

# Investigation of perinatal asphyxia in term newborns with postnatal feeding intolerance

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## ABSTRACT

**Aim:** Perinatal asphyxia affects whole body systems and depending on compensation mechanisms, the central nervous system is primarily protected. In this study, we aimed to evaluate brain electrophysiological activity in cases with postnatal feeding intolerance due to perinatal asphyxia and to investigate whether the compensation mechanism is adequate or whether there is a minimal electrophysiological disorder.

**Methods:** This study was conducted prospectively to compare the amplitude electroencephalography (EEG) recordings of 22 patients who were followed up with the diagnosis of feeding intolerance due to perinatal asphyxia and 10 control groups. Eeg probes were applied by gluing. Conventional EEG was performed in the patient group and the recordings were evaluated with an amplitude integrated electroencephalography (aEEG). It was also compared with feeding time, length of hospital stay, maternal ages, cord blood gas pH and base deficit values, electrolyte values at the 24th hour, appearance pulse grimace activity and respiration (APGAR) and Burdjalov scores.

**Results:** When aEEG Vmin values, Burdjalov scores, and 1st min APGAR scores were compared, statistically significant difference was found between the patient and control groups. There was an inverse weak correlation between the patients' aEEG Vmin values and their length of hospital stay. A weak correlation was found between the cases' cord blood gas base deficit and aEEG Vmax values. When cases were divided into two groups as less than 7 days of hospitalization and more than 7 days of hospitalization, a statistically significant difference was found between the groups in terms of maternal age.

**Conclusion:** In our study, it was aimed to show whether there is a minimal effect of perinatal asphyxia on EEG findings in newborns with nutritional deficiency. The difference in the aEEG Vmin values of the case and control groups indicates that brain electrical activity is affected. This is also supported by the fact that those with higher Vmin values had shorter hospital stays.

**Keywords:** aEEG, cEEG, feeding intolerance, perinatal asphyxia

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## INTRODUCTION

Perinatal asphyxia criteria include cord blood gas pH and base deficit values. Neurological examination, amplitude integrated electroencephalography (aEEG), and near infrared spectroscopy (NIRS) are used to monitor whether or not the central nervous system is affected. Conventional EEG (cEEG) is an important diagnostic tool, which is a detailed and complementary examination method in the clinical, neuroradiologic and electrophysiologic evaluation of newborns. cEEG is used to determine the level of brain damage and to determine the possibility of permanent neurologic sequelae. However, its use in the neonatal intensive care units is limited (1).

Continuous monitoring of cerebral activity can contribute to the assessment of the degree of cerebral damage and evaluation of prognosis, monitoring of seizure activity and response to treatment (2-5). In addition, electroencephalographic monitoring helps early identification of neonates suitable for neuroprotective treatment such as hypothermia (5,6).

In the early period following perinatal asphyxia, aEEG tracing is very effective in predicting neurological prognosis in term infants (7). There are many studies in the literature reporting that the background rhythm in aEEG is compatible with the neurological examination (8).

Electrical seizures should be screened with aEEG monitoring in term newborns at risk, and if suspected or when an electrical seizure is detected, this should be confirmed by cEEG or video EEG monitoring before starting antiepileptic treatment (5,9,10).

In this study, it was aimed to investigate perinatal asphyxia in term newborns with postnatal feeding intolerance and its effects on the central nervous system. The CNS impact was evaluated by investigating whether the compensation mechanism was sufficient

with aEEG or whether the electrophysiological impactation was minimal.

## MATERIAL AND METHODS

In this study, patients with insufficient suction, swallowing coordination or feeding intolerance in the postpartum days were evaluated, between 2020-2022 in the Bolu Abant İzzet Baysal Education and Research Hospital. The cases that are clinical decided or proven early neonatal sepsis were excluded, and only the cases with inadequate feeding were evaluated. Amplitude EEG recordings were compared in 22 patients who were thought to have feeding intolerance as a result of compensation due to perinatal asphyxia and 10 healthy controls, these records were compared for feeding time, hospitalization duration, maternal ages, cord blood gas pH and base deficit values, electrolyte values at the 24th hour, Apgar and Burdjalov scores. At the same time, cEEG recording were obtained to the case group, and it was checked for compatibility with the aEEG recordings. The study was conducted prospectively. aEEG and cEEG probes were applied by gluing.

