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Original Article

The Role of Long Monitoring EEG in Detection of Interictal Epileptiform Discharge in Idiopathic Epilepsy

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ABSTRACT

Background: Epilepsy is a common chronic neurological disorder affecting around 5 million people each year worldwide. It is estimated that nearly 70% of people with epilepsy could live seizure free if properly diagnosed and treated, so early diagnosis and treatment is very helpful.

Methods: This cross sectional observational prospective study included 36 epileptic patients underwent long term Electroencephalographic monitoring for at least sixty minutes and epilepsy severity was measured by National Hospital Seizure Severity Scale.

Results: 52% of studied patients had late IED beyond 20 minutes of EEG recordings, while 30.1% of our patients had early IED in the first 20 of EEG recording .also Interictal Epileptiform discharge (IED) latency had significantly increased with earlier age of epilepsy onset (22.13 ± 12.8 vs. 42.33 ± 4.2, P= 0.01) and longer duration of epilepsy (13.40 ± 4.6 vs. 8.50 ± 3.9, P= 0.027).

Conclusions: Our data concluded that age of onset and duration of epilepsy were significant factors related to the presence of IED, as patients with IED had an earlier onset and longer duration of epilepsy.

Keywords: EEG; IED; Epilepsy

INTRODUCTION

Electroencephalogram (EEG) is considered as an important tool for diagnosis and evaluation of seizures and spells. Epileptiform abnormalities on EEG are useful in assessing the risk of seizure recurring after a first unprovoked seizure and helpful in differentiating epileptic from nonepileptic events, **[1].** According to the American Academy of Neurology practice parameters for evaluation of a first unprovoked seizure, the presence of epileptiform abnormalities on EEG were associated with a greater risk of recurrence in both adult and children **[2].**

Despite EEG is a cornerstone in epilepsy diagnosis, routine EEG is frequently non-diagnostic as epileptiform abnormalities on a single routine EEG are detectable in only 29-55% of patients, so that serial recordings are advised **[3,4].** The length of a conventional EEG can vary from practice to practice. American clinical Neurophysiology However, the organization recommends at least 20 minutes of artifact-free recording **[5],** however the international league against epilepsy (ILAE) suggested 30 minutes of recordings for better visualization of brain activity **[6].** Additionally prolonged EEGs is occasionally utilized to detect IEDs, or interictal epileptiform discharges, in patients with normal or non-epileptiform routine EEGs **[7].**

This work aims at determining the diagnostic role of long EEG monitoring, by extending the duration of EEG recordings beyond 20 minutes in adults and children, in order to detect interictal epileptiform discharge.

PATIENTS AND METHODS

36 epileptic patients were included in this cross-sectional observational study. The patients' ages ranged from 7 – 46 years and a mean of 27.03 ± 11.09 years. The patients were 19 (52.78%) female and 17 (47.22%) male, they attended Neurophysiology unit for EEG in Neurology Department, Zagazig University hospital, during the period from August of 2022 till February 2023

Patients with brain disorders causing secondary epilepsy as metabolic encephalopathy, CNS infections, head trauma, electrolyte disturbance and brain tumor were excluded from the study.

Written consent was obtained from all participants after an explanation of the procedure. The Institutional Review Board, Faculty of Medicine Zagazig University approved this study (ZU-IRB #9665(27/7/2022). The study was done according to the code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All patients underwent full history taking with focusing on age at seizure onset, type/s of seizures, frequency of attacks, duration of attack, history of status epilepticus and semiology of seizures. Complete neurological examination and assessment of the severity of the epileptic seizures were done using the National Hospital Seizure Severity Scale-NHS3 and it's relation to the frequency of interictal epileptiform discharge. The National Hospital Seizure Severity Scale (NHS3) contains seven seizure-related factors and generates a score from 1 to 27. A seizure severity score is generated for each seizure type the patient experiences. NHS3 instructions recommend that the interview includes a witness to seizures, in addition to the person with epilepsy. Higher scores reflecting increased severity of epilepsy **[8].**

Plain computed (CT scan) brain with or without contrast or Magnetic Resonance Imaging (MRI) brain with or without contrast was done to exclude 2ry epilepsy.

