EEG Changes in Neonatal Hypoxic Ischemic Encephalopathy

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Abstract

Background: Traditional multichannel EEG is an integral part of the evaluation of neonates diagnosed with neonatal hypoxic ischemic encephalopathy (HIE). HIE is well-defined as the clinical appearance of reduced neonatal brain function after asphyxia due to perinatal and/or an antenatal adverse incident. It is prevalence ranging from 1 to 8 per 1000 worldwide. **Objectives:** To evaluate EEG changes in neonates with hypoxic ischemic encephalopathy.

Method: A cross sectional study conducted from Aug. 2018 till June 2019. The patient included ,term neonate with gestational age from (37 to 42 weeks) admitted in Neonatal Care Unit(NCU) in Babylon teaching hospital for maternity and children , with diagnosis of hypoxic Ischemic Encephalopathy(HIE) . with total number of 47 were enrolled in the study. Full assessment, including: clinical assessment (history and full examination) and electrophysiological (EEG) were done to all Patients. First EEG was done at age ranged from (2 to 7 days) while second EEG was done at age ranged from (21 to 28 days).

Result: In this study, first EEG showed that 8 (17.02%) normal EEG and 39 (82.9%) abnormal EEG results, while second EEG was shown that 15 (31.9%) normal EEG, 17 patients get improvement and 7 get worse. This study was shown that, there are a strong significant statistical deference between the EEG background activity in the first week and developmental mile stone, stage of HIE, neurological examination, age of patients and seizure with p value less than 0.05.

Conclusion: EEG of neonates with HIE provides early prognostic and objective information.

Key words: *EEG, neonatal hypoxic ischemic encephalopathy*

Introduction

HIE has significant detrimental effects on the growing brain and is between the leading causes of death among neonates, as well as the major original cause of seizures in term neonates [1] . HIE is still a serious situation that is unresolved and causes significant mortality and long-term morbidity [2]. Neonatal HIE can also be considered as damage that occurs in the immature brain, producing in delayed cell death via excitotoxicity, oxidative stress and inflammation. These adverse happenings in the evolving brain often lead to long lasting detrimental neurological defects afterward in life such as mental retardation, learning disabilities, epilepsy, cerebral palsy, and other neurophysiological handicaps [3].

The "EEG picture" of a disease is frequently a visual waveform or an atypical frequency or abnormalities in waveform amplitude or a hyper synchrony [4]. The EEG in neonates with HIE reveals the severity of brain damage and changes over time [5].

Method

Inclusion criteria:

1-Term (37-42 weeks of gestation).

2-HIE occur in neonatal period 28 days.

3- fitting within 7 days of delivery.

The patients were selected according to the American Academy of Pediatrics and American College of Obstetrics and Gynecology [6] criteria, a patient with

hypoxic ischemic encephalopathy require 3 or more of the following criteria.

(a) Neonatal encephalopathy.

(b) Apgar score ≤ 3 for elongated than 5 minutes.

(c) Intense metabolic acidosis (pH < 7.0) in umbilical artery blood.

(d) Multiorgan system failure.

(e) Fetal bradycardia. Patients in this study have low Apgar score, neonatal encephalopathy and fetal bradycardia

Exclusion criteria:

1- Infant with cerebral Sino venous thrombosis.

2- Newborns with other structural CNS abnormalities.

3- Encephalopathy due to genetic disorders, infections and inborn error of metabolism.

EEG Procedure

An EEG was done in department of neurophysiology in the hospital of Imam AL Sadiq. A neonate was lied on a bed and the EEG electrodes were located to the scalp at FP1, FP2, F3, F4, C3, C4, P3, P4, F7, F8, T5, T6, T3, T4, O1, O2, and CZ permitting to the international 10-20 system of electrode placement using adhesive paste. A pair of electrodes is required in order to get a voltage potential difference. Most EEGs was taken about 1 hour. Before the procedure, the patient's parents are requested to wash their child hair the night before the test and stop taking certain medications before the test. The parents of neonates satisfying the criteria were approached and informed consent was achieved as soon as after the birth or with the start of clinical seizures. All EEGs were given a grade depended on background activity, which has been described Table below.

Table 1 Classification of EEG Background Activity [7].

Grade	Results	Description
0	Normal EEG	EEG results Continuous background arrangement with normal physiologic features for example anterior slow waves.
1	Normal/mild abnormalities	Continuous background arrangement with slightly abnormal activity (slight asymmetry, slight voltage depression).
2	Moderate abnormalities	Discontinuous activity by way of interburst interval of <10 s, or clear asynchrony or asymmetry.
3	Major abnormalities	Discontinuous activity with interburst interval of 10–60 s, marked Reduction of background patterns.
4	Inactive EEG findings	Background action of <10 μV or severe discontinuity with IBI of >60 s

Results

The patient's age ranged from 2 – 7 days and most of them are male and have birth weight more than 3.75 kg shown in table below.

