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Amplitude - Integrated EEG Recorded at 32 weeks Postconceptional age Correlated with MRI at Term

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ABSTRACT

Introduction: Preterm birth significantly increases the risk of neurodevelopmental disorders due to the brain's vulnerability during critical gestational weeks. Early detection of brain injuries is essential to facilitate interventions that improve long-term outcomes. While cranial ultrasound (CUS) is commonly used, it may miss subtle brain injuries, whereas MRI provides more detailed structural insights. Amplitude-integrated EEG (aEEG) complements MRI by offering real-time, functional monitoring in the NICU, enhancing neurocritical care and enabling a more comprehensive approach to protecting neonatal brain health. **Objective:** This study aims to determine the predictive value of aEEG recorded at 32 weeks postconceptional age and its correlation with MRI findings at term-equivalent age, evaluating aEEG's potential in predicting neurodevelopmental outcomes for preterm neonates. **Methods:** A prospective observational study was conducted at Rajarajeswari Medical College and Hospital, Bengaluru, from August 2022 to April 2024. Forty-five preterm neonates born before 32 weeks were assessed with aEEG, and MRI was performed at term-equivalent age. Statistical analyses included correlation assessments between aEEG parameters (continuity, cyclicity, amplitude) and MRI findings. **Results:** The study demonstrated significant correlations between aEEG parameters and MRI-detected abnormalities in cerebral white matter, grey matter, and cerebellum. Lower a EEG scores correlated with severe brain injuries. Continuity and cyclicity were notably predictive of brain health, with higher continuity scores linked to greater gestational maturity. **Conclusion:** This study highlights aEEG as an effective tool for early neurodevelopmental risk assessment in preterm neonates, particularly when used with MRI. Integrating aEEG into NICU protocols offers a more comprehensive assessment of neonatal brain health, allowing for timely interventions that may significantly improve neurodevelopmental outcomes in this vulnerable population.

INTRODUCTION

Preterm birth poses a significant risk for neurodevelopmental disorders, such as cerebral palsy and intellectual disabilities owing to the vulnerability of the developing brain during the critical gestational period from 24 to 40 weeks. This phase encompasses rapid and intricate developmental processes, and disruptions can lead to lasting neurological challenges. Recognizing these risks, early detection of brain injuries in neonates is crucial, as it allows for proactive intervention. Identifying high risk infants at the earliest stages can lead to tailored care strategies that support more favourable developmental outcomes, which can profoundly impact the quality of life for these vulnerable neonates [1].

Traditionally cranial ultrasound (CUS) has been the primary tool used to detect brain lesions in preterm neonates in the Neonatal Intensive Care Unit (NICU). This non invasive accessible technology provides bedside imaging and helps identify certain types of brain injuries. However, CUS has limitations in sensitivity and resolution especially for subtle or deep brain lesions and some injuries that could influence long term neurodevelopment might remain undetected. Magnetic Resonance Imaging (MRI) offers an alternative with a higher resolution and a more comprehensive assessment of the brain, particularly beneficial for examining white matter an essential area for neurodevelopment. Unlike CUS, however MRI often requires specialized equipment skilled technicians and transport to imaging facilities, making it less commonly used in routine neonatal care. As a result MRI is typically reserved for specific cases or performed at term equivalent age rather than during the immediate postnatal period [2].

The growing recognition of MRI's detailed imaging capability in assessing brain structure has sparked interest in integrating it more systematically for preterm infants who are at higher risk. By including MRI in routine evaluations, healthcare providers could identify potential brain injuries more accurately at an earlier stage, which would help facilitate timely interventions and support services. Advanced imaging tools may thus enhance diagnostic precision, enabling healthcare teams to make better informed decisions that could improve long-term outcomes for infants at high risk of neurodevelopmental disorders. This approach underscores a shift towards combining advanced imaging with early monitoring to optimize neonatal care [3].

