Annals of Reviews and Research

Juniper Publishers key to the Researchers

Research Article
Volume 12 Issue 2 - October 2024
DOI: 10.19080/ARR.2024.12.555834

Ann Rev Resear
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Role of Early aEEG Abnormalities in Predicting Brain Injury and Neurodevelopmental Outcomes in Preterm Neonates.

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Submission: October 09, 2024; **Published:** October 22, 2024

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Abstract

Aims and Objectives: To determine the prognostic value of Amplitude integrated electroencephalography (aEEG) for the identification of preterm infants at risk for subsequent adverse neurodevelopment with the objective for those at high risk to be targeted for early interventions.

Methods: This Prospective observational study of 175 neonates born between 24-32 weeks gestation was conducted from June 2018 through December 2020 a level IV NICU in Kuwait. aEEG was applied during the first 72 hours of life. Background was assessed as the most prominent pattern and classified into 1) normal voltage (continuous normal voltage (CNV)/ Discontinuous normal voltage (DNV) 2) low voltage 3) burst suppression and 4) the presence of sleep-wake cycling (SWC). To improve prediction, Ultrasonography head (HUS) and brain magnetic resonance imaging (MRI) were used in combination to assess short-term outcomes in relation to aEEG abnormalities with long-term neurodevelopmental outcomes assessed at 18- 24 months corrected age using Bayley Scales of Infant Development III (BSIDIII).

Results: Neonates with low voltage aEEG (N=31) had high risk of white matter injury (WMI) adjusted odd ratio (aOR) 5.3 (95%CI: 1.5-17.7); 0.007, intraventricular hemorrhage (IVH) aOR 9.2 (95%CI: 2.5-22.7); 0.028 and lower motor composite scores adjusted beta coefficient -5.3 (95%CI: -12, 1.5); 0.05. Those with burst suppression background (N=23) were at higher risks of IVH aOR 15.5 (95%CI: 2.7-8.9); 0.002 and lower motor composite scores -5.3 (95%CI: -12, 1.5); Absence of SWC was associated with white matter injury and lower cognitive scores adjusted beta coefficient -4.6 (-0.3, -8.9); p = 0.036.

Conclusion: aEEG abnormalities were associated with neuroimaging abnormalities and abnormal neurodevelopmental outcomes at 24 months.

Keywords: aEEG; IVH; MRI; SWC; Neurodevelopment

Abbreviations: aEEG: Amplitude Integrated Electroencephalography; CNV: Continuous Normal Voltage; DNV: Discontinuous Normal Voltage; HUS: Ultrasonography head; SWC: Sleep-Wake Cycling; MRI: Magnetic Resonance Imaging; BSIDIII: Bayley Scales of Infant Development III; WMI: White Matter Injury; IVH: Intraventricular Hemorrhage; CP: Cerebral Palsy; TR: Repetition Time; TE: Echo Time; AOR: Adjusted Odds; DWMI: Diffuse White Matter Injury; TAS: Total Abnormality Score

Introduction

Although the survival of preterm infants has improved to a great extent in the last few decades; however, they continue to remain at high risk of neurological disabilities and cognitive dysfunction which can exceed 50% [1]. A lot of these infants need a high level of specialized care. Prevention of the learning disabilities associated with cognitive deficiencies in this group is an important

goal for modern perinatal care and their families. Amplitude-integrated electroencephalography (aEEG) monitoring reveals abnormal brain activity that would otherwise pass unrecognized, such as subclinical seizure activity or transient background deterioration during hypoglycemia or pneumothorax. Although in the recent past, early postnatal aEEG has emerged as an increasingly used tool in preterm infants, there is no clear evidence to confirm its prognostic value in preterm infants of <30 wk GA [2]. The most predominant characteristic of the extremely preterm infants is a discontinuous baseline EEG, with scarce validated reference criteria with regards to maturation and appearance of sleep-wake cycling (SWC). Recently, MRI has been shown to be of increasing value in the evaluation of brain damage in preterm infants and offers high predictive values (sensitivity 84%, specificity 89%) when performed at term equivalent [3]. Sequential HUS is less reliable for mildly and moderately abnormal White matter injury [4]. Kidokoro et al. suggested a scoring system and simple brain metrics to characterize brain injury and impaired development in very preterm infants [5]. There always remains a subset of infants with impairments in childhood who demonstrate no significant brain injury or alterations upon neuroimaging. It is necessary to explore therefore other methods of early prediction of brain injury in preterm neonates. Neural dysfunction may be reflected by aberrations in aEEG and can be used as an early marker of brain injury in preterm neonates as in term neonates.