All patients were subjected to long monitoring or extended EEG examination (at least for 60 minutes) where encephalographic epileptiform abnormalities were detected and recorded in each EEG which was done under standard conditions during resting-wakefulness state with closed eyes, in addition to the hyperventilation and photic stimulation as a provocative tests, and then was reviewed for presence of interictalepileptiform discharges, which includes spikes sharp waves, temporal intermittent rhythmic delta activity and generalized spike and wave discharges **[7].**

EEGs of all subjects were visually inspected; and the epileptiform activities were detected in most of the patients. The patients' EEG records4 were analyzed in the first 20 minutes (early) and then after 20 minutes (late).

Interictal Epileptiform discharge (IEDs) and events of interest:

IEDs were defined as spikes, sharp waves, temporal intermittent rhythmic delta activity, and generalized spike and wave discharges, IEDs were classified as multifocal if they appeared within both cerebral hemispheres independently over at least 3 head regions **[9].**

Events of interest were defined as any clinical or electrographic event that occurred during the EEG that were potentially of diagnostic value. When identified, the data were retrieved about the event through the formal EEG report.

Interictal Epileptiform discharge (IEDs) was classified into early IEDs if occurring within the first 20-minutes of EEG record and late IEDs if they occurred only after 20 minutes **[10].**

Statistical Analysis:

Statistical analysis was done by SPSS v27 (IBM©, Armonk, NY, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Unpaired student t-test, Mann Whitney-test (U), Chi-square test or Fisher's exact test and multiple regression were used.

RESULTS

Table (1) demonstrated that most of patients (61.1%) had focal epilepsy, followed by tonic, clonic (22.2%). Regarding the postictal state,

sleepiness was the most frequent sequale representing (30.6%). Among the studied patients, only (19.4%) patients had a history of status epilepticus. NHS3 scoring ranged from 4 – 22 with a mean of 14.07 ± 5.78. As shown in Table (2) focal epileptiform activity were detected in (27.78%) patients, focal epileptiform waves with generalized slowing were detected in (13.89%) patients, focal sharp waves with secondary generalization were detected in (27.7%) patients, generalized epileptiform waves were detected in (13.89%) patients and normal long monitoring EEG was found in (16.67%) patients. The overall latency duration ranged from 5 – 60 minutes. With a mean of 29.63 ± 18.42 minutes. 11 (30.1%) patients had early IED < 20 min, 19 (52.8%) patients had late IED > 20 min. A non- significant difference between adult and children epileptic patients regarding EEG findings, early and late IED and NHS3 scoring was found Table(3).Regarding factors related to the presence of IED, patients with IED had an earlier onset of epilepsy (22.13 ± 12.8 vs. 42.33 ± 4.2, P= 0.01) and longer duration of epilepsy (13.40 ± 4.6 vs. 8.50 ± 3.9, P= 0.027). Age and frequency of epilepsy were insignificantly different between patients with presence or absence of IED as shown in table (4). On multiple regression analysis, age of onset of epilepsy, duration of epilepsy and NHS3 scoring were significant predictors of latency of IED (P<0.05) whereas other variables were insignificant predictors as shown in table (5).

Table (1): Characteristic of epileptic attack in the studied patients

		Total (n=36)
Types of epilepsy	Tonic	2 (5.6%)
	Tonic, clonic	8 (22.2%)
	Focal	22 (61.1%)
	Atonic	2 (5.6%)
	Myoclonic	1 (2.7%)
	Absence	1 (2.7%)
Postictal state	Amnesia, Todd's paralysis	4 (11.11%)
	Confusion, amnesia, vomiting	3 (8.33%)
	Headache, confusion, amnesia	4 (11.11%)
	Sleepiness	11 (30.6%)
	Sleepiness, headache, confusion	4 (11.1%)
	NAD	10 (27.7%)
History of status		7 (19.4%)
NHS3 scoring	Mean ± SD	14.07 ± 5.78
	Range	4 - 22
	Median (IQR)	13 (10- 18.2)

NAD: no abnormality detected, NHS3: national hospital severity scale.

Table (2): Long monitoring EEG findings and IED of the studied patients during one hour

		Total (n=36)	
EEG findings			
Focal epileptiform activity		10 (27.78%)	
Focal epileptiform waves with generalized slowing		5 (13.89%)	
Focal sharp waves with secondary generalization		10 (27.7%)	
Generalized epileptiform waves		5 (13.89%)	
Normal long monitoring EEG		6 (16.67%)	
Overall latency duration (min)		**Mean ± SD**	29.63 ± 18.42
		Range	5 - 60
		Median (IQR)	26.5 (15-39.5)
IED	**No**		6 (16.7%)
	Early	**< 20 min**	11 (30.1%)
	Late	**> 20 min**	19 (52.8%)

EEG: electroencephalogram, IED: interictalepileptiform discharges.

