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Correlation of Electroencephalography (EEG) Findings with Clinical Seizures in Children

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ABSTRACT

Objective: To determine the sensitivity, specificity and diagnostic accuracy of electroencephalography in predicting the development of a second/recurrent seizures/epilepsy within one year of first attack, in children who have developed their first unprovoked seizure.

Study Design: Cross-sectional validation study.

Place and Duration of Study: Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan from Jan to Dec 2022.

Methodology: This study was conducted on 126 paediatric patients who reported with a first unprovoked seizure. All patients aged between 4 and 12 years, of both genders. All participants underwent the recording of an EEG, for thirty minutes with photic and hyperventilation stimulation. All patients were followed-up for a period of one-year.

Results: Mean time from onset of seizure to presentation was 22.89±13.37 hours. An abnormal EEG was seen in 57(45.2%) patients: seizure activity was seen in 11(8.7%) cases, focal and generalized spike-waves in 11(8.7%) and 10(7.9%) cases, respectively, while slowing was seen in 31(24.6%) cases. Seizure recurrence was seen in 66(52.4%) cases. An abnormal EEG as a predictor for the development of recurrent seizures/epilepsy in children, who have had their first episode of unprovoked seizure, had a sensitivity of 57.58%, a specificity of 68.33%, a positive predictive value of 66.67%, a negative predictive value of 59.42% and a diagnostic accuracy of 62.70%.

Conclusion: Electroencephalographic findings alone in paediatric patients suffering from their first unprovoked seizure carries inadequate sensitivity, specificity and diagnostic accuracy in predicting the development of future seizures.

Keywords: Electroencephalogram, Epilepsy, Paediatric Patients, Recurrent Seizures.

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INTRODUCTION

Paediatric seizures are a common occurrence with as many as 102 incident cases in 100,000 children annually, worldwide i.e., at least 5% of all children will experience one unprovoked seizure during their lifetimes,[1] and approximately half of these patients will go on to develop epilepsy.[2] Pakistan has been noted to have a high prevalence of this disease.[3] The diagnosis of the disorder is usually clinical: patients are observed to have recurrent seizures, typically with no observable provoking factor, and are placed on prophylactic medication, which is sometimes continued life-long: treatment has to be initiated in a timely manner to prevent the occurrence of permanent damage to the neurons of the central nervous system.[4] While a majority of these children will have a clinically benign course, a minority may develop cognitive dysfunction, as well as emotional disorders, poor concentration and low self-esteem, in addition to the risk of development of injuries as a result of seizures.[5]

The electroencephalogram (EEG) is a non-invasive modality wherein electrodes are applied over the scalp of a patient to measure voltage potentials over different areas of the brain, in essence it is the average of the sum of the voltage potentials produced by radially oriented pyramidal neurons in the cerebral cortex.[6,7] In epilepsy, patients may demonstrate EEG findings such as diffuse or focal slowing, posterior dominant rhythm absence, focal or generalized periodic discharges, and focal or generalized epileptiform activity.[8,9] Thus, in theory, the EEG forms an important part of the diagnosis of patients presenting with onset of first episode of unprovoked seizures, in predicting whether the patient will develop future seizures and is currently suffering from epilepsy.[10]

We conducted this research study with aim of determining the diagnostic utility of the EEG in paediatric patients presenting with their first episode of an unprovoked seizure in predicting the development of future seizures and establishing the diagnosis of epilepsy. To our knowledge, determining

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the diagnostic yield of EEG in this population has never been assessed. Understanding whether the EEG is a useful diagnostic modality in this scenario or not will help to dictate its role in the diagnostic algorithm of this ubiquitous disorder in an effort to make timely and accurate diagnoses and provide appropriate management, to prevent both short- and long-term morbidity associated with this disease.

METHODOLOGY

The study was conducted from January to December 2022 at the Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan on 126 paediatric patients who reported with a first unprovoked seizure, after obtaining informed consent from their parents or guardians. Institutional ethical review committee approved the study protocol (ERC # 333/CMH Rwp dated 09 Feb 2022) Patients were selected via non-probability, consecutive sampling. The EPI tools sample size calculator was used to calculate the sample size keeping an test sensitivity of 0.578, test specificity of 0.696, expected prevalence of 0.66, which were the sensitivity, specificity, and prevalence of occurrence of recurrent seizures/epilepsy after an initial attack based on EEG findings, from Bouma *et al*.[11]

Inclusion Criteria: All paediatric patients aged between 4 and 12 years, of both genders, reporting with their first unprovoked seizure (occurring within the previous 48 hours of presentation), which was defined as the first transient occurrence of loss of consciousness with signs and symptoms of an epileptic seizure, were included.