We aimed to determine the prognostic value of aEEG for the identification of preterm infants at risk for subsequent adverse neurodevelopment in the current perinatal care and medicine with the objective that those at high risk could be targeted for early intervention services.

Methodology

This Prospective study cohort of 175 neonates born between 24-32 weeks' gestation was conducted from June 2018 to December 2020 in a level IV NICU in Kuwait. The parents or legal guardians of neonates were informed of the study's objectives and a written informed consent was taken. All procedures were in line with the Declaration of Helsinki and ethical approval was granted by the local ethics committee at Farwaniya Hospital (PI_2018/111). aEEG was applied during the first 72 hours of life. Exclusion criteria included major congenital malformations, genetic anomalies, congenital viral infections, and death within the first week of life.

The aEEG was recorded as a single-channel EEG during the first 72 hours from the bi-parietal surface using needle electrodes with a CFM (CFM Olympic 6000 Devices Ltd, UK). The electrodes were placed by the nursing staff in the standard locations C3, P3, C4, and P4 with a reference electrode on the back. The median duration of the aEEG recordings was 54(14-71) hours and the median impedance of the tracings was 2 kOhm [mean: 2.8 kOhm (0 –11 kOhm)]. Tracings were evaluated visually and classified according to the method previously described by Hellström-Westas et al. [2]. We grouped continuous and discontinuous voltages together as normal voltage due to discontinous pattern evolving over time to continuous pattern in extreme preterm neonates until at least 28-30 weeks of age. The tracings were evaluated for any relevant artifacts and impedance >15 kΩ. The aEEG tracings were evaluated independently by the two researchers who were blinded to the patient's details as well as to each others assessment. Each investigator analyzed the background pattern, presence of sleep wave cycles, seizures, and any differences using the classification by Hellström-Westas independently. There was a good agreement between the two raters with weighted $\kappa = 0.7589$ (CI: 0.7177–0.8001).

Cerebral ultrasound: Ultrasonography head (HUS) scans were performed on Days 1, 3, 5, 7, and 10 of life and then once a week, using an Ultrasound Envisor (Philips)SN#USN0302322 with a 7.5-MHz transducer. IVH and periventricular leukomalacia were classified according to Papile et al. [6] and de Vries et al. [7], respectively. Normal HUS was defined when no white matter abnormalities and no signs of IVH were present. IVH any was classified as the presence of Grade 1 or Grade 2 IVH, IVH moderate to severe was classified as Grade 3 or Grade 4 IVH.

MRI was done in 168 neonates between 32 -34 weeks (median GA 33 weeks) and brain injury was assessed using Miller's score [8]. Our routine protocol is to perform an MRI when indicated in extreme and very preterm babies at 32 weeks gestational age. All studies were performed on a 1.5 Tesla Signa Echo (GE Medical Systems). The brain MRI studies included 1) T1-weighted sagittal spin-echo images (4mm thick) using repetition time (TR) =500ms, echo time (TE)= 11ms, 1 excitation, and 192×256 acquisition matrix; and 2) T2 weighted dual-spin echo(3 mm thick) with TR =3000ms, echo time (TE)= 60 and 120 ms, and 192×256 acquisition matrix; and 3) SWI images TR=25-50ms, TE = 20-40ms, flip angles = 15-20. Two pediatric neuroradiologists interpreted each MRI study blinded to the subject's clinical condition and ultrasound findings. The inter-rater reliability for classification of white matter abnormalities was high k= 0.85(CI 0.81-0.88). Assessment of neurodevelopmental outcome was done by developmental psychologist and a pediatrician unaware of the aEEG-findings between 18 and 24 months of corrected age, using the Bayley Scales of Infant Development III (BSIDIII) and a standardized neurological examination [9]. Abnormal neurodevelopmental outcome was defined as a diagnosis of Cerebral Palsy (CP) or if any of the three subscales (motor, cognitive, and language) showed a standardized score value <85 on BSIDIII.