Table (3): Prolonged EEG findings among the patients regarding the age

			Adult (n=24)	Children (n=12)	Test of sig	P value
EEG findings						
Focal epileptiform activity			7 (29.17%)	3 (12.5%)	0.525	0.999
Focal epileptiform waves with generalized slow			3 (12.5%)	2 (8.33%)		
Focal sharp waves with secondary generalization			7 (16.6%)	3 (50%)		
Generalized epileptiform waves			3 (12.5%)	2 (8.33%)		
Normal long monitoring EEG			4 (16.67%)	2 (8.33%)		
IED	**No IED**		4 (16.7%)	2 (16.7%)	-	-
	Early	**< 20 min**	7 (29.2%)	4 (33.3%)	Fisher	0.63
	Late	**> 20 min**	13 (54.2%)	6 (50%)	Fisher	0.68
NHS3 scoring		**Mean ± SD**	13.77 ± 5.93	14.68 ± 5.66	U=128.0	0.602
		Range	4 - 22	4 - 22		
		Median (IQR)	12.5 (10-18.2)	14.5 (10.9-18.2)		

EEG: electroencephalogram, IED: interictalepileptiform discharges, NHS3: national hospital severity scale

Table (4): Risk factors for the presence of interictalepileptiform discharges (IED) in long-term EEG.

	IED present (n=27)	IED absent (n=9)	P value
Age (years)	26.77 ± 10.3	28.33 ± 15.3	0.819
Age of onset of epilepsy (years)	22.13 ± 12.8	42.33 ± 4.2	**0.001***
Duration of epilepsy (years)	13.40 ± 4.6	8.50 ± 3.9	**0.027***
Frequency of epilepsy	15.10 ± 3.1	15.8 ± 3.4	0.971

IED: Interictalepileptiform discharges, EEG: electroencephalogram,

Table (5): Multiple regression analysis for factors predicting IED latency

	Coefficient	SE	t	P	$r_{partial}$	$r_{semipartial}$
Age (years)	-0.010	0.005	-1.882	0.070	-0.330	0.203
Age of onset of epilepsy (years)	-0.012	0.003	-3.799	**0.001***	-0.577	0.409
Duration of epilepsy (years)	0.049	0.012	4.208	**<0.001***	0.616	0.453
Frequency of epilepsy	0.000	0.001	0.028	0.978	0.005	0.003
NHS3 scoring	0.017	0.007	2.369	**0.025***	0.403	0.255

SE: standard error, EEG: electroencephalograph, NHS3: national hospital severity scale, *: statistically significant as P value <0.05

DISCUSSION

A cross-sectional observational study was conducted with 36 individuals of idiopathic epilepsy were included as a comprehensive sample with their age ranged from 7 – 46 years with a mean of 27.03 ± 11.09 years, the age of onset of epilepsy ranged from 6 – 45 years with a mean of 21.67 ± 13.24 years.

It is known that age of onset of idiopathic epilepsy is variable across different studies. In agreement with our results, **Arteaga-Rodríguez et al. [11]** found that primary epilepsy was more common in age <20 years. Also, **Marini et al. [12] a**nnounced that 28% of patients with primary epilepsy were identified as having adult-onset IGE with an onset age above 20 years.

On the other hand **Asadi-Pooya et al. [13]** reported a bimodal peak age of onset with a modest peak at age 2 and a significant peak at age 15, and that the age of seizure beginning was 12.4 6.9 years. The observed differences may be biological (such as genetic variances across various groups) or technical (such as changes in definitions applied and cut off ages used).

Upon analysis of our results, we found that idiopathic epilepsy is a bit more common in females (52.78%) versus (47.22%) in males. This results were also reported by **Burkholder et al. [7]** who found that 53% of their epileptic patients were females. **also ,Werhahn et al. [14]** registered that females represent a percentage of 55.2% of their epileptic patients .Additionally, **Liu et al. [15]** investigated a total of 255 patients. They were distributed as 38% male and 62% were female. The gender differences in seizure susceptibility could be attributed to chemical, genetic factors, Neuroplasticity in their receptor signaling systems, variations in

neurosteroids, and acquired epileptogenesis **[16].**

In the current study, most common type of seizures among the studied populations was focal seizures (61.1%), followed by tonic, clonic seizures (22.2%)**.**

In agreement with our study, **Mathew et al. [17]** found that 42.4 % of patients had focal seizures that was the most common type of seizures: 15.5% focal to bilateral tonic-clonic, 27.3% generalized tonic-clonic, and 15% focal motor seizures.

