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Amplitude integrated electroencephalography, preterm infant, neurological outcomes, Sarnat score, Thompson score, NICHD score, SIBEN score, NE-RS

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A Comparison of Scoring Systems and Amplitude Integrated Electroencephalography in Neonates with Hypoxic Ischemic Encephalopathy to Predict Adverse Neurological Outcome: A Prospective Cohort Study

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ABSTRACT

Early identification of HIE in newborns is very crucial for the decision to start Hypothermia and subsequent outcome. AEEG has been proved to be a useful tool in predicting Neuro developmental outcome and to select infants for cooling as it is easy to perform bedside and gives continuous real time monitoring. Objective of present study is Comparison of clinical scoring systems (with and without AEEG) and AEEG to assess the severity of HIE based on adverse neurological outcome before discharge. 41 Babies who had clinical signs and symptoms of HIE, required resuscitation at birth (PPV or more) and admitted to NICU who fulfil the inclusion criteria are enrolled into the study. Each baby enrolled into the study is assigned clinical scoring within 6 hours and before the initiation of TH or usage of AED for seizure episodes. Scoring will be done at 1, 3 and 6 hrs and the maximum score will be taken for the analysis . AEEG will be done for all the babies being recruited for the study and quantified as normal or abnormal (before the initiation of TH). The sensitivity and Negative Predictive Value (NPV) for abnormal scores in all scoring systems was 100%. The specificity was highest for normal NICHD score. Positive Predictive Value (PPV) was highest for abnormal Thompson and NE-RS Score. We found that Scoring systems used in the study and AEEG both useful predictor for short term neurologic outcome in preterm infants.

INTRODUCTION

The survival rate of newborn has a significant increase as a result of advancements in neonatal intensive care^[1-3]. The survival rate has increased but there is a corresponding rise in prevalence of brain damage and neurodevelopmental abnormalities^[4,5]. Therefore, monitoring of cerebral function has acquired significance. For several decades, conventional electroencephalography (CEEG) has served as the widely accepted and established method for monitoring brain function. The utilization of neonatal continuous electroencephalography (CEEG) has been the subject of investigation, with a focus on its association with neurodevelopmental outcomes in infants, both full-term and preterm, who have intracranial lesions^[6-10]. Due to the necessity of specialized interpretation skills and the presence of certain technical challenges the routine implementation of continuous electroencephalography (CEEG) in neonatal intensive care units poses difficulties^[11]. In contrast, amplitude-integrated electroencephalography (AEEG) can be acquired using a single-channel EEG and is readily comprehensible. Utilization of amplitude-integrated electroencephalography (AEEG) has emerged as a prominent technique for monitoring infants who have experienced asphyxia at birth^[12]. AEEG is considered as gold standard because it is a simplified method of brain monitoring having high sensitivity and specificity in predicting neurodevelopmental outcome in HIE infants within first 6 hours of life^[13]. Multiple studies have demonstrated that an atypical aEEG reading during the initial days of life can serve as a prognostic indicator for encephalopathy^[14-17]. In recent times, a number of studies have documented a correlation between early AEEG parameters and neurological outcome^[18-23].

Various scoring systems have been employed to evaluate the severity of hypoxic-ischemic encephalopathy (HIE) and offer prognostic insights. These include Thompson Score, NE-RS, NICHD score, SIBEN score and Sarnat Staging. Predictive outcomes of these scoring systems are dependent upon clinical observations and assessments of diverse physiological parameters. The accuracy and reliability of their predictions in identifying neonates who are at risk of experiencing adverse neurological outcomes have been a subject of discussion.