The study protocol was approved by the Abant İzzet Baysal University Clinical Research Ethics Committee (13.07.2021 / 2021/168).

The data obtained from the study were recorded and analyzed using the standard program "Statistical Package for Social Sciences for Windows 20.0". Microsoft Excel was used for some graphs. The Pearson correlation test was used to measure the relationship between variables. The Mann-Whitney U test was used for nonparametric data. P-value <0.05 was considered significant.

In the study, aEEG scores, cEEG grading results, neurological examination findings, cord blood gas values, aEEG voltage values, feeding initiation times, hospitalization duration and maternal ages were compared.

## RESULTS

Twenty-two patients in the neonatal intensive care unit were included in the study. Nine (40%) of the patients were female and 13 (60%) were male. The boy/girl ratio was 1/1.4. The median Vmin value of the patient group was 7.5 (6-8.25) and the median Vmin value of the control group was 9.5 (7.75-13.5). The median Vmax value of the patient group was 53.5(47.25-76.25) and the median Vmax value of the control group was 67.5 (58.75-90) (Table 1).

An inverse correlation was found between the patient's aEEG Vmin values and their length of hospital stay ( $r=-0.507$ ,  $p=0.003$ ). A correlation was detected between cord blood gas base values and aEEG Vmax values of the patients ( $r=0.450$ ,  $p=0.01$ ) (Table 2).

A statistically significant difference was found between the case and control groups when comparing 1st minute APGAR scores ( $p<0.05$ ) (Figure 1), aEEG Vmin values ( $p<0.05$ ) (Figure 2) and Burdjalov scores ( $p<0.05$ ) (Figure 3).

A statistically significant difference was found in maternal ages between the patients hospitalized for less than 7 days and those hospitalized for more than 7 days ( $p<0.05$ ) (Figure 4).

## DISCUSSION

In our study, we aimed to evaluate brain electrophysiological activity in cases with postnatal feeding intolerance due to perinatal asphyxia and to investigate whether the compensation mechanism is adequate or whether there is a minimal electrophysiological effect on the brain. aEEG Vmin values, APGAR score in first minute and Burdjalov scores were lower in the patient group. There was no difference between the groups in aEEG Vmax, APGAR fifth minute scores, feeding time, cord blood gas pH and base deficit values and electrolyte values at the 24th hour.

In a study of 89 newborns with perinatal asphyxia, a correlation was found between aEEG scores and APGAR 1st and 5th minute scores. In our study, we found no correlation between aEEG scores and 5th minute APGAR scores. However, we found a statistically significant difference between the aEEG and 1st minute APGAR scores of the patient and control groups ( $p<0.05$ ). We did not include moderate and severe asphyxia cases in the study. There may have been no difference in APGAR scores because the patients did not have significant asphyxia (11).

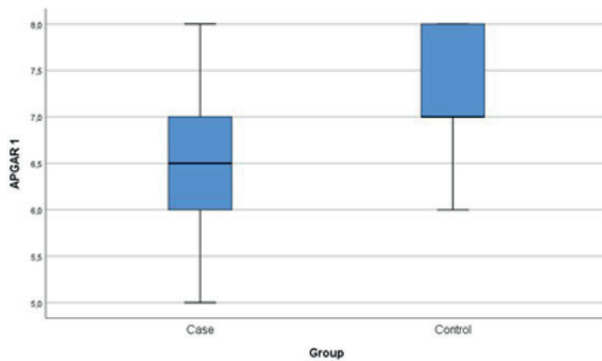
**Table 1.** Results of patient and control groups

	Patient Median (IQR 25-75)	Control Median (IQR 25-75)
pH of the cord	7.31 (7.16-7.36)	7.33 (7.3-7.36)
pCO <sub>2</sub> of the cord (mmHg)	39.5 (37-61.25)	44.55 (37-51.48)
HCO <sub>3</sub> of the cord (mEq/L)	20.35 (17.9-21.77)	22.3 (19-25.53)
Base deficit of the cord (mmol/L)	-6.5 (-11.62- -2.8)	-5.3 (-6.5-3.13)
Lactate of the cord (mmol/L)	3.19 (1.94-5.98)	2.70 (1.5-4.17)
Hospitalization duration (day)	9.5 (7-11)	1 (1-1)
Time to start feeding (day)	1.5 (1-2.25)	1 (1-1)
Voltage minimum (μV)	7.5 (6-8.25)	9.5 (7.8-13.5)
Voltage maximum (μV)	53.5 (47.25-76.25)	67.5 (59-90)
Burdjalov score	12.5 (12-13)	13 (13-13)
APGAR score (1.min)	6.5 (6-7)	7 (7-8)
APGAR score (5.min)	8 (7-9)	8.5 (8-9)
Maternal age	30.5 (25.75-37)	30 (28-34)

