

RESEARCH ARTICLE



Study of electroencephalography in people with generalized epilepsy in a Saudi population

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ABSTRACT

Background: Electroencephalography (EEG) remains a vital tool in the diagnostic evaluation of patients with epilepsy (GE), however, there is scarcity of information on the yield and potential clinical variables that are associated with EEG abnormalities in people with GE.

Objective: The study aimed to evaluate the yield and pattern of EEG abnormalities in patients with GE with the view to determining factors that are independently associated with abnormal EEG in them.

Methods: We characterized EEG features and evaluated associated factors in a sample of people with GE in a Saudi population. Standard definition of interictal epileptiform discharges was used.

Results: A total of 1105 (77%) out of 1436 GE patients had EEG. Five hundred and ninety-five (53.85%) patients had abnormal EEG. Factors associated with EEG abnormalities before adjustment for confounders were age, gender, duration of epilepsy, and seizure frequency. However, only frequency of seizure ($P = 0.0018$), gender ($P < 0.0001$), and age ($P < 0.0001$) were independently associated with EEG abnormalities.

Conclusion: The study showed a modest yield (54%) of abnormal EEG in the cohort of patients with GE. Frequency of seizure, age, and gender, independently predicted the presence of EEG abnormality in people living with GE.

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1. Introduction

In Saudi Arabia, about seven out of every thousand citizens live with epilepsy [1]. As common as it is, this chronic neurological disorder is often accompanied by a remarkable socioeconomic burden to the healthcare system, the people living with epilepsy (PWE), and their care givers [1–3]. Over 60% of cases of epilepsy in Saudi Arabia had no clear etiology [1] but more than half of those with identifiable etiology are static encephalopathy whereas cerebral trauma and pediatric intracranial infection were also common etiologies in Saudi communities [1,4]. Generalized seizure semiology is more frequent than partial seizure [4]. Like in many developing countries, the pattern of neurophysiological features and their association with clinical factors have not been fully studied.

Although the diagnosis of epilepsy is largely clinical, electroencephalography (EEG) is a well-established tool in the evaluation of patients with epilepsy. It is of value in distinguishing epileptic seizures from paroxysmal nonepileptic events, localizing seizure origin, and classifying epilepsy and epileptic syndromes [5]. Moreover, certain electroclinical syndromes and epileptogenic zones require EEG for proper identification [6–8].

Regardless of its role as a guide in the selection and discontinuation of antiepileptic drugs (AED), EEG is of value in prognostication of epilepsy. Despite the remarkable advances in the area of neurodiagnostic, however, EEG maintains its relevance in the management of epilepsy.

In the literature, the proportion of abnormal EEGs in a given population of people with epilepsy depends on the type of epileptic syndromes, the methodology of the study, the type of population studied, and the size of the sample of population studied [9]. The prevalence of EEG in patients with epilepsy ranges between 25% and 56% [9–12]. EEG changes may appear infrequently and may not appear during the relatively brief period of routine EEG recording. Nonetheless, the diagnostic yield of EEG could be enhanced by ramping up the recording time, applying activation procedures such as hyperventilation, photic stimulation, and sleep deprivation [13].

Despite the invaluable importance of EEG in the diagnostic workup and management of PWE, there is paucity of data on the utility, yield, and determinants of abnormal routine EEG.

We, therefore, set out to evaluate the yield, pattern, and also determine the factors that are associated with EEG abnormality.

2. Methods

2.1. Study site and patient population

The EEG procedures were conducted at the King Abdullah Hospital, Bisha, Saudi Arabia. King Abdullah Hospital, Bisha is the first reference hospital in the region, serving the residents of Bisha, Bilqarn, Raniah, and Tathlith[14]. It has a 365-bed capacity and provides all medical specialties in and out-patient services[14]. The hospital has electro diagnostic centers with electromyography and EEG machines. Because the laboratory is a reference laboratory for the region, it receives patients, children, and adult alike, for EEG and EMG from Bisha and all the neighboring towns. The center has three neurophysiology technologists and five neurologists that interpret EEG. The EEGs were from patients that were predominantly Saudis from the region and fewer non-Saudis from the Middle East and North Africa.

We included in the study only the first EEG of the patients with clinical diagnosis of generalized epilepsy (GE) while patients with the other types of epilepsy and those whose seizure types were uncertain were excluded from the study.

