MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2024.3.154.159

OPEN ACCESS

Key Words
Amplitude integrated electroencephalography, preterm infant, neurological outcomes, sarnat score, thompson score, NICHD score SIBEN score NE-RS

Corresponding Author
Mohit Sharma,
Department of Neonatology , Govt Chengalpattu Medical College, Tamil Nadu India
Drmohitsharma15@gmail.com

Author Designation
[1]SR
[2]Assistant Professor
[3]Associate Professor
[4]Professor

Received: 25 November 2023
Accepted: 31 December 2023
Published: 4 January 2024

Citation: Mohit Sharma, S. Manikumar, S. Ramya and N. Muthukumaran, 2024. A Comparison of Scoring Systems and Amplitude Integrated Electroencephalography in Neonates with Hypoxic Ischemic Encephalopathy to Predict Adverse Neurological Outcome A Prospective Cohort Study. Res. J. Med. Sci., 18: 154-159, doi: 10.59218/makrjms.2024.3.154.159

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

[1]Mohit Sharma, [2]S. Manikumar, [3]S. Ramya and [4]N. Muthukumaran

[1-4]Department of Neonatology , Govt Chengalpattu Medical College, Tamil Nadu India

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. Forty one 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 hrs and before the initiation of TH or usage of AED for seizure episodes. Scoring will be done at 1-3 and 6 hours 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. Amplitude-integrated electroencephalography, preterm infant, neurological outcomes, Sarnat score, Thompson score, NICHD score, SIBEN score, NE-RS.

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 hrs 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-June 2022-2023 (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 $\geq$36 weeks of gestation, birth weight $\geq$2 kg, Requirement of PPV at birth (need for resuscitation) $\leq$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 hours 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 $\geq$30 min within 6 hrs of birth[13-26].

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.

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 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%) infants required invasive ventilation for more than 72 hours 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,

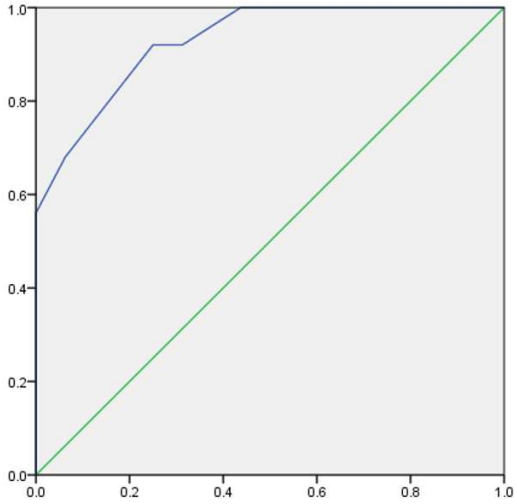

Fig. 1: AUC for Thompson score

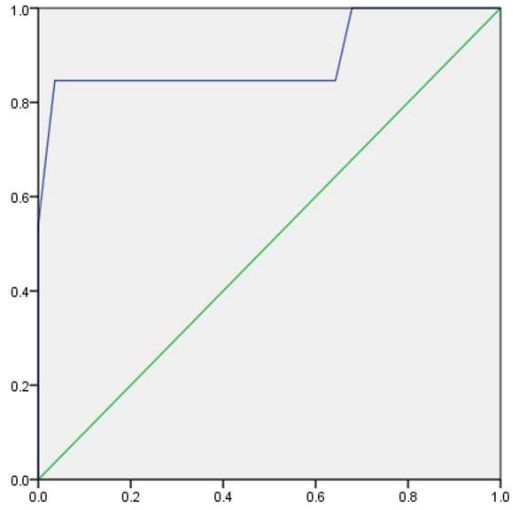

Fig. 2: AUC for NE-RS score

with the use aEEG (at admission) in order to determine their effectiveness in predicting adverse neurological 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 ($p>0.90$) 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

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	<24 hr	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%)

Table 2: Association between scoring systems and EEG findings

	EEG findings			
Scoring	Sub optimal	Optimal	Total	p-value
Thompson score				
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%)	

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 *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 hrs 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

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 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.