**Table 2.** Correlation values between patients and controls EEG Vmin, Vmax, cord blood base deficits, day to start feeding, and their hospitalization duration values

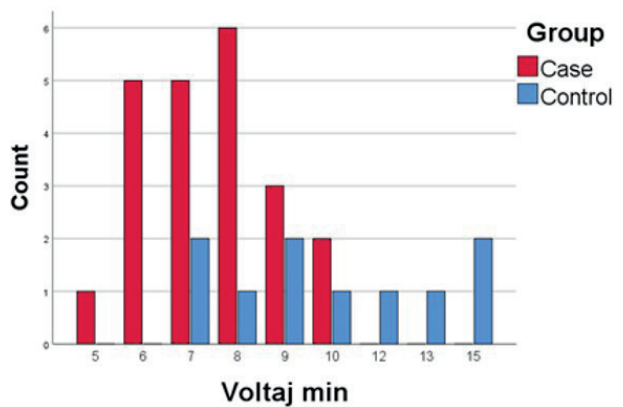
		pH	V min	V max	Base deficit
V min	r	0.036			
	p	0.843			
V max	r	0.231	0.158		
	p	0.203	0.388		
Base deficit	r	0.768	0.084	<b>0.450</b>	
	p	0.000	0.648	<b>0.010</b>	
Day to start feeding	r	-0.024	-0.148	-0.267	-0.017
	p	0.895	0.418	0.139	0.926
Hospitalization day	r	-0.175	<b>-0.507</b>	-0.309	-0.180
	p	0.339	<b>0.003</b>	0.085	0.324

r: Pearson correlation, p: p value



**Figure 1.** Comparison of the 1st minute APGAR scores between patient and control groups.

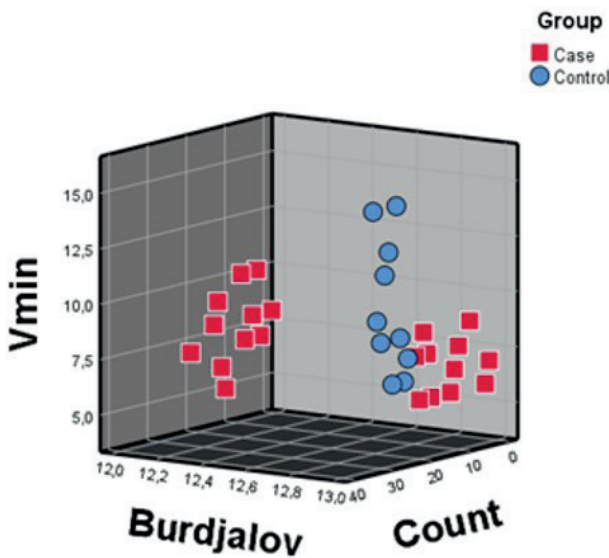
In the study conducted by Pichler et al.<sup>12</sup> when the aEEG Vmin and Vmax values of newborns with and without postnatal resuscitation were compared, the Vmin and Vmax values of those without resuscitation were found to be higher. In our study, a statistically significant difference was found between the patient and control groups when the aEEG Vmin values of the cases were compared, ( $p < 0.05$ ). At the same time, a weak inverse correlation was found between Vmin values and the length of hospital stay ( $r = -0.507$ ,  $p = 0.003$ ). This suggests that there was a decrease in Vmin values due to perinatal asphyxia and that patients needed longer hospitalization. There was no difference in Vmax values between the groups. The reason why we did not detect a difference in Vmax values may be that there



**Figure 2.** Comparison of aEEG Vmin values between patient and control groups.

was no significant decrease in the Vmax values of the patients because we did not include moderate and severe asphyxia cases. The difference in Vmin values may also be due to insufficient blood supply to the brain and damage from free oxygen radicals. We think that in mild asphyxia, there may be CNS involvement without short-term sequelae.

