severe HIE. Ten patients with severe HIE and one patient with moderate HIE displayed cerebral palsy.

We observed typical neurodevelopment in the TN in whom the EEG was normal during the neonatal period. Thus, 61.3% (19 patients) with a normal EEG did not present with a cognitive deficit; we observed similar findings in behavioral outcomes and language development (58.1%, 18 patients and 60.0%, 18 patients, respectively). Only one patient with a normal EEG had hearing disturbances.

Concerning EEG findings, we observed all the patients with focal abnormalities presented with language disorders at the consultation. Four of them (80%) had cognitive and behavioral alterations, and one patient (20%) suffered from visual/hearing disturbances. Moreover, 12 patients who had generalized abnormalities in the EEG presented later with language, cognitive, and behavioral disorders, and five of them (41.6%) had visual/hearing disturbances. We explored the relationship between the reported neurodevelopmental deficits and several independent variables using logistic regression multivariable analysis. Sex, presence of seizures, the HIE staging based on clinical features and EEG results, ultrasound/MRI findings, and the cause of hypoxia were the independent variables. Clinical HIE staging was the variable most significantly associated with the development of longterm (2 years) cognitive deficits (OR = 9.5; 95% CI 2.5, 36.4; p=0.001). However, when the clinical HIE staging was included in the model, the HIE staging based on EEG was the only variable that maintained an association with longterm cognitive deficits (OR = 4.3; 95% CI 1.8, 10.4; p=0.001) and language difficulties (OR=2.7; 95% CI 1.4, 5.3; p=0.030).

**DISCUSSION** This study shows a diagnostic and prognostic value model in predicting the neurodevelopmental outcomes in newborns with suspected perinatal HIE. Based on electroclinical findings during the neonatal period, we could predict the longterm neurological outcome in a broad sample of patients [6,7]. HIE is a condition that presents with an increase in morbidity and mortality and, in survivors, there is a significant occurrence of neurological impairment [8]. Several clinical reports have confirmed that therapeutic hypothermia before 6 hours of life decreased mortality and improved outcomes at 18 months of follow-up in TN with moderate to severe HIE [12–15]. Nevertheless, therapeutic hypothermia only resulted in improvement in 20-35% of children at risk [16]. Hence, all TN with HIE, regardless of therapeutic hypothermia during the neonatal period, must be included in monitoring schemes up to two years of age [17].

Since researchers first described HIE, they have used staging criteria to predict the neonates' outcomes. However, this approach has limitations due to the non-uniformity of encephalopathy criteria. This fact leads to an overlap between mild to moderate categories and moderate to severe categories that can fog the prognosis. In this sense, complementary tests such as EEG, neuroimaging tests, and biochemical markers could be useful to estimate future neurological outcomes [18].

Our study analyzed results from 58 patients with a suspicion of HIE based on clinical HIE staging and HIE staging based on EEG at birth. There are limitations in the initial physical examination in neonates, highlighting how crucial an EEG is in determining the potential severity of TNs' neurological outcomes at an early stage. Our work revealed a high electroclinical correlation to severe HIE and, to a lesser extent, to moderate HIE in TNs. This finding occurred in 37.5% of patients with clinically moderate HIE presented with EEG signs of severe HIE.

As described above, 27.8% of patients with moderate HIE and 50.0% of patients with severe HIE exhibited cognitive deficits at two years of follow-up. Regarding behavioral issues, 27.8% of patients with moderate HIE and 50.0% of patients with severe HIE suffered these problems at two years of age. This percentage of TN's cognitive-behavioral difficulties is similar to data previously published [12,19,20]. The prevalence of language delay at two years of age was 26.3% with moderate HIE and 47.4% with severe HIE. In children with severe HIE, the rate of developing cerebral palsy was 73.3%. This percentage was similar to another series of cases, with 50-75% of survivors with ganglio-thalamic damage [17]. Visual and hearing disturbances had a prevalence of 14% in all TNs in our series, which is a slightly smaller proportion compared to other reports [12,13,17].