Statistical Analysis Categorical variables were summarized as numbers and percentages. Numerical variables of birth weight, gestational age, as median with inter-quartile ranges and others as mean with standard deviation. Pearson's Chi-square test was used to assess the association of outcomes. Fisher exact test was used when frequency was less than 5. Regression models were used to estimate the Adjusted Odds (aOR) ratio and adjusted beta coefficient (aβ) to determine abnormalities in aEEG as predictors for abnormalities in MRI and abnormal neurodevelopmental

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outcome, after adjusting to GA, BW, sex, APGAR, use of sedatives, mode of ventilation, NEC, hypotension, BPD, postnatal infection, and use of steroids. To quantify the reliability of an aEEG background in predicting brain injury on MRI and neurodevelopmental outcomes, sensitivity, specificity, and positive and negative predictive values were calculated. In addition, the predictive value of aEEG was assessed using multivariable logistic and linear regression analysis. Values of $p < 0.05$ were considered to indicate significance in all the statistical analysis, which were performed using STATA14IC.

Results

The perinatal characteristics of the 168 infants are shown in (Table 1). Among 168 neonates enrolled, 81 (48.2%) were males and 87 (51.7%) were females. IVH any was found in 3(2.7%) in CNV group, 4 (12.9%) in low voltage group, 2 (8.6%) in burst suppression group, 8 (7.2%) in a sleep-wake cycling group , 3 (11.1%) in non-cycling group, while Grade III/IV IVH was found in 1(0.9%) in the CNV group, 14 (45.1%) in the low voltage group, 11 (47.8%) in the burst suppression group, and 5 (4.5%) in the sleep-wake cycling group, 14 (51.8%) in non-cycling group WMI any was found in 6(5.4%) in CNV group, 5 (16.9%) in low voltage group and 4 (17.3%) in burst suppression group, 7 (6.3%) in the sleep-wake cycling group, 4 (14.8%) in non- cycling group. Moderate to severe WMI was found in 3(2.7%) in the CNV group, 16 (51.6%) in the low voltage group and 11(47.8%) in the burst suppression group, and 4 (3.6%) in the sleep-wake cycling group, 15 (55.5%) in non-cycling group (Figure 1).

Table 1: Perinatal characteristics of neonates.

GA (wks) median+ IQR	27.6(26.1-29.7))
Wt (median+ IQR)	920(805- 1255)
Males: Females	81:87
Antenatal steroids	162 (96.5%).
APGAR 1 min, median IQR	7(6-8)
APGAR 5min, median IQR	8 (7-9)
Sedation	
Morphine	4(2.3%)
Midazolam	1(0.005%)
Low flow [a]	33(19.6%)
CPAP /NIPPV	37(22.2%)
Ventilation/HFO	60(35.7%)
Postnatal corticosteroids	15(8.9%)
CLD at 36 wks [b]	47(27.9%)
NEC Bell stage >2 [c]	16(9.5%)
Postnatal infection [d]	42 (25%)
PDA [e]	61(36.3%)
Cystic PVL	8(4.7%)
aEEG Background pattern	
Continuous/Discontinuous normal voltage	114(67.8%)
Low voltage	31(18.4%)
Burst suppression	23(13.6%)
Presence of sleep-wake cycling	110(65.4%)
Absence of sleep-wake cycling	27 (16.1%)
Seizures	2 (0.011 %)

Values are expressed as numbers and percentages (%) or median and interquartile range (IQR)

[a]Low flow was defined as a flow rate < 2LPM, fio2 <25%

[b]CLD was defined as the need for oxygen or any respiratory support at 36 wks PMA.

NEC [c] was defined as infants diagnosed with NEC ≥ IIA (Bell's classification).

[d]Postnatal infection was diagnosed if culture-positive sepsis, urinary tract infection, or meningitis was diagnosed.