Table 2 Distribution of the study patients according to child characteristics.

variables	Mean	percentage
Age	Mean	5.45 (±1.47)
Gender	Male	31 (66%)
	Female	16 (34%)
Gestational age	Mean	38.6 (± 1.33)
	Mean	3.14 (±0.78)
Birth weight	Less than2.5 kg	7 (14.9%)
	2.5-3.750 kg	19 (40.4%)
	More than 3.750kg	21 (44.7%)
Mode of delivery	Home delivery	3 (6.4%)
	Hospital vaginal delivery	34 (72.3%)
	Cesarean section	10 (21.3%)

This study was shown that most of patients have moderate HIE scale 48.9%, the staging was done according to modified sarant scale and have normal development mile stone 66% (patients were followed up from age ranged from 3-11 months).

Table 3 Distribution of the study group according to the neurological characteristics

characteristics	**group**	**NO. (%)**
HIE	Mild	20 (42.6%)
	Moderate	23 (48.9%)
	Severe	4 (8.5%)
Neurological examination	Normal	13 (27.7%)
	Hypotonic	23 (48.9%)
	Spastic (hypertonia)	11 (23.4%)
Developmental milestones	Normal	31 (66%)
	delayed	16 (34%)
Presence of Seizure	Yes	23 (49%)
	No	24 (51%)

Table 4 Distribution of study patients in the first and second EEG.

	Type	1st week		4th week	
		No	%	No	%
EEG	normal	8	17.0	15	31.9
	mild	13	27.7	10	21.3
	moderate	12	25.5	8	17.0
	major	12	25.5	10	21.3
	inactive	2	4.3	4	8.5
	Total	47	100.0	47	100.0

In this study there are positive association between EEG background activity in the 1st week and age of patient p value less than 0.05 while there are no significant association between EEG background activity in the 1st week and gender, mode of delivery, birth weight and gestational age.

Table 5 The association between different child characteristics and EEG findings in the 1st week

normal abnormal			abnormality of EEG		Total	P Value
Age of the baby	2-7 days	No.	8	39	47	0.011
		%	17.02%	82.9%	100.0%	
Gender	Male	Count	6	25	31	
		% within gender2	19.4%	80.6%	100.0%	0.963
	Female	Count	2	14	16	
		% within gender2	12.5%	87.5%	100.0%	
Birth weight	Less than 2.5 kg	Count	0	7	7	0.451
		% within Wt2	.0%	100.0%	100.0%	
	2.5 to 3.750 kg	Count	3	16	19	
		% within Wt2	15.8%	84.2%	100.0%	
	More than 3.750 kg	Count	5	16	21	
		% within Wt2	23.8%	76.2%	100.0%	
Gestational age	less than 39 wks	Count	4	19	23	1.00
		% within G.age2	17.4%	82.6%	100.0%	
	39-40 wks	Count	3	16	19	
		% within G.age2	15.8%	84.2%	100.0%	
	41 or more	Count	1	4	5	
		% within G.age2	20.0%	80.0%	100.0%	
Mode of Delivery	Home delivery	Count	0	3		0.808
		%	.0%	100.0%		
	Hospital Vaginal Delivery	Count	7	27		
		%	20.6%	79.4%		
	Cesarean section	Count	1	9		
		%	10.0%	90.0%		

This study was shown that, there are a strong positive association between the EEG background activity in the first week and development mile stone, stage of HIE, neurological examination and seizure with p value 0.0001.

Table 6 The association between neurological characteristics and the EEG findings in the 1st week.

normal mild			**EEG background activity in the 1st week**						
			moderate	**major**	**inactive**				
development mile stones	Normal	No.	8	13	8	2	0	31	0.0001*
		%	25.8%	41.9%	25.8%	6.5%	.0%	100.0%	
	delay	No.	0	0	4	10	2	16	
		%	.0%	.0%	25.0%	62.5%	12.5%	100.0%	
Seizure	Absent	No.	8	10	5	0	1	24	0.0001*
		%	33.3%	41.7%	20.8%	.0%	4.2%	100.0%	
	Present	No.	0	3	7	12	1	23	
		%	.0%	13.0%	30.4%	52.2%	4.3%	100.0%	
stage of HIE	mild	No.	8	9	3	0	0	20	0.0001*
		%	40.0%	45.0%	15.0%	.0%	.0%	100.0%	
	moderate	No.	0	4	8	9	2	23	
		%	.0%	17.4%	34.8%	39.1%	8.7%	100.0%	
	severe	No.	0	0	1	3	0	4	
		%	.0%	.0%	25.0%	75.0%	.0%	100.0%	
Neurological examination	normal	No.	7	4	2	0	0	13	0.0001*
		%	53.8%	30.8%	15.4%	.0%	.0%	100.0%	
	hypotonic	No.	0	2	9	10	2	23	
		%	.0%	8.7%	39.1%	43.5%	8.7%	100.0%	
	spastic	No.	1	7	1	2	0	11	
		%	9.1%	63.6%	9.1%	18.2%	.0%	100.0%	