This study is done to enhance the current understanding by conducting a systematic assessment and comparison of the predictive abilities of different scoring systems and amplitude-integrated electroencephalography (AEEG) in neonates diagnosed with hypoxic-ischemic encephalopathy (HIE). Total number of babies born in a year in our hospital are approximately 10,000. Out of which admission was done for 3000 babies. Among those inborn babies, 290

babies were given PPV and 45 babies were diagnosed as hypoxic ischemic encephalopathy (HIE). According to HELIX trial therapeutic hypothermia should not be given as treatment for neonatal encephalopathy^[24]. On the contrary, recent studies suggest that AEEG is a better tool to predict moderate to severe encephalopathy for therapeutic hypothermia. We have done this study as very few other studies have analysed the clinical scoring systems to predict the need for therapeutic hypothermia. Also AEEG is a part of few scoring systems but it is not easily available at every centre, therefore our study is choosing a system that is comparable to aEEG in resource limited settings to initiate therapeutic hypothermia early.

MATERIALS AND METHODS

A Diagnostic study was conducted from July 2022- June 2023 (12 months for enrollment, combining to 12 months of study duration) at Department of Neonatology, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India. Total 41 babies were studied and study protocol was approved by the Institutional Ethical Committee.

Inborn neonates ≥ 36 weeks of gestation, birth weight > 2 kg, Requirement of PPV at birth (need for resuscitation), < 6 hrs of life, and parents ready to give Informed consent were included while neonates with any congenital malformations, prophylactic phenobarbitone given at referral centre, sedation before enrolment, discontinuation of treatment before the study were excluded. AEEG patterns consistent with Encephalopathy like BS, CLV, FT are taken as abnormal, DNV and CNV are taken as normal aEEG patterns.

Procedure: Babies who had clinical signs and symptoms of Encephalopathy, required resuscitation at birth (PPV or more) and admitted to NICU who fulfil the inclusion and exclusion criteria are enrolled into the study. Treatment protocol followed as per the unit guidelines. Babies enrolled into TH according to the clinical criteria and availability of cooling device. Each baby enrolled into the study is assigned clinical scoring within initial 3-5 hrs of birth^[25] and before the initiation of TH or usage of AED for seizure episodes. AEEG will be done for all the babies being recruited for the study and quantified as normal or abnormal (before the initiation of TH). Criteria for therapeutic hypothermia was AEEG with voltage pattern of burst suppression, low voltage or flat trace for ≥ 30 min within 6 hrs of birth^[26,13]. Before the initiation of study the NICU residents will undergo formal training in assigning scoring for HIE babies and reading the AEEG findings. Online training sessions will be conducted for residents in scoring systems and AEEG. The scoring assigned to each baby and the AEEG findings will be cross checked by neonatologist.

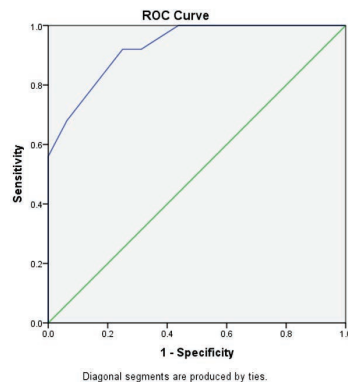


Fig. 1: AUC for Thompson score

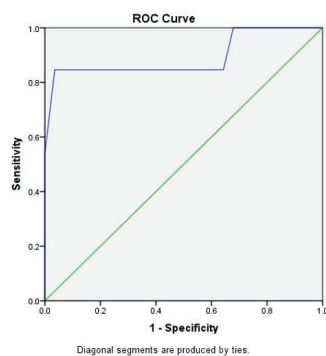


Fig. 2: AUC for NE-RS score

Scoring systems used in the study:

- Sarnat score
- Thompson score
- NICHD score
- SIBEN score
- NE-RS

Statistical analysis: All the scoring systems are staging systems except Thompson score and NE-RS. The sensitivity and specificity of TS and NE-RS will be obtained by using the ROC curve as they are continuous variables and correlated with aEEG findings. The obtained cut-off from the ROC curve will be used to decide the severity of HIE as mild/moderate to severe. The sensitivity, specificity, PPV, NPV and accuracy of all the other scoring systems will be compared with AEEG using the 2/2 table to access the mild vs moderate to severe HIE. In the same way sensitivity, specificity, PPV and NPV for all the secondary outcomes will be decided.