The two most important parameters in the assessment are the pH and base deficit, which show metabolic acidosis (13). In our study, a weak correlation was detected between cord blood gas base deficit values and aEEG Vmax values ( $r = 0.450$ ,  $p = 0.01$ ). Changes in

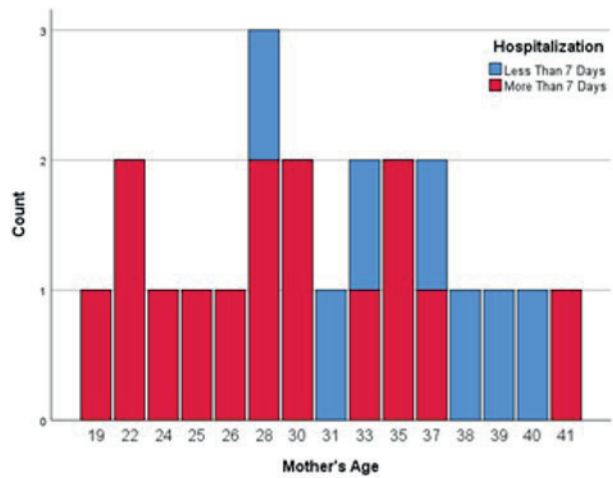


**Figure 3.** Comparison of Burdjalov scores between patient and control groups.

this base deficit and Vmax values in the cases support the minimal effect of perinatal asphyxia.

Burdjalov et al.<sup>14</sup> developed a different scoring system with 146 aEEG recordings in 30 newborns. Scores were created by rating the continuity, sleep-awake, lower-limit amplitude value and upper-limit value components. In our study, a statistically significant difference was found between the patient and control groups when Burdjalov scores of the patients were compared ( $p < 0.05$ ). The significant difference between Vmin, APGAR 1st minute scores and Burdjalov scores supports that the patient group was exposed to minimal asphyxia.

Comparative studies on the effectiveness of aEEG in seizure detection have concluded that electrical seizures in term newborns at risk should be screened with aEEG monitoring and, if suspected or when an electrical seizure is detected, this should be confirmed by cEEG or video EEG monitoring before starting antiepileptic treatment (5,9,10). In our study, no seizure activity was detected on aEEG and cEEG. Normal detection of cEEG was a finding we expected since moderate and severe asphyctic cases were not included in the study.



**Figure 4.** Comparison of mother's ages between patient and control groups.

In a study by Topçuoğlu et al.<sup>15</sup>, the use of assisted reproductive techniques, multiple pregnancies, gestational diabetes and pre-eclampsia were found to be higher in older mothers compared to other age groups. In our study, when the cases were divided into two groups with a hospitalization period of less than 7 days and more than 7 days, a statistically significant difference was found between the groups in terms of maternal age ( $p < 0.05$ ). Fetuses are exposed to more prenatal stress in the uterus, which disrupted maturation and development, and as risk factors increase with maternal age. Therefore, the length of stay of newborns in intensive care may be extended.

A study reported that the development and implementation of better evidence-based nutrition support practices in newborns led to improved nutrient intake and decreased growth, length of hospital stay and related costs (16). In our study, the feeding initiation times of the patient groups were found to be similar.

This study shows cerebral involvement as assessed by early aEEG. We included only term infants and excluded moderate and severe asphyctic patients. The relatively small study population is a limitation, and the findings need to be reproduced in larger cohorts. It is known that the brain is severely affected in asphyctic

patients. In our study, we showed that there were changes in brain electrophysiological activity even in mild asphyctic cases.

The limitations of this study are the small number of patients and the selection of term newborns to reduce effect of other risk factors.

Nutritional deficiency is observed in newborns with perinatal asphyxia. In perinatal asphyxia, the central nervous system is protected by compensatory mechanisms. However, although the CNS is preserved, this does not mean that it is not affected. In our study, it was aimed to show whether there is a minimal effect of perinatal asphyxia in newborns with nutritional deficiency. The difference in the aEEG Vmin values between the case and control groups indicates that the electrical activity of the brain is affected. This is also supported by the fact that those with higher Vmin values had shorter hospital stays.

### Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date 13.07.2021, number 2021/168). Written informed consent was obtained from the participants.

### Author contribution

Concept: AE, ST; Design: AE, ST; Data Collection or Processing: AE, ST, AD, FH, MD; Analysis or Interpretation: AE, MD; Literature Search: AE, ST, MD; Writing: AE, ST, AD, FH, MD. All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

### Conflict of interest

The authors declare that there is no conflict of interest.

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