[e]PDA was defined as an internal ductus diameter ≥1.5mm or a PDA: left pulmonary artery diameter ≥ 0.5) and 1 or more of the any of following criteria: LA/AO ≥ 1.5, ductus flow velocity ≤2.5m/sec or mean pressure gradient across ductus ≤ 8mmHg, left pulmonary artery diastolic flow velocity ≥0.2m/sec and/or reverse diastolic flow in the descending aorta.

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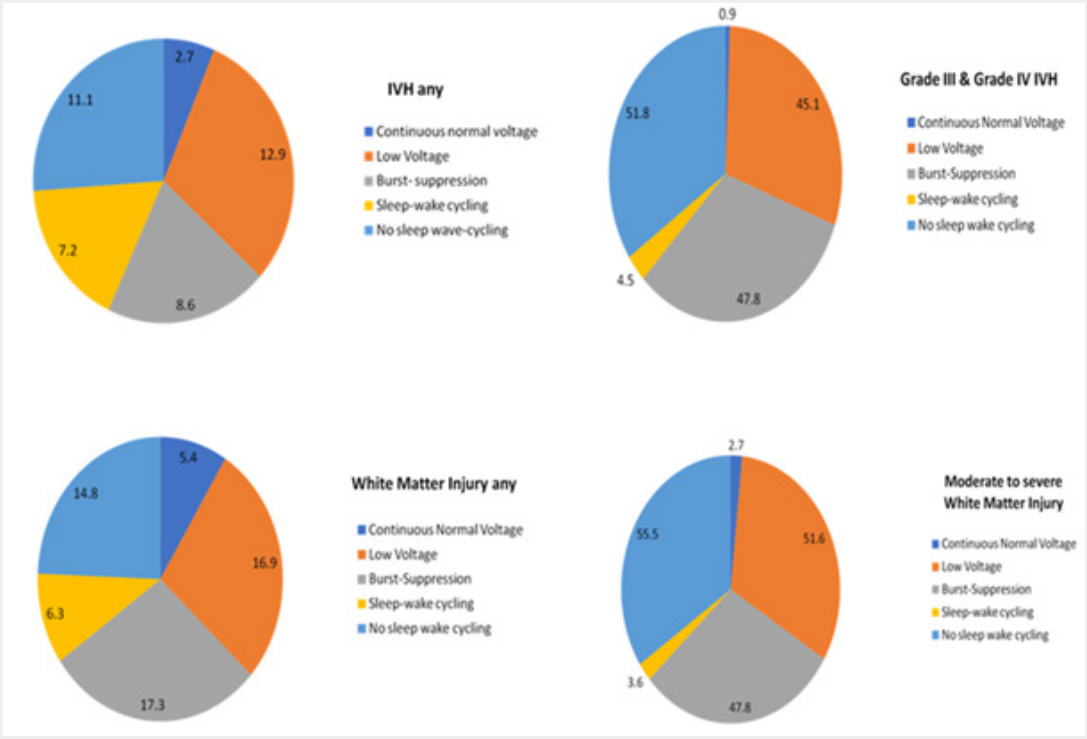

Figure 1: Shows IVH and WMI across neonates with different aEEG backgrounds.

Table 2: aEEG background as predictors of MRI brain injury.

	[a]OR(95%CI); p- value	Sensitivity %	Specificity %	Positive Predictive Value %	Negative Predictive Value %
Low voltage					
WMI any	5.3 (95% CI 1.5- 7.7); 0.007	86.70%	95.80%	92.70%	83.30%
WMI moderate-severe	4.2 (95% CI 0.11- 8.3); 0.322	91.40%	94.70%	91%	85.40%
IVH any	9.2 (95% CI 2.5- 22.7); 0.001	87.60%	91.10%	89.30%	80.90%
IVH moderate to severe	4.3 (95%CI 1.2 - 16.3); 0.0028	88.60%	88.20%	91.80%	83.30%
Burst suppression					
WMI any	3.3 (95%CI 0.615- 18.2); 0.162	85.70%	82.70%	83.50%	80%
WMI moderate-Severe	3.8 (95%CI 0.7- 5.3);0.279	91.40%	83%	81.50%	90%
IVH any	13 (95%CI 3-70); 0.001	93.60%	97.20%	91.80%	88%
IVH moderate to severe	15.5 (95%CI 2.7- 89); 0.002	94.60%	92.20%	90.80%	95%
Sleep awake cycling					
WMI any	0.43 (95% CI 0.71-0.88);0.006	86.70%	79.30%	85.50%	81.50%
WMI moderate-Severe	0.72 (95% CI 0.21-1.8);0.312	84.50%	83.20%	86.80%	90%
IVH any	0.382 (95%CI 0.19-2.1); 0.211	83.10%	77.10%	80.90%	77.80%
IVH moderate to severe	0.382 (95%CI 0.19-2.1); 0.211	78.10%	72.10%	81.70%	70.80%