2.2. Procedure and definition of terms

Routine, scalp, and interictal EEG recording was performed on all the patients following a detailed explanation on the procedure. Surface electrodes were applied with collodion, according to the 10–20 system with linked mandibular references. The EEG was conducted in the wakeful and alert states in most cases and also with sedation using chloral hydrate in the case of uncooperative children. Hyperventilation and photic stimulation activation procedures were carried out on patients that were suitable for them. Hyperventilation and photic stimulation lasted for 5 minutes each. We used common average referential, longitudinal, and transverse bipolar montages for the procedure. EEG recording was filtered with 1 Hz high-pass, 30 Hz low-pass, and 60 Hz notch filters at a paper speed of 30 mm/s.

During the recordings, the patients were instructed to remain relaxed but alert. In eye-open recordings, the patients were instructed to fixate on a particular point in order to inhibit ocular movements. The behavior of the patient during the EEG recording was noted. The EEG recording was performed for 30 min. The EEG procedure was carried out using 16-channel digital recording Natus EEG machines. The EEGs were reported by four neurologists, with adequate skills of EEG interpretation, two of whom were dedicated to the study and inter-rater agreement was determined. The reporting protocol adopted in the study was based on the standard definitions of the EEG features commonly

assessed in clinical practice[15]. The report included the general background activity which was classified as normal or abnormal based on the presence of excessive generalized slow activity. Non-epileptiform focal features including focal theta and slow wave activity as well as significant background interhemispheric asymmetries were recorded. Interictal epileptiform discharges were defined as sharp waves that were clearly distinguished from the background activity, spike or polyspike discharges, spike and wave complexes, sharp and wave patterns. Benign epileptiform transients of sleep, 6/s spike and wave, 14 and 6/s positive spikes, psychomotor variant, and wicket spikes were considered normal variants[16]. We classified Interictal epileptiform discharges as generalized if they were diffuse, i.e., involved the entire brain, focal if they were localized, i.e., limited to a region of the brain, and multifocal if three or more discrete brain regions were involved. Abnormal findings during photosensitivity such as photo paroxysmal responses as well as IED and asymmetric slowing during hyperventilation were noted. In the current study abnormal background, inter-ictal epileptiform discharges (IED) during rest EEG or activation procedures were categorized as abnormal. Standard definition of inter-ictal epileptiform activity (IEA) was adopted in the study [16,17].

3. Statistical analysis

Statistical analysis was performed using STATA version 12 (Stata Corp, Texas, USA). Descriptive statistics including means with standard deviation or median with interquartile range for continuous variables and proportions for categorical variables were computed. Chi-square or Fisher's exact test, in case of infrequent measures, was used for comparison of categorical variables such as gender, status of findings (normal or abnormal), and age category (children or adults) while the differences in means of parametric and Mann–Whitney U-test (nonparametric) for numerical variables such as age, and frequency of seizure were assessed using student *t*-tests. We estimated adjusted odds ratio and 95% confidence interval (CI) for the association of different demographic and seizure-related variables with EEG end point (normal or abnormal). Associations reaching a *p*-value of 0.05 were entered into a multivariable model. We used multivariable-adjusted unconditional logistic regressions and the covariates were adjusted for each independent (regression) variable to find independent predictors of EEG abnormality with their adjusted odds ratio (aOR) and 95%CI. All statistical tests of hypotheses were two-sided at 5% significance level.

4. Ethical approval

Ethical approval for this study was granted by the University of Bisha Ethical Review Committee and informed consent was obtained from the patients.

5. Results

5.1. Demographic and seizure characteristics

A total of 1105 (77%) out of 1436 patients with GE comprising 674 (61%) males and 431 (39%) females had EEG during the study period. Their age ranged between 2.4 months and 78 years with a median age of 14 years and an interquartile range (ir) of 25 years. The median age of males and females were 18 (ir = 26) and 10 (ir = 22) years, respectively. Table 1 summarizes the age and sex distribution of the study participants. The patients comprise 1051 (95%) Saudis, 16 (1.5%) Egyptians, 16 (1.5%) Sudanese, 6(0.5%) Pakistani, 6 (0.5%) Yemenis, 7 (0.7%) Bangladeshi, and 3 (0.3%) Indians.

There were 926 (74.8%) generalized tonic clonic seizure, 20 (1.8%) generalized tonic 27 (2.4%) seizure, 45 (4.1%) Absence seizure, 10 (0.9%) Myoclonic seizure, 2 (0.2%), atonic seizures, seizure type was unspecified in 175 (15.8%) cases (Table 2). About 38% of the patients were on antiepileptic drugs before the EEG procedure.