CONCLUSIONS

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.

REFERENCES

1. Blaymore-Bier, J., J. Pezzullo, E. Kim, W. Oh, C. Garcia-Coll and B. Vohr, 1994. Outcome of extremely low-birth-weight infants: 1980-1990. Acta. Paediatrica., 83: 1244-1248.
2. McCall, T.A., B. Conrad, B. Badman and T. Wright, 2007. Volar versus dorsal fixed-angle fixation of dorsally unstable extra-articular distal radius fractures: A biomechanic study. The J. Hand Surg., 32: 806-812.

3. Piecuch, R.E., C.H. Leonard, B.A. Cooper and S.A. Sehring, 1997. Outcome of extremely low birth weight infants (500 to 999 grams) over a 12-year period. Pediatrics., 100: 633-639.
4. Olischar, M., K. Klebermass, T. Waldhoer, A. Pollak and M. Weninger, 2007. Background patterns and sleep-wake cycles on amplitude-integrated electroencephalography in preterms younger than 30 weeks gestational age with peri-/intraventricular haemorrhage. Acta. Paediatrica., 96: 1743-1750.
5. Wilson-Costello, D., H. Friedman, N. Minich, A.A. Fanaroff and M. Hack, 2005. Improved survival rates with increased neurodevelopmental disability for extremely low birth weight infants in the 1990s. Pediatrics, 115: 997-1003.
6. Tharp, B.R., F. Cukier and N. Monod, 1981. The prognostic value of the electroencephalogram in premature infants. Electroencephalography Clin. Neurophysiology, 51: 219-236.
7. Marret, S., D. Parain, E. Jeannot, D. Eurin and C. Fessard, 1992. Positive rolandic sharp waves in the eeg of the premature newborn: A five year prospective study.. Arch. Dis. Childhood, 67: 948-951.
8. Maruyama, K., A. Okumura, F. Hayakawa, T. Kato, K. Kuno and K. Watanabe, 2002. Prognostic value of eeg depression in preterm infants for later development of cerebral palsy. Neuropediatrics, 33: 133-137.
9. Kato, T., A. Okumura, F. Hayakawa, K. Kuno and K. Watanabe, 2004. Electroencephalographic aspects of periventricular hemorrhagic infarction in preterm infants. Neuropediatrics, 35: 161-166.
10. Diepgen, T.L., K.E. Andersen, F.M. Brandao, M. Bruze and D.P. Bruynzeel, *et al*., 2009. Hand eczema classification: a cross-sectional, multicentre study of the aetiology and morphology of hand eczema. Br. J. Dermatol., 160: 353-358.
11. El-Dib, M., A.N. Massaro, P. Glass, D. Bulas, N. Badrawi, A. Orabi and H. Aly, 2011. Early amplitude integrated electroencephalography and outcome of very low birth weight infants. Pediatr.s Int., 53: 315-321.
12. Chalak, L.F., N.C. Sikes, M.J. Mason and J.R. Kaiser, 2011. Low-voltage aeeg as predictor of intracranial hemorrhage in preterm infants. Pediatr. Neurol., 44: 364-369.
13. Toet, M.C., L. Hellstrom-Westas, F. Groenendaal, P. Eken and L.S. de Vries, 1999. Amplitude integrated eeg 3 and 6 hours after birth in full term neonates with hypoxic-ischaemic encephalopathy. Arch. Dis. Childhood Fetal Neonatal Edition, 81:
14. Rowe, J.C., G.L. Holmes, J. Hafford, D. Baboval and S. Robinson et al., 1985. Prognostic value of the electroencephalogram in term and preterm infants following neonatal seizures. Electroencephalography. Clin. Neuro., 60: 183-196.
15. Lieshout, H.B.M., J.W.F.M. Jacobs, J.J. Rotteveel, W. Geven and M. v't Hof, 2009. The prognostic value of the eeg in asphyxiated newborns. Acta Neurologica Scand., 91: 203-207.
16. Benavente-Fernández, I., S.P. Lubián-López, G. Jiménez-Gómez, A.M. Lechuga-Sancho and M. Garcia-Alloza, 2014. Low-voltage pattern and absence of sleep-wake cycles are associated with severe hemorrhage and death in very preterm infants. Eur. J. Pediatr.s, 174: 85-90.
17. Lowry, K.,J.B.J. Gainor and J.S. Hoskins, 2000. Extensor tendon rupture secondary to the AO/ ASIF titanium distal radius plate without associated plate failure: a case report. Am. J. Orthop., 29: 789-791.
18. Bajaj, A.K., 1983. Contact dermatitis hands. Ind. J. Dermatol. Venereol. Leprol., 49: 195-199.
19. Klebermass, K., M. Olischar, T. Waldhoer, R. Fuiko, A. Pollak and M. Weninger, 2011. Amplitude-integrated eeg pattern predicts further outcome in preterm infants. Pediatr. Res., 70: 102-108.
20. Rozental, T.D., P.K. Beredjiklian and D.J. Bozentka, 2003. Functional outcome and complications following two types of dorsal plating for unstable fractures of the distal part of the radius. Ovid Technologies (Wolters Kluwer Health), The J. Bone Joint Surg.-Am. Volume., 85: 1956-1960.
21. Soubasi, V., K. Mitsakis, K. Sarafidis, M. Griva, C.T. Nakas and V. Drossou, 2012. Early abnormal amplitude integrated electroencephalography (aeeg) is associated with adverse short-term outcome in premature infants. Eur. J. Paediatric Neurol., 16: 625-630.
22. Welch, C., J. Helderman, E. Williamson and T.M. O'Shea, 2013. Brain wave maturation and neurodevelopmental outcome in extremely low gestational age neonates. J. Perinatology, 33: 867-871.
23. Wikström, S., I.H. Pupp, I. Rosén, E. Norman, V. Fellman, D. Ley and L. Hellström-Westas, 2012. Early single-channel aeeg/eeg predicts outcome in very preterm infants. Acta Paediatrica, 101: 719-726.
24. Yu, Y.R., M.C. Makhni, S. Tabrizi, T.D. Rozental, G. Mundanthanam and C.S. Day, 2011. Complications of low-profile dorsal versus volar locking plates in the distal radius: A comparative study. J. Hand Surg., 36: 1135-1141.