Amplitude-integrated electroencephalography (aEEG) has emerged as a complementary tool to MRI and CUS, providing real-time monitoring of brain function in NICU settings. aEEG allows for continuous bedside monitoring, which makes it possible for clinicians to track changes in brain activity and identify abnormalities that could signal the onset of neurological complications. This form of electroencephalography is sensitive to the evolving patterns of brain function in neonates, enabling early detection of potential brain injuries or epilepsy like patterns. Since its introduction into neonatal care, aEEG has proven invaluable in assessing the neurological status of at risk infants and has become an essential tool for guiding therapeutic interventions that support optimal neurodevelopment [4].

In addition to injury detection aEEG provides insights into the ongoing development of neonatal brain function. Its continuous monitoring capability gives clinicians a detailed view of brain activity, allowing for rapid intervention if irregularities arise. This approach adds a vital dimension to neonatal care, as aEEG provides a window into cerebral health that supports a more holistic understanding of brain function and maturation. Combining this technology with other diagnostic tools strengthens clinicians' ability to monitor, diagnose and intervene effectively to support positive neurodevelopmental outcomes [5].

eEEG's utility is especially evident when recorded within the first 72 hours of life, which represents a sensitive period for identifying brain injuries in preterm neonates, particularly those born around 32 weeks of gestational age. The early days of life are critical, and aEEG recordings taken during this window can yield valuable information regarding cerebral function. While its predictive value is clear during this period, aEEG's role in identifying more subtle or evolving brain lesions beyond the first few days remains an area of ongoing research. Clinicians often supplement early aEEG findings with MRI scans conducted at term equivalent age, which provide a structural evaluation that further informs long term neurodevelopmental assessments [6].

MRI conducted at term equivalent age (TEA) provides a detailed structural overview of the brain, identifying abnormalities and developmental delays with implications for long term outcomes. Integrating information from aEEG monitoring within the initial days of life with MRI findings at TEA may bridge the gap between early functional assessments and later anatomical evaluations. Such a combined approach would enhance the understanding of neonatal brain health, enabling healthcare providers to better tailor interventions for neonates who are at a higher risk of neurodevelopmental challenges [7].

Despite aEEG's promising real time capabilities, its long-term predictive power is best utilized within a comprehensive framework. This includes considering established clinical factors, such as gestational age and the presence of intraventricular hemorrhage, which remain fundamental for prognosis. By integrating aEEG with other clinical indicators, clinicians can make more informed predictions regarding an infant's neurodevelopmental risks allowing for more targeted interventions that can support improved outcomes [8].

For preterm neonates, amplitude integrated electroencephalography (aEEG) patterns provide valuable early indicators of neurodevelopmental outcomes. Specific patterns like cycling and changes in background frequency, correlate with neurological health and can predict short-term outcomes.Classification systems, such as those by Hellstrom Westas and Burdjalov, help clinicians interpret these patterns, aiding in early diagnosis and guiding timely interventions to support long term cognitive health [9].

When combined with Magnetic Resonance Imaging (MRI), the diagnostic power of aEEG is further enhanced. Research shows correlations between aEEG parameters and MRI findings, with metrics like spectral edge frequency reflecting brain maturation and aligning with postmenstrual age. Together, aEEG and MRI offer comprehensive insights into neonatal brain health integrating real time functional data with detailed structural imaging. This dual approach enables healthcare providers to create more personalized care plans, supporting early interventions that can optimize neuro-developmental outcomes for at risk preterm neonates [10].

The aim of this study is to determine if amplitude integrated electroencephalography (aEEG) patterns within the first weeks of life can reliably predict neurodeve-lopmental outcomes in preterm neonates born at 32 weeks of gestational age. Additionally, the study seeks to identify the optimal timing for aEEG assessment and to evaluate its diagnostic sensitivity and specificity compared to Magnetic Resonance Imaging (MRI) at term equivalent age, aiming to enhance early detection and intervention strategies for at risk neonates.