RESULTS

The mean gestational age of the study participants was 38.47 ± 1.07 weeks, mean birth weight was 2964.75 ± 361.4 Gms. The APGAR score at 1 min was 3.87 ± 1.3 and at 5 mins was 7.1 ± 1.31 . 16 (39.02%)

Table 1: Baseline characteristics of study participants

Baseline Characteristics	Mean (SD)
GA(weeks)	38.47 (1.07)
Birth weight (gm)	2964.75 (361.4)
APGAR score 1 min	3.87 (1.3)
APGAR score 5 min	7.1 (1.31)
Clinical score (at the time of admission)	
Thompson score	
Normal	9 (21.95%)
Abnormal	32 (78.05%)
NICHD score	
Normal	5 (12.19%)
Abnormal	36 (87.81%)
SIBEN score	
Normal	7 (17.07%)
Abnormal	34 (82.93%)
NE-RS score	
Normal	9 (21.95%)
Abnormal	32 (78.05%)
SARNAT Staging	
Normal	7 (17.07%)
Abnormal	34 (82.93%)
Invasive ventilation	
<24HR	7 (17.07%)
24-48 HRS	18 (43.9%)
>72 HRS	16 (39.02%)
Inotropes required	
Yes	37 (90.24%)
No	4 (9.76%)
Therapeutic hypothermia	
Yes	34 (82.93%)
No	7 (17.07%)
EEG Findings	
Sub-optimal	13 (31.71%)
Optimal	28 (68.29%)

infants required invasive ventilation for more than 72 hrs and 90.24% required inotropes. 82.93% infants required therapeutic hypothermia.

AEEG and Thompson score were compared in 41 infants. All infants with normal score in all scoring systems had optimal EEG findings, while among those with abnormal Thompson score, 13 (40.63%) and 19 (59.38%) infants had suboptimal and optimal EEG respectively ($p < 0.001$, highly significant). 13 (36.11%) and 19 (63.89%) with abnormal NICHD score had optimal and suboptimal EEG respectively ($p < 0.001$). In the SIBEN scoring system, 13 (38.24%) and 21 (61.76%) with abnormal score had suboptimal and optimal findings on EEG ($p < 0.001$). Similarly, among those with abnormal NE-RS score, 13 (40.63%) had suboptimal EEG while 19 (59.38%) had optimal EEG ($p < 0.001$). In the Sarnat staging, among those categorized as abnormal, 13 (38.24%) and 21 (61.76%) had suboptimal and optimal EEG respectively ($p < 0.04$).

The sensitivity and Negative Predictive Value (NPV) for abnormal scores in all scoring systems was 100%. The specificity was highest for normal NICHD score. Positive Predictive Value (PPV) was highest for abnormal Thompson and NE-RS Score.

DISCUSSIONS

The current study conducted a comparison between various clinical scoring systems, including Thompson Score, NE-RS Score, NICHD neurological assessment, SIBEN score and SARNAT staging systems, with the use AEEG (at admission) in order to determine their effectiveness in predicting adverse neurological

Table 2: Association between scoring systems and EEG findings

Thompson score	Scoring Sub optimal	EEG Findings Optimal	Total	p-value
Normal	0 (0%)	9 (100%)	9 (100%)	<0.001
Abnormal	13 (40.63%)	19 (59.38%)	32 (100%)	
NICHD score				
Normal	0 (0%)	5 (100%)	5 (100%)	<0.001
Abnormal	13 (36.11%)	19 (63.89%)	36 (100%)	
SIBEN score				
Normal	0 (0%)	7 (100%)	7 (100%)	<0.001
Abnormal	13 (38.24%)	21 (61.76%)	34 (100%)	
NE-RS score				
Normal	0 (0%)	9 (100%)	9 (100%)	<0.001
Abnormal	13 (40.63%)	19 (59.38%)	32 (100%)	
SARNAT staging				
Normal	0 (0%)	7 (100%)	7 (100%)	<0.04
Abnormal	13 (38.24%)	21 (61.76%)	34 (100%)	