Abbreviation: White matter injury: WMI. Intraventricular hemorrhage (IVH)

Data are expressed in adjusted odd ratio (aOR) and 95% confidence interval (95% CI) in relation to continuous normal voltage and to no cycling. Adjusted for gestational age, birth weight, sex, Apgar score, use of sedatives, mode of ventilation, necrotizing enterocolitis, chronic lung disease, postnatal infection, and the use of post-natal steroids.

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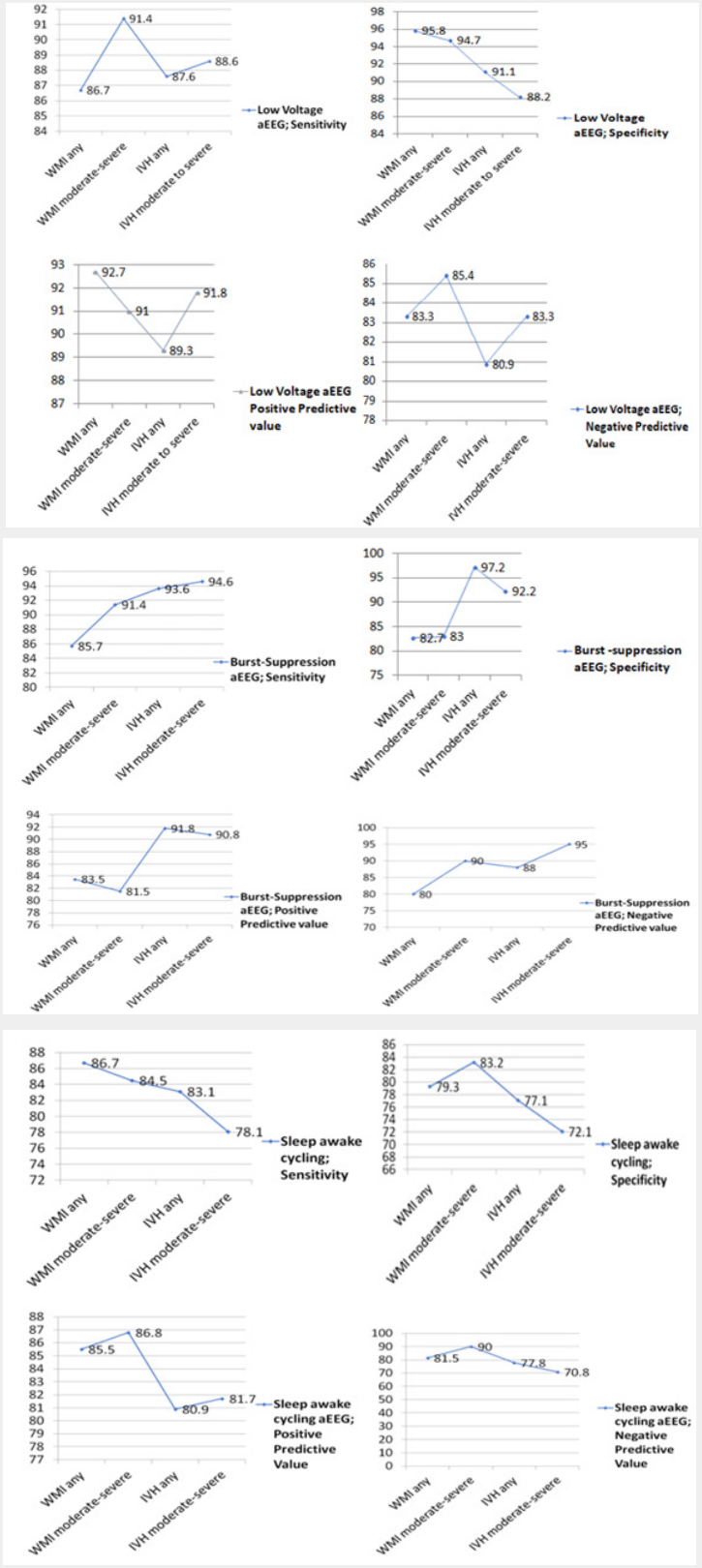

