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Original Article

Electroencephalography findings in childhood epilepsy in a Saudi population: Yield, pattern and determinants of abnormality

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المخلص

أهداف البحث: صممت الدراسة لتقييم النتائج والنمط والعوامل التي ترتبط بشكل مستقل بتشوهات التخطيط الدماغية في صرع الطفولة لدى السعوديين.

طرق البحث: وصفنا السمات الأولى لمخطط كهربية الدماغ وقيمنا العوامل المرتبطة بها في عينة من الأطفال المصابين بالصرع في المجتمع السعودي. اعتمد الاتحاد الدولي لجمعيات تخطيط كهربية الدماغ والفيزيولوجيا العصبية السريرية تعريف التصريفات الصرعية بين النشبات (نشاط الصرع بين النشبات) في الدراسة.

النتائج: كان 756 مريضاً من الأطفال منهم 427 (56.5%) من الذكور و329 (43.5%) من الإناث مع التشخيص السريري للصرع لديهم تخطيط كهربية الدماغ. سريريا، النوبة كانت معممة في 619 (81.9%) مريضاً وبؤرية في 137 (18.1%) مريضاً. عانى 397 (52.51%) من شذوذ في مخطط كهربية الدماغ، بينما كان مخطط كهربية الدماغ طبيعياً عند 359 (47.49%) مريضاً. كان تواتر النوبة والجنس ووجود تاريخ عائلي للصرع والعمر مميزات مستقلة لوجود تشوهات تخطيط كهربية الدماغ.

الاستنتاجات: كشفت الدراسة أن نتائج 52% من مخطط كهربية الدماغ غير طبيعي لدى الأطفال المصابين بالصرع. وكان العمر والجنس والتاريخ العائلي وتواتر النوبات مميزات مستقلة لوجود شذوذ في مخطط كهربية الدماغ في صرع الطفولة.

الكلمات المفتاحية: تخطيط كهربية الدماغ؛ أطفال؛ صرع؛ نتائج؛ مميزات

Abstract

Objective: The study was designed to evaluate the yield, pattern, and factors that are independently associated with electroencephalography (EEG) abnormalities in childhood epilepsy in a Saudi population.

Methods: We characterised the features of the first EEG and evaluated the associated factors in children with epilepsy in a Saudi population. The features of interictal epileptiform discharges (interictal epileptiform activity (IEA)) adopted by the International Federation of Societies for Electroencephalography and Clinical Neurophysiology were used in the study.

Result: A total of 756 paediatric patients, comprised of 427 men (56.5%) and 329 women (43.5%) with a clinical diagnosis of epilepsy, underwent EEG. Clinically, seizure was generalised in 619 (81.9%) patients and focal in 137 (18.1%). Among the patients, 397 (52.51%) had an abnormal EEG, while EEG was normal in 359 (47.49%) patients. Seizure frequency, gender, family history of epilepsy, and age were independent predictors of the presence of EEG abnormalities.

Conclusion: This study revealed a yield of 52% abnormal EEG findings in children with epilepsy. Age, gender, family history, and seizure frequency were independent predictors of the presence of EEG abnormalities in childhood epilepsy.

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Keywords: Children; Electroencephalography; Epilepsy; Predictors; Yield

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Introduction

Epilepsy is a common neurological disorder in children, and it affects between 0.5% and 1% of children.¹ In the KSA, the prevalence rate for active epilepsy was 6.54 per thousand in the regional population.² It is often associated with a considerable socioeconomic burden to the healthcare system and the people living with epilepsy (PWE), as well as their relations and caregivers.^{2–4} The cause of the disorder is unknown² in six out of ten cases of epilepsy in KSA.² In Saudi communities, the most common aetiologies include static encephalopathy, cerebral trauma, and paediatric intracranial infection.^{2,5}

A flawless diagnosis of epilepsy requires the differentiation of epileptic seizures from provoked seizures and other paroxysmal events. Given that childhood epilepsy has a wide spectrum of clinical manifestations and that several other conditions may masquerade as epilepsy, the diagnostic process remains dauntingly, with a high risk of misdiagnosis in children.^{6–8}