MATERIALS AND METHODS

This prospective observational study, conducted at Rajarajeswari Medical College and Hospital, Bengaluru, aimed to assess the predictive value of amplitude integrated electroencephalography (aEEG) recorded at 32 weeks

Spanning from August 2022 to April 2024, the study included 45 preterm neonates admitted to the NICU all born before 32 weeks of gestation and presenting high-risk factors like intraventricular hemorrhage birth asphyxia and neurological complications. Exclusion criteria included neonates with severe congenital nervous system malformations or those unable to be followed until 40 weeks gestation or death.

RESULTS

The study involved 45 preterm neonates (25 males, 20 females) with a mean birth weight of 1346.22g and a median gestational age of 31 weeks. Antenatal steroids were given to 44 mothers, chorioamnionitis was prevalent (82.22%), and sepsis occurred in 24.44%. Significant associations were found with chorioamnionitis sepsis and postnatal steroid use.

Table 1: Descriptive Statistics for the aEEG Findings

aEEG Findings	Mean	Standard Deviation (SD)	Range
Continuity	1.04	0.74	0-2
Cyclicity	2.22	1.31	0-5
Amplitude of lower border	1.51	0.63	0-2
Band Width span	2.36	0.48	2-3
Total aEEG score	7.11	2.51	0-12

This study included 45 preterm neonates (25 males, 20 females) with a median gestational age of 31 weeks and mean birth weight of 1346.22g. Antenatal steroids were administered in 97.78% of cases, with high rates of chorioamnionitis (82.22%) and sepsis (24.44%), both significantly associated with postnatal steroid use.

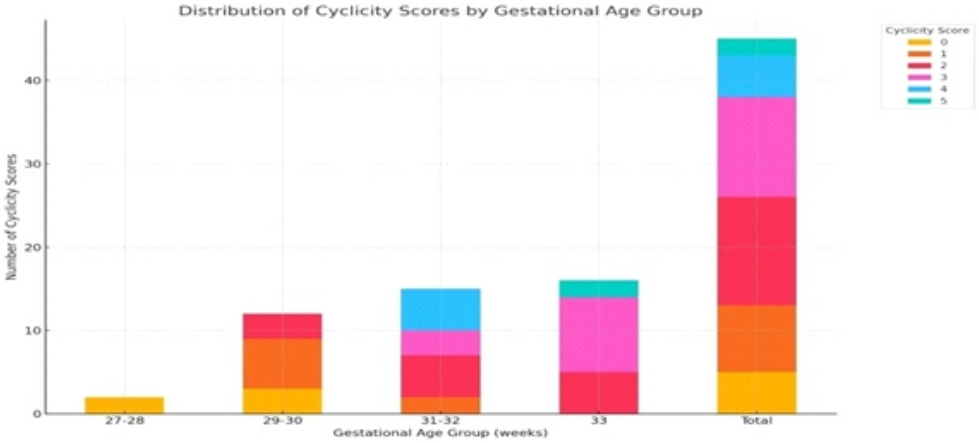

Figure 2: Distribution of Cyclicity Burdjalov Scores by Gestational age Group

Gest age (wks)	Continuity Score 0	Continuity Score 1	Continuity Score 2	Total
27-28	2	0	0	2
29-30	9	3	0	12
31-32	0	11	4	15
33	0	7	9	16
Total	11	21	13	45

The distribution of Burdjalov continuity scores shows that lower gestational ages (27–28 weeks) have only score 0 instances while 29–30 weeks have more score 0 and some score 1 cases. At 31–32 weeks scores 1 and 2 appear and at 33 weeks scores are balanced between 1 and 2 suggesting a link between gestational maturity and higher continuity scores.

Table 3: Distribution of Amplitude of Lower Border Burdjalov Scores by Gestational age Group

Gest age (wks)	ALB Score 0	ALB Score 1	ALB Score 2	Total
27-28	1	1	0	2
29-30	2	5	5	12
31-32	0	10	5	15
33	0	0	16	16
Total	3	16	26	45

The distribution of Amplitude of Lower Border (ALB) scores shows that the 33-week group has the highest count of ALB Score 2, indicating generally higher amplitudes. In con-trast the 27–28 week group has lower counts and greater variability, while the 29–30 and 31–32-week groups display moderate to high amplitude scores.