Exclusion Criteria: Children with ages less than 4 or greater than 12 years, with a past history of diagnosis of epilepsy, had a history of drug or alcohol abuse, or those who had reported with cranial trauma, status epilepticus, meningoencephalitis, abnormal levels of Sodium, Potassium, Magnesium or Calcium, or hypoglycaemia, patients with abnormal brain imaging, or those who were lost-to-follow up were excluded.

All patients underwent a clinical session during which their relevant demographic data/history was documented and they received a clinical examination. Laboratory investigations and magnetic resonance imaging (MRI) were carried out. All participants subsequently underwent the recording of an EEG (Neurofax EEG-1200J, Nihon Kohden; Tokyo, Japan) for thirty minutes with photic and hyperventilation stimulation, which was then read by two consultant paediatric neurologists separately, and any disagreements in between both readers were settled by consensus. Assessors evaluated the EEG record for the presence of seizure activity, focal spike-waves, generalized spike-waves and slowing and made a final comment on whether the EEG record was normal or not. All patients were followed-up for a one-year period during which they remained under observation for recurrence of seizures, and a single further episode established the diagnosis of epilepsy.

Data was analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows version 26, IBM Corp; Armonk, USA). Mean and standard deviation was calculated for quantitative variables specifically patient age and time since seizure occurred. Qualitative variables like gender, occurrence of nocturnal seizure, whether EEG was abnormal or not, type of abnormality (if any) seen on EEG, and whether there was a recurrence of seizures were recorded in terms of frequency and percentage. The 2 x 2 table was constructed to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of EEG in predicting the development of recurrent seizures/epilepsy.

RESULTS

This study was conducted on a total of 126 paediatric patients reporting with their first, unprovoked seizure. with a mean age of 7.25±2.97 years. The total number of males were 69(54.8%). Mean time from onset of seizure to presentation was 22.89±13.37 hours. The frequency of occurrence of a nocturnal seizure was 9(7.1%). An abnormal EEG was seen in 57(45.2%) patients: seizure activity was seen in 11(8.7%) cases, focal and generalized spike-waves in 11(8.7%) and 10(7.9%) cases, respectively, while slowing was seen in 31(24.6%) cases. Seizure recurrence was seen in 66(52.4%) cases. Table-I shows the patient characteristics and study results, distributed according to gender.

Table-II displays the 2 x 2 table used for EEG to calculate the various test characteristics. An abnormal EEG as a predictor for the development of recurrent seizures/epilepsy in children, who have had their first episode of unprovoked seizure, had a sensitivity of 57.58%, a specificity of 68.33% and a diagnostic accuracy of 62.70%.

Table-I: Patient Characteristics (n=126)

Variable	Male (n=69)	Female (n=57)
Gender	69(54.8%)	57(45.2%)
Age (years)	7.01±2.99	7.53±2.97
Time Since Seizure (hours)	3(4.3%)	6(10.5%)
Abnormal Electro-encephalogram	33(47.8%)	24(42.1%)
Type of Electroencephalogram Abnormality seen		
Normal	36(52.2%)	33(57.9%)
Seizure Activity	7(10.1%)	4(7.0%)
Focal Spike-Wave	6 (8.7%)	4(7.0%)
Generalized Spike-Wave	5 (7.2%)	-
Slowing	15(21.8%)	16(28.1%)
Seizure Recurrence	37(53.6%)	29(50.9%)

Table-II: Diagnostic Accuracy Table for Calculation of Test Characteristics for EEG

	Clinically Positive (n=66)	Clinically Negative (n=60)
EEG Positive	38 (57.6 %)	19 (31.7%)
EEG Negative	28 (42.4%)	41 (68.3%)

Sensitivity= 38/(38+28)*100=57.58%
Specificity= 41/(41+19)= 68.33%
Positive Predictive Value= 38/(38+19)*100= 66.67%
Negative Predictive Value= 41/(41+28)*100)= 59.42%
Diagnostic Accuracy=(38+41)/126*100= 62.70%

DISCUSSION

Early diagnosis of recurrent seizures is paramount in preventing morbidity associated with epilepsy,[12] however, the current study demonstrated that the EEG lacked the appropriate sensitivity, specificity and diagnostic accuracy to be of reliable use, in such cases, as a diagnostic or even a screening test.