5.2. The yield and pattern of EEG abnormalities

Five hundred and ninety-five (53.85%) patients had abnormal EEG, while EEG was normal in 510 (46.15%) patients. However, 557 (50.3%) patients had IEA. Table 3 shows the distribution of EEG abnormalities in the study. Hyperventilation activated epileptiform EEG recording was observed in 20% of those that had the procedure, while 3% of the patients who had photic stimulation recorded photo-induced EEG abnormalities.

5.3. Factors associated with EEG abnormalities

Regarding the factors that are associated with EEG abnormalities, before adjustment for confounders, age, gender, duration of epilepsy, seizure frequency were found to be associated with EEG abnormalities (Table 4). On adjustment for confounders, however, frequency of seizure, gender, and age were independent predictors of EEG abnormalities.

6. Discussion

This study suggests that the yield of EEG in generalized epilepsy is modest. This finding is in agreement with reports from studies elsewhere [11,15]. Nonetheless, the yield of EEG in generalized epilepsy

Table 1. Distribution of age by gender.

Age category (yrs)	Sex		Total
	Male	Female	
≤10	274	214	488
11–20	69	67	136
21–30	146	66	212
31–40	6	18	24
41–50	60	50	110
51–60	19	6	25
61–70	46	0	46
≥70	54	10	64
Total	674	431	1105

Table 2. Distribution of seizure types.

Seizure types (clinical)	Frequency	Percentage
Generalized tonic clonic	826	74.8
Generalized tonic	20	1.8
Generalized clonic	27	2.4
Absence Seizure	45	4.1
Myoclonic	10	0.9
Atonic	2	0.2
Unspecified	175	15.8
Total	1105	100

could be as low as 18% and as high as 81% [12,17–19]. The yield of EEG in PWE was investigated in a community setting of Rochester, Minnesota using the resources of the Rochester Epidemiology Project. The study showed that the cumulative yield of epileptiform abnormalities was 53% after the first EEG procedure[20].

It is noteworthy, however, that the results obtained in our study were from the first EEG ever undertaken by the patients in the study. There is a high possibility that the EEG procedure could have yielded a higher figure if serially undertaken in the study population. Conceivably, the yield of EEG is enhanced by multiple EEGs[21]. In another study, the prevalence of EEG abnormality was as high as 90% among PWE on fourth EEG[21]. In a review of 1201 multiple EEG records from 429 adult patients, Salinsky *et al.* reported that 50% of the patients had IEA on first EEG, 84% on third EEG, and 92% on fourth EEG[21]. A similar trend was shown in another study that involved 308 PWE in which multiple EEGs were conducted. The study found abnormal EEG in 56% of the patients on first EEG examination and an additional 26% on subsequent EEGs[22].

The prevalence of interictal epileptiform activities observed in our study conforms with the classical EEG findings in generalized epilepsy. Such findings are often bisynchronous, symmetric, and generalized spike-wave pattern. However, focal, irregular epileptiform discharges are infrequently seen[23]. The other EEG features seen in the current study included polyspike, polyspike-wave discharges, and occipital intermittent rhythmic delta activity.

The reason behind the generation of epileptic discharges on scalp EEG is not fully known. Nevertheless,

Table 3. Distribution of electroencephalography abnormalities across age groups.

Age group	BW (abnormal)	FSW	GSW	3 HZ	NSSW	FSIW	BS	NSF	HYPS	Total
≤10	42	01	255	29	99	12	8	17	29	492
11–20	13	06	30	2	18	1	2	12	0	84
21–30	2	40	135	0	135	13	0	06	0	331
31–40	1	01	08	0	17	1	0	02	0	30
41–50	2	02	50	0	30	1	0	04	0	89
51–60	0	01	06	0	12	0	0	10	0	29
61–70	0	0	33	0	21	1	8	08	0	71
≥70	8	01	24	0	10	2	0	06	0	51
Total	68	52	541	31	342	31	18	65	29	1177

*Some of the patients had more than one abnormality. BW = Background wave, FSW = Focal spike/sharp and wave, GSW = Generalized spike/sharp wave, NSSW = Nonspecific slow wave, FSLW = Focal slow wave, BS = Burst suppression, NSF = Nonspecific findings

Table 4. Relationship between common variables and abnormal EEG (unadjusted) and independent predictors of abnormal EEG (adjusted).