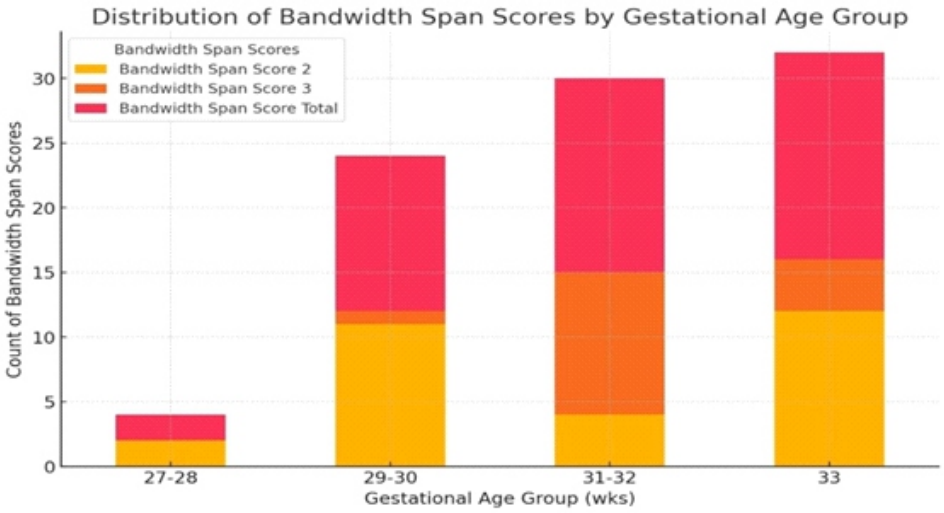

Figure 2: Distribution of Band width Span Burdjalov Scores by Gestational age Group

The Bandwidth Span score distribution shows that the 29–30 and 31–32-week groups have a balanced mix of Scores 2 and 3 indicating varied bandwidth spans. The 33-week group mostly has Score 2, reflecting narrower spans, while the 27–28-week group has fewer cases, primarily with

Table 4: Correlation Analysis between the MRI Findings and TMS

MRI Finding	Correlation with TMS (r)
Cerebral White Matter Cystic Lesion (CWMCL)	0.75
Focal Signal Abnormality (FSA)	0.65
Myelination Delay (MD)	0.43
Deep Grey Matter Signal Abnormality (DGMSA)	0.65
Cerebellum Signal Abnormality (CSA)	0.59

MRI analysis shows strong correlations between the Total MRI-Kidokoro Score (TMS) and brain abnormalities, with the highest for Cerebral White Matter Cystic Lesion (r = 0.75). Focal and Deep Grey Matter Signal Abnormalities ® = 0.65) and Cerebellum Signal Abnormality (r = 0.59) also strongly correlate, while Myelination Delay (r = 0.43) has a moderate association.

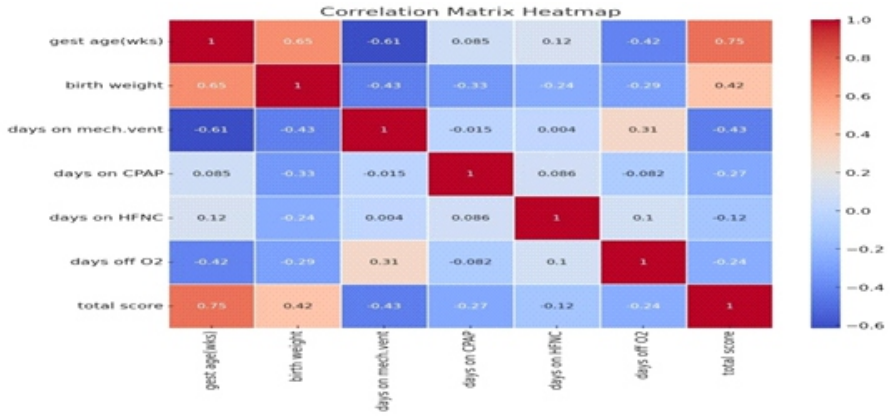

Figure 3: Correlation Matrix Heat Map

The correlation matrix shows gestational age positively linked to birth weight (0.653) and aEEG score (0.748), suggesting better outcomes with maturity. Conversely gestational age negatively correlates with ventilation days (-0.615), highlighting greater respiratory needs in more premature neonates.