Our study sample had a mean age at onset of first, unprovoked seizure of 7.25±2.97 years. de Rezende-Machado *et al*., reported that the age-of-onset of first, unprovoked seizure in children in their study was between 5 and 10 years of age, which was in keeping with our study.[13] Klotz *et al*., reported in their study on paediatric patients with onset of first, unprovoked seizure, that the mean age of onset of such seizures was 7.27±5.04,1 while Crevier-Sorbo *et al*., reported that the mean age of onset of seizures in such patients was a similar 7.5 years in their study.[14] However, Khan *et al*., reported on a slightly younger, but still similarly aged, population of 5.6±5.1 years.[15] While the literature is mostly in agreement with our study in this aspect, the minute variability in age-at-presentation may be attributable to ethnic and environmental differences.

The current study had a sample composed of a slight male majority of 54.8%. Studies such as Hu *et al*., have noted that males have a higher burden of epilepsy than women, while the reasons for this are unclear, it is thought that a higher exposure to steroid hormones may be associated with an increased risk in males; it is pertinent to note here that this study reported on epilepsy in all ages, and these conclusions may not be applicable to the paediatric population.[16] Reddy *et al*., noted that these differences may have arisen due to differences in the distribution of intra- and inter-hemispheric neuronal connections between males and females.[17] de Rezende-Machado *et al*., reported a population of children with first, unprovoked seizures with a slight male majority of 55.4%,[13] while Klotz *et al*. also reported a slight male majority of 60.7%.[1] We believe that while male gender does appear to have a higher frequency of occurrence of unprovoked seizures in-general, and epilepsy in particular, further study is required before concrete assertions can be made in the paediatric population. A total of 52.4% participants developed seizure recurrence in the present study. de Rezende-Machado *et al*., reported a recurrence rate of 56.7% in their study,[13] while Al-Momani *et al*., also reported a similar figure of 55.3% for recurrence in their study.[18] Pellino *et al*., in their meta-analysis, reported that a recurrence rate 50.0% was seen at three years of follow-up in paediatric patients reporting with first, unprovoked seizures.[19] Thus, it is safe to conclude that roughly half of all children reporting with a first, unprovoked seizure will experience a second episode during their lifetime.

Our study showed that an abnormal EEG in fore-casting the occurrence of recurrent seizures/epilepsy in children after their first, unprovoked seizure carried a sensitivity of 57.58%, a specificity of 68.33%, a positive predictive value of 66.67%, a negative predictive value of 59.42% and a diagnostic accuracy of 62.70%. Bouma *et al*., reported similar figures for EEG in paediatric patients and noted that it had a sensitivity of 57.8% and a specificity of 69.6% in predicting the occurrence of future seizures.[11] Chowdhury *et al*., reported a sensitivity and specificity of 66.0% and 79.0% for EEG in prediction of presence of epilepsy, with a positive predictive value of 58.0% and a negative predictive value of 41.0%,[20] however, its is pertinent to note here that this study looked at both adults and children, which may account for the slight difference in our results. Smith, noted that the test characteristics of EEG varied wildly: EEG had a relatively low sensitivity in epilepsy, ranging between 25.0% to 56.0%, with a specificity ranging from 78.0%

to 98.0%, again this included adult data as well,[5] and we can safely conclude that EEG carries a low sensitivity and a moderate specificity in predicting the occurrence of future seizures in children with a first, unprovoked seizure.

LIMITATIONS OF STUDY

EEGs are open to subjective interpretation, and while we employed two different interpreters for this study and discrepancies between the two were sorted through discussion, differences in interpretation may have led to the possibility of confounding within the results. Secondly, homeopathy is routinely practiced in Pakistan which patients regularly practice and do not disclose to the healthcare professionals attending to them, and while the guardians/study participants were strictly instructed to avoid homeopathic medication during the course of this study, some may still have employed these treatments methods which may have had unknown effects on our results.

CONCLUSION

The use of electroencephalography in predicting the presence of epilepsy or the development of future seizures in children who have suffered from their first, unprovoked episode is not particularly useful in isolation as this testing modality lacks the appropriate sensitivity, specificity and diagnostic accuracy to make precise predictions. Use of this testing method in conjunction with other parameters such as history/examination, laboratory tests and imaging techniques may prove to be more accurately predictive and should be the subject of future research.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

BA & EQ: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

HA & AK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FI & SHN: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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