25. Horn, A.R., G.H. Swingler, L. Myer, L.L. Linley and M.S. Raban et al., 2013. Early clinical signs in neonates with hypoxic ischemic encephalopathy predict an abnormal amplitude-integrated electroencephalogram at age 6 hours. BMC Pediatr.s, Vol. 13. 10.1186/1471-2431-13-52
26. al Naqeeb, N., A.D. Edwards, F.M. Cowan and D. Azzopardi, 1999. Assessment of neonatal encephalopathy by amplitude-integrated electroencephalography. Pediatrics, 103: 1263-1271.
27. Weeke, L.C., A. Vilan, M.C. Toet, I.C. van Haastert, L.S. de Vries and F. Groenendaal, 2017. A comparison of the thompson encephalopathy score and amplitude-integrated electroencephalography in infants with perinatal asphyxia and therapeutic hypothermia. Neonatology, 112: 24-29.
28. Koval, K.J., J.J. Harrast, J.O. Anglen and J.N. Weinstein, 2008. Fractures of the distal part of the radius. J. Bone Joint Surg.-Am. Vol., 90: 1855-1861.
29. kumar Bhagwani, D., 2016. To study the correlation of thompson scoring in predicting early neonatal outcome in post asphyxiated term neonates. J. Clin. Diagn. Res., Vol. 10. 10.7860/jcdr/2016/22896.8882
30. Garcia-Alix, A., J. Arnaez, G. Arca, T. Agut and A. Alarcon *et al*., 2021. Development, reliability, and testing of a new rating scale for neonatal encephalopathy. J. Pediatrs., 235: 83-910.