Variable	Frequency (Abnormal EEG/Total)	Unadjusted		Adjusted	
		Odds ratio (95%CI)	P	Odds ratio (95%CI)	P
Age	18/10 ^m	-----	0.0136*	1.2 (1.087–1.208)	0.0001*
Age category					
Adult	308/525	1 reference			
Pediatric	287/590	1.5 (1.13–1.85)	0.0025	0.2(0.122–0.356)	0.0001*
Family history of epilepsy					
Yes	24/47	1 reference			
No	571/1058	0.9(0.47–1.67)	0.7655	0.4(0.192–0.871)	0.0200*
Sex					
Male	298/674	1reference			
Female	297/431	0.4(0.27–0.47)	0.00001*	0.2(0.148–0.285)	0.0001*
Duration of epilepsy					
< 6 months	284/466	1 reference			
6–12 months	265/542	1.6(1.25–2.11)	0.0001*	1.0(0.809–1.293)	0.8550
>12 months	46/97	1.7 (1.09–2.75)	0.0139*		
Frequency of seizure					
Once/day	43/142	1 reference			
Once/week	261/592	0.6(0.36–0.83)	0.0027*	0.3(0.205–0.319)	0.0001*
Once/month	183/259	0.2(0.11–0.29)	0.00001*		
≥ once/3 month	108/112	0.02(0.004–0.047)	0.00001*		

m = median age in abnormal EEG and normal EEG category, *Statistically significant. EEG = Electroencephalography, OR = Odds ratio, CI = Confidence interval

epileptiform discharges that are bilaterally synchronous and symmetric spikes would indicate a deep-seated generator of these discharges in generalized epilepsy. This centrencephalic epilepsy was first proposed by Morison and Dempsey[24], not disregarding the other studies that demonstrated the role of cerebral cortex in the generation of epileptic activity in generalized epilepsy[25].

It is clearly desirable to find effective ways of predicting the presence of EEG abnormality. To this end, demographic and seizure characteristic factors with a potential of predicting abnormal EEG in PWE on first EEG were explored in our study. Age of the patient with epilepsy was found to be an independent predictor of the presence of EEG abnormality in our study. This finding conforms with reports from studies elsewhere that showed an age-dependent effect of a linear trend for the detection of higher rates of epileptiform patterns with increasing age [23,26].

In this study, frequency of seizure predicts the presence of seizure abnormality in generalized seizure. The association between frequency of seizure

and EEG abnormality found in our study further corroborates the concept that seizure begets seizure [27]. The mechanism underlying this concept is not completely clear, however, there are suggestions that seizures alter the brain functions in such a way that each seizure increases the risk for further EEG abnormality and seizures and hence abnormal EEG [28]. Interestingly, the duration of epilepsy from the first seizure that showed a significant association with the occurrence of EEG abnormality initially proved not to be so on adjustment for confounders. This finding offers for consideration the possibility that what determines the presence of EEG abnormality in epilepsy is not the duration of epilepsy but how frequently seizures occur.

7. Limitations and strength of the study

Our study is not without limitations. First, our data was based on collection of a single routine EEG in people with generalized epilepsy. Thus, our finding is most applicable to first EEGs as serial EEG might

have provided a higher diagnostic yield. Second, for logistic reasons, the other activation methods such as sleep and sleep deprivation that could have resulted in a better yield were not done in the current study considering that an EEG obtained after a period of sleep deprivation improves detection of epileptiform abnormalities[29].

Nonetheless, the large sample size selected in our study provides sufficient power to measure associations between demographic and seizure characteristic factors and the presence of EEG abnormality. Furthermore, the use of a standard protocol for collection as well as interpretation of EEGs by more than one experienced neurologists are arguably a major strength of the current study.

When a physician considers ordering EEG as a diagnostic support for patients who might have generalized epilepsy, there is room for expectation as regards the yield and predictions of positive findings. The current study provides one good piece of information in this respect.

8. Conclusion

Electroencephalography abnormalities are common in generalized epilepsy in Saudi population. Abnormalities on first EEG are independently associated with frequency of seizure, gender, and age. The utility of EEG in supporting diagnosis of epilepsy and in discriminating between epileptic syndromes cannot be overemphasized. Future studies should explore these EEG findings along with other clinical and neuroimaging characteristics in order to improve the understanding as well as management of epilepsy in Saudi Arabia.

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Author's contribution

Conceptions and designs: OLF, RAA. Manuscript drafting: All authors. Manuscript Revision: All authors. Approval of the final version of the manuscript: All authors.

Disclosure statement

No potential conflict of interest was reported by the authors.

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