Table 5: Correlation Analysis between aEEG and MRI Findings

aEEG Findings / MRI Findings	Continuity		Cyclicity		Amplitude of Lower Border		Band Width Span	
	Spearman	p-value	Spearman	P value	Spearman	p-value	Spearman	p-value
White Matter	-0.551	0.000	-0.504	0.000	-0.451	0.001	-0.237	0.116
Grey Matter	-0.591	0.000	-0.614	0.000	-0.423	0.003	-0.211	0.163
Cerebellum	-0.472	0.001	-0.539	0.000	-0.251	0.096	-0.112	0.463

The correlation analysis shows that MRI abnormalities are strongly linked to poorer aEEG parameters. Continuity and cyclicity exhibit strong negative correlations with abnormalities in white matter, grey matter and cerebellum while amplitude has moderate correlations. These findings suggest aEEG parameters, especially continuity and cyclicity, as potential biomarkers for neurodevelopmental outcomes.

Table 6: Comparison of Severity between Total MRI Score and aEEG Score

Severity	Total MRI Score	Total aEEG Score
Normal (score 0-3)	24	7
Mild (score 4-7)	15	14
Moderate (score 8-11)	3	22
Severe (score >11)	3	2
Total	45	45

In comparing MRI and aEEG scores, MRI classifies more neonates as normal (24 vs. 7 for aEEG), while aEEG identifies a higher number as moderately abnormal (22 vs. 3 for MRI). This suggests aEEG may detect subtler neurological differences, highlighting the benefit of using both methods.

DISCUSSION

Preterm birth is a leading cause of neurodevelopmental disorders, including cerebral palsy and intellectual disabilities. Brain injury risk spans from 24 to 40 weeks, necessitating early diagnostics to identify high-risk neonates. Cranial ultrasound and MRI help detect brain lesions, with ongoing studies focusing on neurodevelopmental outcomes into early childhood and beyond [11].

Amplitude integrated electroencephalography (aEEG) prov-ides continuous monitoring of neonatal brain function in NICUs, particularly within the first 72 hours for high-risk preterm infants (Soubasi et al., 2012). This study evaluated aEEG's predictive value at 32 weeks postconceptional age for brain maturation at term with MRI, finding significant correlations between chorioamnionitis, sepsis, ROP, and EEG scores. An MRI tool adapted from Kidokoro et al. assessed term brain abnormalities. Kristina Stuikiene and Elke Griesmaier et al. (2024) noted EEG scores rising with gestational age, whereas our study showed lower scores with severe brain injury [12,13].

Jihae Kim's study emphasizes that mechanical ventilation while reducing mortality in preterm neonates, negatively affects brain development and correlates with injuryechoed in our findings where prolonged ventilation linked to adverse outcomes. Unlike Kim's findings on magnesium sulfate's protective effects, our study found no significant correlation. Tang et al. (2021) noted improved motor outcomes with a "New Nesting Device," while Roberta Pineda et al. (2024) linked lower aEEG and Burdjalov scores to cerebral injury and sociodemographic factors. Reynolds et al. and our study found strong associations between aEEG outcomes, sepsis, and ventilation duration, supporting aEEG's predictive neurodevelopmental value [14,15,16].

Our study found that absence of EEG cyclicity in the first 24 hours is predictive of brain injury, such as intraventricular hemorrhage. Using Burdjalov criteria, continuity scores were analyzed across gestational groups (27-33 weeks), showing an increase in cyclicity with gestational age. Han et al. (2016) confirmed data accuracy and inter-rater agreement in scoring, while Stuikiene et al. (2024) observed a positive association between Burdjalov scores and gestational age, with lower gestational age neonates displaying higher scores across all aEEG dimensions at each time point [17,18].