Electroencephalogram (EEG) remains a veritable tool in the diagnostic workup of seizures and childhood epileptic syndromes; hence, it has an invaluable place in the proper management of a child with epilepsy.⁹ Aside from its diagnostic role, it is important in decision making regarding the discontinuation of treatment and drug monitoring. EEG may also be abnormal in a normal child and normal in a child with clinically diagnosed epilepsy.⁹ However, the diagnostic yield of EEG could be improved by increasing the recording time and applying activation procedures, such as hyperventilation, photic stimulation, and sleep deprivation, as well as by repeating the procedure.¹⁰

Though the diagnosis of epilepsy or epileptic syndrome is largely a clinical one, EEG has a significant role in substantiating the clinical suspicion of epilepsy, the classification of seizures, and the management of childhood epilepsy.⁹

Despite the invaluable role of EEG in the diagnostic workup and management of childhood epilepsy, there is a scarcity of information on the utility, the profile of EEG abnormality, and the determinants of abnormal routine EEGs in children with epilepsy in KSA.

We therefore set out to evaluate the yield, pattern, and influence of sociodemographic and seizure characteristic factors on EEG abnormality among the paediatric age group in a Saudi population.

Materials and Methods

Study site and patient population

The EEG procedures were carried out at the King Abdullah Hospital, Bisha, KSA. The King Abdullah Hospital is the region's first reference hospital, serving the residents of Bisha, Bilqarn, Raniah and Tathlith.¹¹ It has a 365-bed capacity and provides all medical specialties, including paediatric in- and out-patient services.¹¹ The hospital has electrodiagnostic centres equipped with electromyography and EEG machines. Given that the laboratory is the region's only reference laboratory, it receives patients for EEG and EMG from Bisha and all the neighbouring towns. The centre has three neurophysiology technologists and five neurologists that interpret EEGs. The patients included in this study are aged less than 18 years with a clinical diagnosis of epilepsy; older patients and those with other indications, as well as those with unconfirmed seizure types, were excluded from the study. Only each patient's first EEG undergone in our hospital was considered for analysis.

Procedure and definition of terms

Routine, scalp, and interictal EEG recordings were performed on all the patients, following a detailed explanation of the procedure. Cap 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 recordings were filtered with 1,000 Hz high-pass, 30 Hz low-pass, and 60 Hz notch filters at a paper speed of 30 mm/s. The minimum technical standards for paediatric EEG were followed.¹²

Patient behaviour during EEG recording was noted. The routine EEG recording was performed for 30 minutes. The EEGs were carried out using 16-channel digital recording Natus EEG machines. The EEGs were reported by four trained neurologists with adequate skills of EEG interpretation, two of whom were dedicated to the study. 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.¹³ The report included general background activity, which was classified as normal or abnormal based on the presence of an excess of generalised slow activity. Non-epileptiform focal features, including focal theta and slow-wave activity, as well as significant background interhemispheric asymmetries, were recorded.

This study adopted the definition of interictal epileptiform discharges (IEDs) as sharp waves that can be clearly distinguished from background activity. Spike or polyspike discharges, spike and wave complexes, and sharp and wave patterns were considered abnormal. 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.¹⁴ IEDs were classified as generalised if they were diffuse, i.e. if they involved the entire brain; focal if they were localised i.e. limited to a single region of the brain; and multifocal if three or more discrete brain regions were involved.

Abnormal findings during photic stimulation, such as photo paroxysmal responses, as well as IEDs and asymmetric slowing during hyperventilation, were noted. In the current study, abnormal background and IEDs during rest EEG or activation procedures were categorised as abnormal. The study adopted the International Federation of Societies for Electroencephalography and Clinical Neurophysiology's definition of inter-ictal epileptiform activity (IEA).¹⁵ Age was categorised into neonate infant, toddler, pre-schooler, school age, and adolescent. Seizure frequency was classified into less than 6 months, 6–12 months, and greater than 6 months. Seizure semiology was classified into focal and generalised seizure types.

Statistical analysis

Statistical analyses and graphics were produced using STATA version 12 (Stata Corp, Texas, USA). Descriptive statistics, including means with standard deviation or medians with an interquartile range for continuous variables and proportions for categorical variables, were computed. For infrequent measures, either a Chi-squared or a Fisher's exact test was used to compare categorical variables, such as gender, status of findings (normal or abnormal), and age category (children or adults), while comparison was done using students' t-tests for parametric numerical variables and the Mann–Whitney U (Ranksum) test for non-parametric numerical variables. Inter-rater reliability, kappa, was determined for the independently interpreted EEGs.