Figure 2: Shows Sensitivity, Specificity, PPV & NPV of aEEG backgrounds in predicting brain injury.

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However, after adjustment, neonates with low voltage aEEG (N=31) had high risk of white matter injury (WMI) any adjusted odd ratio (aOR) 5.3 (95%CI: 1.5-17.7); 0.007, intraventricular hemorrhage (IVH) any aOR 9.2 (95%CI: 2.5-22.7); 0.028 and IVH moderate to severe aOR 4.3 (95%CI 1.2 – 16.3); 0.0028. Those with burst suppression background (N=23) were at higher risks of IVH any aOR 13 (95%CI 3-70); 0.001 and IVH moderate to severe aOR 15.5 (95%CI: 2.7-8.9); 0.002. Absence of SWC (N=27) was associated with white matter injury aOR 0.43 (95% CI 0.71-0.88); 0.006. The presence of low voltage or burst suppression aEEG and SWC had high sensitivity, specificity, positive predictive value, and negative predictive value for predicting brain injury (Table 2, Figure 2).

Two neonates, who had electro-clinical seizures, had a burst suppression pattern with HUS showing bilateral Grade 3 IVH and moderate to severe white matter injury. Of the 168 neonates, outcome data in our hospital could be obtained in 164 (97.7%) infants due to loss of follow- up, at a median corrected age of 18.7 months (IQR: 18.3- 22.4 months). Of the 164 infants who underwent assessments, 29 (17.6%) had motor scores <85, 11 (6.7%) had cognitive scores <85, and 11 (6.7%) had language scores <85. Infants in the burst suppression group and low voltage group had lower motor scores (p=0.029) and cognitive scores (p=0.001). Infants who had absent SWC had also lower motor scores (p=<0.001) and cognitive scores (p=0.03). Both aEEG background patterns and SWC had high sensitivity, specificity, positive predictive value, and negative predictive value in the prediction of Bayley-III scores in all domains (Table 3). On multivariable regression analysis, those with burst suppression and low voltage group had lower motor composite scores aOR 15.5 (95%CI: 2.7-8.9); 0.002 and -5.3 (95%CI: -12, 1.5); 0.05 respectively. The absence of SWC predicted lower cognitive scores adjusted beta coefficient -4.6 (-0.3, -8.9); P=0.036 (Table 4).

Table 3: aEEG background in prediction neurodevelopmental outcome.

	Number (%)	Sensitivity %	Specificity %	Positive Predictive Value %	Negative Predictive Value %
Motor <85, n= 29					
Normal voltage	1 (3.4%)				
Low voltage	5 (17.2%)	97.10%	75.70%	70.30%	86%
Burst suppression	6 (20.6%)	97.10%	77%	73%	88.30%
P value	0.029				
No SWC	15 (51.7%)	92.50%	73.30%	68.30%	83.3
SWC	2 (6.8%)				
P value	<0.001				
Cognitive <85, n=11					
Normal voltage	0				
Low voltage	2 (18.1%)	100%	72.80%	63.30%	100%
Burst suppression	5 (45.4%)	100%	70%	61.60%	100%
P value	0.001				
No SWC	3 (27.2%)	97.40%	80.20%	77.90%	96.70%
SWC	1 (9.1%)				
P value	0.03				
Language <85, n=11					
Normal voltage	0				
Low voltage	2 (18.2%)	100%	61.40%	59%	100%
Burst suppression	3 (27.2%)	100%	58%	57.30%	100%
P value	0.093				
No SWC	6 (54.5%)	96.20%	79.50%	76.80%	84.40%
SWC	0				
P value	0.321				

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Table 4: aEEG background as a predictor of neurodevelopmental outcomes.