In preterm neonates, sleep wake cycling patterns are more attenuated typically seen around 30-32 weeks. Anna Tarocco et al. (2021) emphasized brain MRI at term equivalent age (TEA) as a predictor of long term outcomes in very preterm neonates detecting brain volume reduction and lesions. While aEEG is simpler and cost effective it shows predictive value for intraventricular hemorrhage when cyclicity is absent. Our study also using Burdjalov scores, showed strong correlations between early aEEG findings (cyclicity and continuity) and MRI abnormalities in white matter, gray matter and cerebellum, underscoring predictive neurodevelopmental indicators [19].

Our study analyzed Amplitude of Lower Border (ALB) and bandwidth span scores across gestational age groups, showing higher ALB in the 33-week group and variability in lower gestational ages. Kato et al. (2011) observed altered aEEG signals in neonates with cystic white matter injury, similar to our findings, although both studies had limited patient numbers. Gestational age positively correlated with birth weight and total aEEG score, while prolonged ventilation linked to poorer EEG outcomes. Svensson et al. (2023) used EEG to estimate postmenstrual age, applying a regression tree model for feature relevance analysis [20,21].

The Total MRI-Kidokoro Score (TMS) effectively assesses brain injury in preterm neonates, correlating strongly with abnormalities like Cerebral White Matter Cystic Lesion (CWMCL), Focal Signal Abnormality (FSA), and Deep Grey Matter Signal Abnormality (DGMSA). Trevarrow (2021) noted similar patterns in CP patients with somatosensory deficits. Our study found significant negative correlations between MRI abnormalities and aEEG parameters, particularly continuity and cyclicity, supporting aEEG as a potential neurodevelopmental biomarker, as Taubert et al. (2016) observed [22,23].

This study found moderate correlations between aEEG continuity and cyclicity scores with white and grey matter abnormalities, suggesting their predictive value for MRI outcomes. Lower border amplitude and bandwidth span had weaker correlations. Hüning et al. (2018) supports these findings, linking Burdjalov scores with brain volumes and neurodevelopmental indices. Griesmaier et al. (2023) confirmed lower aEEG scores in neonates with severe brain injury. Our findings similarly revealed that lower EEG scores correlate with greater MRI-detected brain injury severity [24,25].

The study compared MRI and aEEG scores in 45 preterm neonates, revealing discrepancies in brain abnormality assessments. MRI showed 24 neonates as normal contrasting with only 7 by aEEG. Mild abnormalities appeared in 15 on MRI, while moderate severity was notably higher in aEEG scores (22 vs. 3 on MRI). Severe scores were consistent across modalities, suggesting aEEG's potential sensitivity to aspects MRI might miss. Griesmaier et al. (2024) observed similar trends, linking lower TMS with more severe injuries. Song et al. found lower aEEG sleep-wake cycling and total scores in severe WMI cases. Correlation analysis highlighted strong inverse associations between “Deep GM signal abnormality” and aEEG, emphasizing the importance of combined imaging moda-

lities. Limitations include sample size, short follow-up, and variability in aEEG interpretation, underscoring the need for larger studies and standardized protocols [25,26].

CONCLUSION

This study highlights the potential of amplitude integrated EEG (aEEG) as a predictive tool for neurodevelopmental outcomes in preterm neonates, particularly when used alongside MRI. Significant correlations between aEEG parameters and MRI-detected brain abnormalities suggest that aEEG can provide early insights into brain function, identifying neonates at risk for neurodevelopmental challenges. aEEG offers real time bedside monitoring, allowing timely interventions to enhance long-term outcomes. Future research with larger cohorts and standardized protocols is essential to validate these findings, incorporating aEEG into neonatal neurocritical care to improve the quality of life for preterm neonates through earlier intervention and support.

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