We estimated the crude odds ratio (cOR) and a 95% confidence interval (CI) for the association of different demographic and seizure-related variables, such as seizure frequency, family history of epilepsy, duration of epilepsy, and seizure types with an 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 regression, and the covariates were adjusted for each independent (regression) variable to find independent predictors of EEG abnormality with their adjusted odds ratio (aOR) and a 95% CI. All statistical tests of hypotheses were two-sided at a 5% significance level.

Results

Demographic and seizure characteristics

A total of 756 paediatric patients, comprised of 427 males (56.5%) and 329 females (43.5%) with a clinical diagnosis of epilepsy, had an EEG. Their ages ranged between 2 weeks and 17 years, with a median age of 4 years and an interquartile range (*ir*) of 7.5 years. The median age of males and females were 4 (*ir* = 6.8) and 4 (*ir* = 7.3), respectively. Table 1 summarises the patients' age and sex distribution. Among the patients, there were 733 Saudis (97%), 4 Egyptians (0.5%), 4 Sudanese (0.5%), 3 Pakistani (0.4%), 5 Yemenis (0.7%), 4 Bangladeshi (0.5%), 2 Indians (0.3%), and 1 other (0.1%).

Clinically, seizure was generalised in 619 patients (81.9%) and focal in 137 patients (18.1%). Of those with generalised epileptic seizures, the diagnosis of distinct childhood epileptic syndrome was made in 87 patients (14.1%), including juvenile myoclonic epilepsy (46), childhood absence epilepsy (31), Lennox Gastaut syndrome (8), and West syndrome (2). About 42% of the patients were on antiepileptic drugs at the time of the procedure.

Prevalence and pattern of EEG abnormalities

Among the patients, 397 (52.51%) had an abnormal EEG, while EEG was normal in 359 (47.49%). IEDs were seen in 376 patients (49.7%). The inter-rater reliability of the EEG interpreters, kappa, was 8.6. Table 2 shows the distribution of EEG abnormalities in the study. As shown in Table 2, multiple epileptiform abnormalities were found in some of the patients. Figure 1 displays the distribution of the patients' median age across the variables of EEG findings, gender, and seizure type. Hyperventilation-activated epileptiform activities were found in 24% of the patients that had the procedure, while among those patients who had photic stimulation, 2% were found to have photo-induced EEG abnormalities.

Table 1: Distribution of Age by Gender.

Age category (years)	Sex		Total
	Male	Female	
Neonate	32	18	50
Infant	74	59	133
Toddler	91	59	150
Pre-schooler	73	45	118
School age	123	97	220
Adolescent	34	51	85
Total	427	329	756

Table 2: Distribution of Electroencephalography Abnormalities Across Age Groups.

Clinical	Age group	BW (abnormal)	FSW	GSW	3HZ	NSSW	FSIW	BS	NSF	HYPs	Total
Generalised	Neonate	—	—	21	—	11	1	1	28	2	64
	Infant	18	—	75	—	63	4	—	79	5	244
	Toddler	23	—	71	1	41	5	2	74	4	221
	Pre-schooler	26	1	30	6	2	1	—	21	2	89
	School age	18	6	86	9	84	14	2	121	—	340
	Adolescent	21	1	17	—	2	5	—	11	—	57
Focal	Neonate	—	—	—	—	—	—	—	—	—	—
	Infant	—	—	—	—	—	—	—	—	—	—
	Toddler	—	—	4	—	2	—	—	7	—	13
	Pre-schooler	5	—	4	—	27	—	1	40	—	77
	School age	8	5	1	—	1	—	—	1	—	16
	Adolescent	6	48	6	—	—	—	—	—	—	60
	Total		125	61	315	16	233	30	6	382	13

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

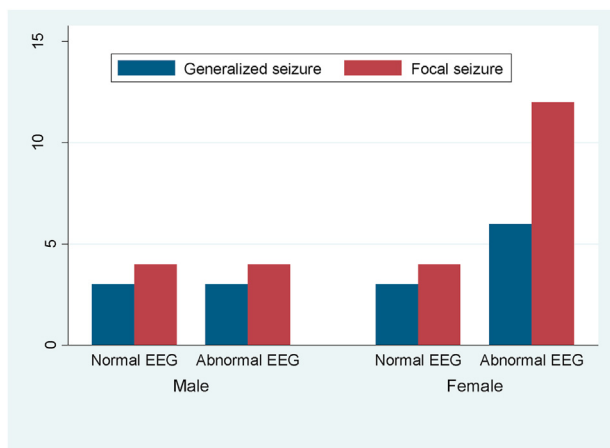


Figure 1: The distribution of the patients' median age across the variables of EEG findings, gender, and seizure type.