Conversely, there was a high percentage of children with clinically mild HIE with normal EEG findings (69.7%) who

presented with no neurodevelopmental issues at two years. Regarding mild clinical HIE, we noted 15 patients (45.4%) with an abnormal EEG. Four of these patients (26.6%) developed language or cognitive disorders as behavioral problems. Similarly, Chalak *et al.* showed a lower rate of disability of diagnosed mild HIE, at 18-22 months (16.6%) [21]. This difference could be related to our consideration of behavioral disturbance as another neurodevelopmental variable in the follow-up. In this context, Lamblin *et al.* considered staging of mild and severe HIE based on the initial EEG findings to be an essential prognostic factor to determine the neurological outcome of children while those categorized as moderate HIE were subject to more significant variability. Implementing other diagnostic measures is necessary to define a precise and accurate staging of HIE and therefore support the treatment and supervision planning for these patients [22–24]. Temko *et al.* described a predictive model based on analytical, clinical, cardiological, and electroencephalographic variables. As we explained, the predictive value of EEG in determining the degree of HIE had an accuracy of 84% in detecting neurodevelopment disorders at 24 months [7].

The presence of neonatal seizures had a high correlation with severe HIE in full-term neonates (73.3%) according to the outcomes presented in this study and in keeping with other published reports [2,25–27]. The risk of developing epilepsy after HIE is not yet known, but overall, 10-20% of children with HIE will develop it in childhood. The most important risk factors are the severity of the encephalopathy, the presence and severity of seizures in the neonatal period, and the extent of lesions in the basal ganglia or white matter and cerebral cortex [17]. Our study observed a trend to develop epilepsy in 88.9% of patients with severe HIE and neonatal seizures.

We found a high correlation between pathological findings (particularly using MRI) and severe HIE (by clinical-EEG staging). Previous reports have documented a significant correlation between abnormalities in MRI, clinical encephalopathy degree, and impaired neurological development [6,27–30]. The physiological basis of this correlation is based on neuronal changes that cause hypoxic-ischemic damage. Therefore, children with isolated injury in the cortex or white matter have a poor motor prognosis and have an increased frequency of cognitive-behavioral issues, visual and hearing problems, and epilepsy development [17].

Two years after diagnosis, we have identified a greater tendency to present with focal paroxysmal abnormalities with or without slowing traces in more than 50% of children with clinically mild HIE. This trend has been described in a small number of cases [8,9,28]. Moreover, we described neurodevelopmental disorders in all patients with focal and generalized EGG abnormalities, with a higher tendency to present visual or hearing disturbances in patients with generalized abnormalities in EEG.

One of the most relevant aspects of our study is the importance of conventional EEG in the differentiation of HIE staging and its prognostic value [14,29] in outlining the different early patterns as well as predicting neurological evolution at longterm follow-up. We have observed a high proportion of TN with clinically mild HIE who had a normal initial EEG (40.3% from all EEG recordings), but who developed focal paroxysmal abnormalities, low voltage tracing, and burst-suppression, on EEGs at follow up. Moreover, although we did not include the clinical HIE staging in the model, the HIE staging based on EEG was the most decisive variable that maintained an association with longterm cognitive deficits and language difficulties.

**Limitations and Contributions**

This study provides a model based on electro-encephalographic findings to determine a patient's prognosis with perinatal hypoxia-ischemia. Previous reports have documented the importance of MRI, amplitude-integrated electroencephalograms, and EEGs. The follow-up for these patients was less than 18 months for neurodevelopmental parameters. For this reason, our study assessed a larger number of neurodevelopmental parameters and increased follow-up time to 24 months. We included initial clinical and neuroimaging parameters to measure each diagnostic parameter's validity as a prognostic value in patient neurodevelopment.

Nevertheless, this study exhibits some limitations, mainly those related to it being a retrospective study, to loss of patients during the follow-up period, and to the limited number of patients included in the therapeutic hypothermia protocol, thus limiting the extrapolated conclusions drawn.

**CONCLUSIONS** This study adds a new perspective regarding the diagnosis, prognosis, and longterm neurodevelopmental follow up of TN with perinatal HIE based on EEG findings not only in the neonatal period but

also longterm EEG assessment (24 months), along with other variables, such as initial clinical data, and neuroimaging results. We highlight the relevance of longterm conventional EEG in the differentiation of HIE staging and its prognostic value in predicting neurodevelopmental outcomes. In this way, we were able to carry out necessary therapeutic and neuropsychological interventions at an earlier stage to improve outcomes for this cohort of patients.

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**DISCLOSURE STATEMENT**

Authors do not report any relevant disclosures or conflict of interest. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

**AUTHOR CONTRIBUTION**

L.L.V., P.N.S., V.F.S. contributed to the conception and design of this study, the acquisition and analysis of data and the drafting of the manuscript and figures. L.R.S., E.B.P., M.P.A.L. contributed to the acquisition and analysis of data and the manuscript's drafting. J.H. and M.A.B.F. contributed to the drafting of the manuscript and figures.

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