On the other hand,**Jawaid et al. [18]** found that Following localized to bilateral tonic-clonic seizures and focal seizures, generalized onset tonic-clonic seizures were the most prevalent overall and were present in 73% of the study sample. Also,**Aziz et al. [19]** reported that focal to bilateral tonic-clonic seizures were the second most frequent group of seizures after generalized onset tonic-clonic seizures. Absence seizures were the least frequent type of seizures (1%).

Regarding the EEG findings, 83.33% of patients had abnormal EEG findings and the most frequent abnormality was focal epileptiform activity followed by, focal sharp waves with secondary generalization, generalized epileptiform waves and lastly focal epileptiform waves with generalized slow. In same line **Owolabi et al. [20]** Considered that the predominant morphology of epileptiform discharges was sharp and slow waves (70.9%)followed by spike and slow(11.02%) polyspikes was detected in(5.2%). Disorganized background and/or asymmetric background were found in (8%) of patients. Also, **Ali et al. [21]** performed EEG on a total of 126 patients; 53.1% had abnormal findings. The most common abnormal EEG findings were sharp and slow waves (47.8%), followed by sharp waves (21%), and slow posterior dominant rhythm (15%).

On the other hand **Burkholder et al. [7]** found in their large study that only 23.6 % had abnormal EEG during the recording time but they did not demonstrate these abnormalities.

Regarding the timing of appearance of IED, it ranged from 5-60 minutes with a mean of 29.63+-18.42 minutes. We recorded that 52% of our patients had late IED>20minutes, while 30.1% of our patients had early IED<20minutes. While, **Burkholder et al. [7]** in a large prospective study of 1.803 patients found only 4.5% out of 23.6% of patients had late IED , but they still advice long term EEG monitoring as increasing the duration of outpatient EEG from 30 to 45 minutes or longer increases the relative yield of new IEDs by approximately 20%. Moreover, these different findings could be attributed to their study population as they included all patients performing EEG for diagnosis of spells and not only epileptics.

This is also supported by one study evaluating IED latency in 171 extended EEG recordings lasting up to 6 hours. In that study, 71% of IED-containing EEGs had the first discharge within 30 minutes, and another 22% of patients between 30 and 90 minutes **[22].** In the same context**, Werhahn et al. [14]** observed that epileptic seizures occurred in 66.6% of all patients with a median latency of 21.6 h.

Those with IED developed epilepsy for a greater period of time and at an earlier age of onset when compared to those without IED. Age and epilepsy frequency were insignificantly different between patients with presence or absence of IED. On the basis of multiple regression analysis, the age of epilepsy onset, duration of epilepsy and NHS3 scoring were significant predictors of latency ($P<0.05$) whereas other variables were reported to be insignificant predictors.

This came similarly with **Werhahn al. [14]** who analyzed the factors associated with IED presence. IEDs started sooner in young patients (20.6 ± 14.0 years vs. 28.3 ± 18.8 years) and longer duration of epilepsy (17.9 ± 14.0 years vs. 11.3 ± 11.3 years).

Owolabi et al. [20] had analyzed the statistical role of different factors in predicting the presence of IEDs and found that longer duration of epilepsy together with pediatric IEDs and other variables, such as female gender, uncontrolled seizures, and

seizure frequency, were linked with age of onset.

In general, IEDs are more common in people with early onset and longer-lasting epilepsy, for example, among other influences **[23].**

Baker et al. [24] demonstrated that epilepsy severity may be used to predict abnormal EEG, but they did it using the updated Liverpool Seizure Severity Scale. compared with NHS3 scale that we used.

On the other hand, **Desai et al. [25]** discovered no correlation between the presence of an IED on an EEG and various clinical seizure data in patients with chronic epilepsy (43% of whom had no seizures and 25% of whom had less than 10 seizures in the six months prior to the EEG recording).

CONCLUSIONS

Our findings indicated that the age of epilepsy onset, duration of epilepsy and NHS3 scoring were significant predictors of IED latency.

Conflict of Interest: None

Financial Disclosures: None

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