Figures 2 and 3 show epileptiform discharges in two patients.

Associated factors and predictors of EEG abnormalities

The sociodemographic and seizure characteristics factors explored, including patient age, age category, family history of epilepsy, sex, duration of epilepsy, seizure frequency, and seizure type, each showed a significant association with the presence of EEG abnormalities before adjustment for confounders (Table 3). However, only seizure frequency, gender, family history of epilepsy, and age were independent predictors of the presence of EEG abnormalities (Table 3).

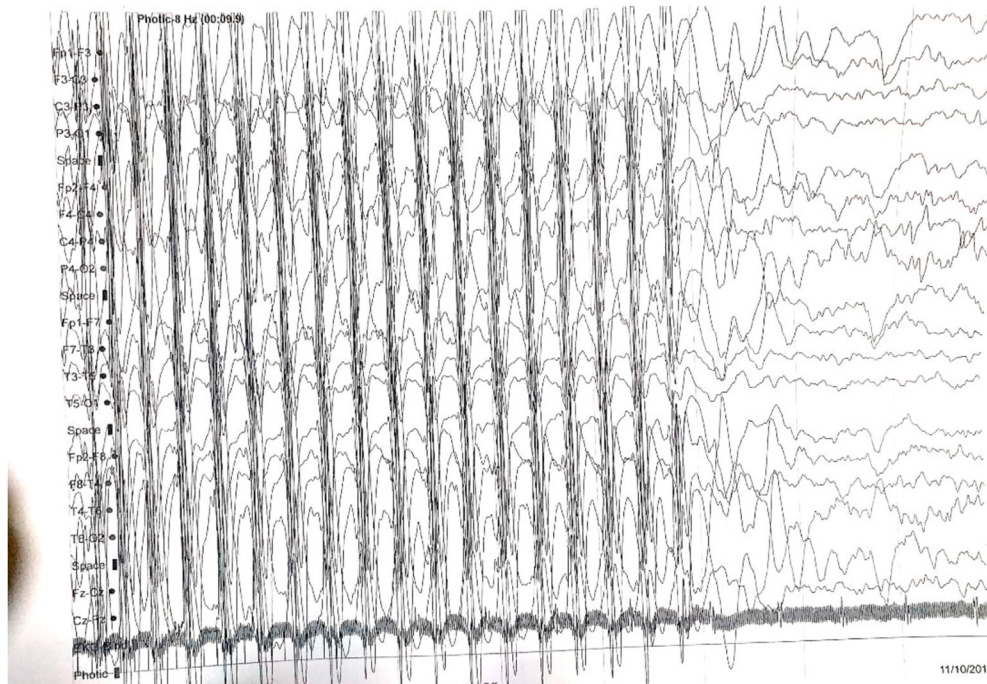


Figure 2: Image showing 3 Hz spike and wave complexes in a child with absence seizures.