Table 3: Validity and predictive values of scoring systems

Scoring	Sensitivity	Specificity	PPV	NPV
Thompson score				
Normal	0.00%	67.86%	0%	59.37%
Abnormal	100%	32.14%	40.62%	100%
NICHD score				
Normal	0.00%	82.14%	0%	63.89%
Abnormal	100%	16.13%	33.33%	100%
SIBEN score				
Normal	0.00%	75%	0%	61.76%
Abnormal	100%	25%	38.24%	100%
NE-RS score				
Normal	0.00%	67.86%	0%	59.37%
Abnormal	100%	32.14%	40.62%	100%
SARNAT staging				
Normal	0.00%	75%	0%	61.76%
Abnormal	100%	25%	38.24%	100%

Table 4: Area under the curve for Thompson score

95% Confidence Interval		
Area under curve	Lower Bound	Upper Bound
0.929	0.851	1.000

Table 5 : Area under the curve for NE-RS score

95% Confidence Interval		
Area under curve	Lower Bound	Upper Bound
0.88	0.79	0.89

outcomes. The results of the receiver operating characteristic (ROC) analysis indicate that the Thompson score is a superior predictor. This is supported by the observation that the Thompson score has a higher area under the curve (AUC) value (>0.90) compared to other scoring systems. During the analysis of the results, factors such as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were considered. Positive Predictive Value (PPV) was highest for abnormal Thompson and NE-RS Score. According to a study conducted by Lauren *et al.*^[27] the utilization of the Thompson score for clinical assessment prior to initiating hypothermia treatment is linked to patient outcomes. The study found that infants who had the highest scores on the Thompson evaluation had a higher likelihood of mortality. This finding aligns with the results of our study. The findings of the Dutch Pharma Cool trial^[28] revealed that a Thompson score of 12 or higher was linked to unfavourable neurological outcomes prior to discharge. Our own results were consistent with this.

Hence, there exists a correlation between elevated Thompson scores and aEEG background pattern suppression, which is indicative of unfavourable outcomes. In accordance with the findings of Dalip Kumar Bhagwani *et al.*^[29], it has been observed that a Thompson score exceeding 10 within the initial seven days of an infant's life serves as a predictive indicator for an adverse outcome. This outcome aligns with the results obtained from our own study. According to Alferado Gracia *et al.*^[30], utilisation of the Neonatal Encephalopathy-Rating Scale (NE-RS) at bedside within the initial six hours following birth proves to be highly applicable, reliable and sensitive which is concordant with our study. Additionally, NE-RS demonstrates a commendable capacity to predict neurological outcomes at the two-year mark. In contrast to nominal scales, such as the Sarnat scale, the NE-RS and other rating scales the NE-RS employs a numerical scale to stratify the severity of NE, rather than relying on nominal categorizations. Our study is in agreement with this previous study. Early recognition of babies who need therapeutic hypothermia should be done by better methods which is followed by careful neurodevelopmental outcome.

CONCLUSION

This study offered valuable insights into the predictive significance of clinical tests conducted shortly after birth in near-term and term infants with perinatal asphyxia, regarding their likelihood of

experiencing adverse neurological outcomes. Scoring systems and neurophysiological tests, such as AEEG or EEG, have shown promise as predictors of adverse outcomes. However, further high-quality studies are needed to confirm the findings for SEPs. To determine if these benefits persist in later childhood, it is crucial to conduct well-designed large prospective studies and closely monitor the children due to the variability in the performance of the tests.

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