* Measured by fissure exact test

In this study, 2nd EEG finding shows that there are a significant association in a group not take AEDs with p value 0.021

Table 7 Significance of difference in EEG Findings after 4 wks. (By willcoxin rank- signed test).

Characteristics	**Group**	**N**	**Mean rank**	**P value**
Both groups	Negative rank	17	12	0.083
	Positive rank	7	13.71	
	No change	23		
	Total	47		
Treated group	Negative rank	7	6	0.796
	Positive rank	5	7.2	
	No change	11		
	Total	23		

Cont... **Table 7 Significance of difference in EEG Findings after 4 wks. (By willcoxin rank- signed test).**

Untreated group	Negative rank	10	6.5	0.021**
	Positive rank	2	6.5	
	No change	12		
	Total	24		

Discussion In our study first EEG shows that 82.9% patients have abnormal EEG and 17% with normal EEG while in the second EEG the numbers of normal EEG became 31.9% and from those with abnormal first EEG 17.9% patients return to normal in second EEG. This mean most of the cases, EEG grades either remained constant or improved between first and second EEG this result agree with [8] in this study was used the same EEG feature we depend on for a classification of EEG background activity (Continuity, asymmetry, voltage depression and interburst interval or asynchrony). [9] tacked 31infants and do EEGs within first week of infant age and founded that 17 normal EEG from them 15 still normal while 2 became abnormal, 13 BS all stayed abnormal. [7] founded that The EEG grade allocated correlated considerably with outcome and EEG abnormalities improved with time, with the worst EEG grade seen on the initial recording in all cases. A substantial problem in the classification of different abnormal EEG features is that there are no universal definition of diverse abnormalities in terms of voltage level, phase or frequency. For instance, voltage levels used to define an abnormality such as low voltage often differ among studies.

In this study there are a significant association between EEG background activity in the 1st week and age of patient with p value 0.011 and there are no significant association with others child characteristics. [10] has similar result to our study while [11,8] show disagreement with our study in that they found there are positive association with mode of delivery. [12] reported high incidence of birth asphyxia in rural area this result shown agreement with our study since 3 patients with home delivery all have abnormal EEG finding, [13] found that home delivery associated with more severe birth asphyxia and abnormal neurodevelopment outcome.

According to development mile stone we found that patients were classified as having mild EEG feature all with normal development which has agreement with [14], also [15] was shown that, infants with mild HIE with a continuous or to some extent discontinuous a EEG with lacking cyclicity are more likely to have the good outcome, while infants with severe HIE have a severely abnormal a EEG background (low voltage, inactive) have a high threat for adverse outcome (death or severe handicap) this result show agreement with our study since patients with severe EEG grade (10 from 12 patients with major EEG grade and all 2 patients with inactive EEG grade) associated with delay development. Explanation to these result are background features of EEG accurately expect long term neurodevelopmental outcome in term neonates with HIE. Burst suppression, flat trace and low voltage do predict neurodevelopmental outcome with a great specificity and sensitivity [14].

Patients with HIE stage one distributed between normal, mild and moderate EEG grades most of them have mild EEG grade 45% while patients with moderate HIE stage two distributed in all EEG grades with most of them have major 39.1% and the patients with severe HIE stage three distributed between moderate 25% and major 75% EEG grade [11] show agreement with our study by finding that, there are positive association between EEG background feature and severity of HIE, While [18] shown disagreement to our study in that all neonates were on hypoxic-ischemic encephalopathy (HIE) Stage I had normal EEG recording; 36.7% with HIE Stage II had abnormal EEG recording while had agreement to our study in that 100% of the neonates with HIE Stage III showed abnormal EEG. Explanation to this, the severity of encephalopathy in asphyxiated neonates correlates well with the abnormalities on EEG records.

Conclusion

EEG regard as the safest mode for a neonate with convulsion and informative tool for routine work up for HIE patient even in neonate without fitting.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the University of Babylon /

Babylon Medical College, Iraq and all experiments were carried out in accordance with approved guidelines.

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