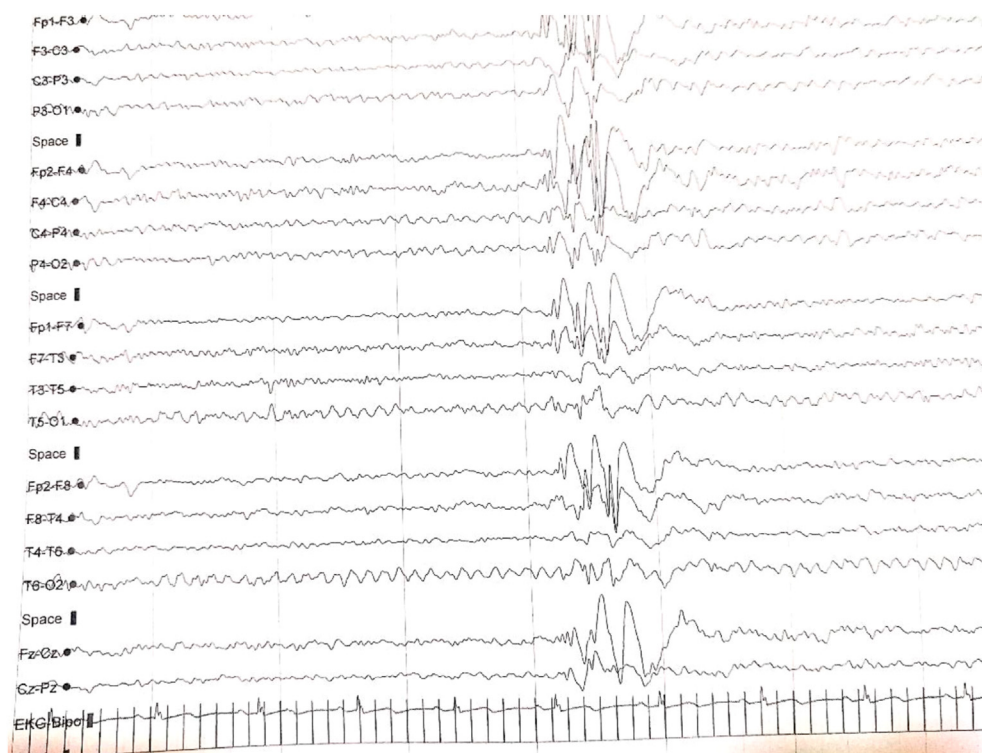


Figure 3: Image showing paroxysms of generalised epileptiform discharges in a child with idiopathic generalised epilepsy.

Table 3: The Relationships 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)	<i>P</i>	Odds ratio (95% CI)	<i>P</i>
Age	4/5 ^m		0.00001*	0.99 (0.902–1.100)	0.919
Age category		1 (reference)			
Neonate	30/50	0.99 (0.49–2.11)	0.9852	1.04 (0.778–1.397)	0.782
Infant	80/133	1.2 (0.62–2.53)	0.5106		
Toddler	82/150	1.3 (0.62–2.63)	0.4915		
Pre-schooler	64/118	1.1 (0.55–2.14)	0.8138		
School age	128/220	8.4 (3.41–20.54)	0.00001*		
Adolescent	13/85				
Family history of epilepsy		1 (reference)			
Yes	16/70	0.23 (0.12–0.43)	0.00001*	0.20 (0.080–0.369)	0.00001*
No	381/686				
Sex		1 (reference)			
Male	194/427	0.52 (0.38–0.70)	0.00001*	0.33 (0.231–0.483)	0.0001*
Female	203/329				
Duration of epilepsy		1 (reference)			
<6 months	228/402	1.9 (1.34–2.62)	0.0001*	1.28 (1.128–1.447)	0.0001*
6–12 months	100/243	0.8 (0.50–1.25)	0.3036		
>12 months	69/111				
Frequency of seizure		1 (reference)			
Once/day	33/212	0.4 (0.36–0.83)	0.00001*	0.23 (0.177–0.299)	0.0001*
Once/week	177/343	0.06 (0.04–0.11)	0.00001*		
Once/month	124/167	0.03 (0.004–0.04)	0.00001*		
≥ once/3 months	63/67				
Seizure type		1 (reference)			
Focal	53/137	2.0 (1.34–2.95)	0.00001*	1.24 (0.766–1.995)	0.3850
Generalised	344/619				

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

Discussion

This study showed that the yield of abnormal EEGs in children with epilepsy is 52.5%, and almost half (49.7%) had IEDs. These findings are in agreement with reports from studies conducted elsewhere. In a similar study, E.C. Wirrell reported that inter-ictal discharges were observed in the first EEG in about 18%–56% of children with new-onset seizures.¹⁶