Bayley-III composite score	Motor	Cognitive	Language
	aβ coefficient (95%CI); P value	aβ coefficient (95%CI); P value	aβ coefficient (95%CI); P value
Normal voltage: Reference			
Low voltage	-5.3 (95%CI: -12, 1.5);0.05	-2.9 (95%CI: -9.5, 3.5);0.364	-2.4 (95%CI: -9.6, 4.8); 0.517
Burst suppression	-9.6(95%CI: -18.8, -0.43);0.04	-5.8 (95%CI: -15.5, 3.8); 0.235	-5.3 (95%CI: -14, 3.4);0.231
Sleep-wake cycling: Reference			
No sleep-wake cycling	3.6 (95%CI: -3.6 -11); 0.324	4.6 (95%CI:0.3 - 0.89); 0.036	3.3 (95%CI-5-11.4); 0.432

Data are expressed as adjusted beta (aβ) coefficient 95% confidence interval (95%CI)

Discussion

Recent studies have elucidated a correlation of early aEEG parameters with short and long-term neurological outcomes [10-12]. Following discharge from neonatal intensive care, the estimated risk of neuro-developmental impairments can be used to target early intervention services to those at high risk. Various clinical risk scores [13], and neuro-imagings [14] in the past have been found useful in assessing early brain function to improve the accuracy index, keeping medium and long-term prognosis in mind. However, mostly only HUS was done to look for neurological lesions, which could miss microscopic areas of necrosis and glial scars of non-cystic PVL & diffuse white matter injury (DWMI), that are below the resolution of ultrasonography [15]. In this single-center prospective cohort of prematurely born infants, between 24 to 32 weeks gestation, we aimed to examine an association between early aEEG background patterns and brain injury using Miller score and neurodevelopmental outcomes by Bayley III scale of infant development at 18-24 months corrected age. To our knowledge, this is the first study that demonstrates the composite role of aEEG backgrounds to predict short-term brain injury using MRI as a modality of choice as early as 32 weeks and long-term neurodevelopmental outcomes. We found that there was a significant association between the classification of aEEG recordings within 72 h after birth and the degree of WMD & IVH in preterm infants with subsequent adverse neurodevelopmental outcomes. Our study also determined an absence of cyclicity to be associated with lower cognition at 18-24 months of corrected age.

The predictive value of early aEEG for long-term outcomes is still controversial. Recent studies [16] reported that abnormal aEEG recordings within 24 hours after birth in infants with GA 22–30 weeks or 27–32 weeks were associated with long-term adverse neurodevelopmental outcomes. However, another study reported that aEEG recordings in preterm infants with GA 28–36 weeks could not predict outcomes at 18 to 22 months of age [17]. The contradictory predictive values could be related to a small sample size & significant loss of follow-up, which might eliminate sick babies with significantly abnormal aEEG tracings. In the current study, we found that abnormalities in aEEG recordings in preterm infants 24 to 32 weeks GA, within 72 h after birth were positively correlated with both short and long-term poor outcomes at 18 months of corrected age.

Benavente et al. [10] determined that lack of sleep-wake cycling during the first 72 hours of life was associated with death in preterm infants ≤1500 g or ≤32 weeks. There was selective monitoring of critical babies in the former study due to the availability of a single device. There was no long-term follow-up of babies in the former study for assessment of neurodevelopment outcomes. Only HUS was used for neuroimaging which is quite unreliable to determine white matter injuries. Our cohort found an absence of sleep-wake cycling to be associated with lower cognition at corrected 18-24 months of age. Klebermass et al. [18] in preterm infants ≤30 weeks determined the significant correlation between the absence of sleep-wake cycle & abnormal outcome at the age of 3 years which was defined as one or more of the following: CP, neurosensory impairment, MDI, and PDI (Bayley Scales <70), without significant mortality.