The magnitude of interictal epileptiform activities in the current study is in conformity with the typical EEG findings for generalised epilepsy. As observed in cases of generalised epilepsy in the current study, bisynchronous and symmetric background and generalised, spike, sharp, spike-wave, or sharp-wave pattern are the classical findings in generalised epilepsy.¹⁷ However, focal irregular epileptiform discharges, which were also observed in our study, are not considered rare in generalised epilepsy.¹⁷ The other EEG features seen in the current study included polyspike, polyspike-wave discharges, and occipital intermittent rhythmic delta activity. Quite commonly, diagnosing epilepsy requires a careful eyewitness account that highlights what transpired during and after the relevant events. However, an eyewitness account of the events may not be available in the case of childhood epilepsy or the child concerned may be too young to provide a reliable history, thus making paediatric patients particularly vulnerable to the misdiagnosis of epilepsy.¹⁸ Consequently, EEG remains a critical tool in evaluating a child who experiences seizures. Thus, awareness of the yield of EEG in children living with epilepsy is of paramount importance, given the occurrence of many nonepileptic events that can mimic seizures, such as sleep disorders, panic attacks and other behavioural events, neurocardiogenic or vasovagal syncope, and neurogenic syncope. Our results support the broader lesson to clinicians that findings on routine electroencephalograms may not necessarily be abnormal in children living with epilepsy at all times.

Our study's results were obtained from the patients' first EEG. Thus, in light of previous studies' findings that the yield of EEG is enhanced with multiple EEGs, the question of whether the EEG test could have resulted in a higher yield if multiple EEGs were done remains unsettled.¹⁹ The prevalence of EEG abnormality that is as high as 90% of PWE has been demonstrated on the fourth EEG.¹⁹

In recent years, there has been a growing research interest in the prediction of EEG abnormality and seizures in patients with epilepsy. In our study, we explored the demographic and seizure characteristic factors that can potentially predict an abnormal EEG in paediatric patients with epilepsy. The patient's age was found to be an independent predictor of the presence of EEG abnormality. 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.^{17,20} It is also in agreement with an earlier study that demonstrated a correlation between the appearance of spike abnormality and a patient's age upon first examination.²¹

In this study, seizure frequency predicts the presence of seizure abnormality in generalised seizure. Our study's

confirmation of an association between seizure frequency and EEG abnormality further corroborates previous reports that higher seizure frequency tends to predispose patients to more intense seizures.²² The relationship between seizure frequency and EEG abnormality is a somewhat bidirectional one. To this end, Ebus et al. reported a significant correlation between epileptiform spikes and reported seizures afterward in patients with epilepsy.²³ The gender difference in the frequency of EEG abnormality observed in the current study is inexplicable, requiring further investigation. Moreover, the duration of epilepsy, starting from the first seizure that appeared to be associated with the occurrence of EEG abnormality, showed no independent association on adjustment for a confounder. This finding raises the possibility that the determinant of the occurrence of EEG abnormality in childhood epilepsy is not really the duration of epilepsy, but rather how frequently seizures occur.

The Study's strengths and limitations

Aside from the general limitations of inter-ictal EEG and the poor spatial resolution of EEGs, the current study has some limitations. First, our data was generated from a single routine EEG in a paediatric population with generalised epilepsy. Therefore, the results of this study may not be generalisable to such cases in which serial or multiple EEGs are done. Second, the current study did not explore the use of other activation methods, such as sleep and sleep deprivation, that could have resulted in a better yield, given the evidence that an EEG obtained after a period of sleep deprivation is better at detecting epileptiform abnormalities.²⁴

An important strength of our study, however, is the large sample size, which is sufficient for measuring the associations between demographic and seizure characteristic factors and the presence of EEG abnormality. Additionally, the use of a standard protocol and the interpretation of EEG by more than one experienced neurologist is a major strength of the current study.

Conclusion

In children presenting with clinical features of epilepsy, approximately one half will show epileptiform abnormalities upon the first EEG and such occurrence is associated significantly and independently with the patient's age and seizure frequency.

Recommendations

EEG should be carried out to support the diagnosis of epilepsy in children, with the proviso that a normal EEG does not totally exclude epilepsy.

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Conflicts of interest

The authors have no conflict of interest to declare.

Ethical approval

Ethical approval for this study was obtained from the University of Bisha Ethical Review Committee (UBCOM/H-06-BH-087(03/05, dated: 25th November, 2019), and informed consents were obtained from the patients.

Authors' contributions

OLF, RE, and RAA conceived and designed the study, conducted research, provided research materials, and collected and organised data, with substantial contributions from OOE, BA, and MA. OLF and BA analysed and interpreted the data, with substantial contributions from RE, RAA, OOE, and MA. OLF, BA, OOE, and MA wrote the initial and final drafts of this article and provided logistical support, with substantial contributions from RE and RAA. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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