Soubasi et al. [11], determined that continuity of aEEG within the first 72 h of life, especially the presence of pathological background pattern correlates with the adverse short-term outcome (IVH °III/IV) in infants between 25 and 32 weeks gestational age. Our study found that neonates with low voltage & burst suppression had not only a high risk of any intraventricular hemorrhage (IVH) including moderate to severe IVH, but the former was also associated with white matter injury. Besides, our study also demonstrated the long-term impact of pathological aEEG backgrounds, those with burst suppression and low voltage backgrounds were at higher risk of lower motor composite scores at 18 months of corrected age. Wikstrom et al also demonstrated, prolonged interburst intervals and burst suppression patterns to be strong predictors of poor neurodevelopmental outcome at 2 years corrected age in preterm infants between 22 and 30 gestational weeks [12].

Burdjalov's total scores from aEEGs obtained within the first 6 weeks of life in infants ≤30 gestational weeks are known to predict adverse neurodevelopmental outcomes [19]. Britta Huning et al. [20] found aEEG parameters classified by Burdjalov Score of the first 72hrs to be significantly associated with altered brain maturation on MRI predicted by total abnormality score (TAS). Also, the combined aEEG and MRI scores predicted the neurodevelopmen-

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tal outcome at 24 months. However, TAS had no predictive value, most likely explained by the small sample and an underestimation of subtle alterations by TAS. We used Miller's score [5], to grade the severity of white matter abnormalities on MRI, which relies more accurately on total lesion volume and quantitative assessment of white matter lesions.

The limitation of our study was that we did not follow the evolution and/or recovery of aEEG over time which could perhaps prove useful and contributory since aEEG is a sensitive marker of developmental outcomes. We recommend future prospective studies to demonstrate such associations. Although we grouped continuous and discontinuous voltages together as a normal voltage due to discontinuous pattern evolving over time to continuous pattern in extreme preterm neonates until at least 28-30 weeks of age, we did not find any significant adverse neurodevelopmental outcomes in them at 18-24 months of age.

Declarations

Ethics approval and consent to participate: A written informed consent was obtained from the parents or legal guardians of neonates. All procedures were in line with the Declaration of Helsinki and ethical approval was granted by the local ethics committee at Farwaniya Hospital (PI_2018/111).

Consent for Publication: The consents for publication had been obtained from the parents or legal guardians of the neonates participated.

Availability of data and materials: All the relevant data and information related to the article is available.

Competing Interests: The authors declare no competing interests.

Funding: None.

Acknowledgements: The authors would like to thank the neonates and their parents for participating in the study.

Contributions MA: Conception and design, data collection, analysis, and interpretation of data; MMM Contribution to design of the study and analysis and interpretation of data, writing the manuscript; MA data collection, HA data collection, RA Analyzing data and editing manuscript. AA data collection, MMM will act as a guarantor for the manuscript.

Compliance with Ethical Standards: Yes

"What is already known on this topic?"

aEEG backgrounds in term newborns and their correlation with the short and long-term neurodevelopmental outcome is well-established.

The predictive value of early aEEG for short and long-term outcomes in preterm neonates is still controversial.

Most studies used only USG as a modality for neuroimaging to predict brain injury which is quite unreliable in determining white matter injuries.

What this study adds?"

To our knowledge, this is the first study that demonstrates the composite role of aEEG in the first 72 hours in preterm neonates to predict short-term brain injury using MRI as a modality of choice as early as 32 weeks and long-term neurodevelopmental outcomes.

A validated Miller's score to determine the severity of white matter abnormalities on MRI.

How might this study affect research, practice, or policy?"

Identification of preterm infants who are at high risk for subsequent adverse neurodevelopment to be targeted for early interventions.

aEEG to be incorporated as a standard of care in NICUs in the management of preterm and extreme preterm neonates.

MRI as a modality of choice of neuroimaging as early as 32 weeks to be as predictive as term equivalent age.

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How to cite this article: Mariam A, Muzamil Mustafa M, Muneera A, Hanadi A, Rima Al S, et al. Role of Early aEEG Abnormalities in Predicting Brain Injury and Neurodevelopmental Outcomes in Preterm Neonates.. Paper Recycling Ann Rev Resear. 2024; 12(2): 555834. DOI: 10.19080/ARR.2024.12.555834

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DOI:10.19080/ARR.2024.12.555834

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