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A STUDY ON CLINICAL, RADIOLOGICAL AND ELECTROPHYSIOLOGICAL PROFILE IN PATIENTS PRESENTING WITH FIRST UNPROVOKED SEIZURE

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Abstract

Background: Epilepsy is defined as a disorder of the brain characterized by an enduring predisposition to generate recurrent seizures. i.e, 1) Atleast 2 unprovoked seizures >24 hrs apart 2) one unprovoked seizure and a probability of further seizures risk of 60% 3) Diagnosis of an epilepsy syndrome. Diagnosis of epilepsy(risk of recurrence of seizures) following First unprovoked seizure depends largely on the EEG study done following the episode. Thus this study is undertaken to analyse the clinical, radiological and electrophysiological features in patients presenting with first unprovoked seizure. **Aim:** To Study the Clinical, Radiological and Electrophysiological profile in patients presenting with First Unprovoked Seizure. **Materials & Methods:** Inpatients or outpatients who had experienced a single first unprovoked seizure presenting between January 2021 and June 2022 were included in the study. Demographic characteristics, Neurological history & examination, Laboratory parameters, Imaging studies and Electrophysiological Studies were analysed. **Results:** Our study included 30 patients, of whom 23(76.7%) were male and 7(23.3%) were female. Mean age was 24.5 +/- 13.76 yrs. 4(13.3%) patients had significant past history ie, Febrile seizures in 3(10%), Migraine in 1 (3.3%). There were 6(20%) patients with family history of seizures in immediate family. The number of patients who presented with more than 1 episode of seizure within 24hrs period was 3. The number of patients presenting with generalized or partial onset seizures (including secondary generalization), were 18(60%) and 12(40%) respectively.MRI Brain was abnormal in 6(20%) patients. The abnormalities noted were mesial temporal sclerosis and volume loss in 2 patients (6.6%), Focal cortical dysplasia in 2 patients (6.6%) and granulomatous lesions in 2 patients (6.6%).Interictal EEG abnormalities were found in 3(10%) patients, with focal IEDs in 1(3.3%) and bilateral IEDs in 2(6.6%) of them during first hour of recording. During overnight recording epileptiform abnormalities were noted in 10(33.3%) patients, with focal IEDs in 5(16.6%), bilateral IEDs in 3(10%) and focal with secondary generalization in 2(6.6%) patients.

INTRODUCTION

An **epileptic seizure** is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. **Epilepsy** was defined conceptually in 2005 as a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures,i.e,(1) At least two unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome[1]

An epileptic seizure can be provoked or unprovoked. Provoked seizure is defined as an event which is caused by an acute CNS insult like Stroke, trauma, infections and neoplasms and Toxins (poisoning and withdrawal). And an unprovoked seizure is of

unknown cause. The clinical guidelines from the American Academy of Neurology for both children[2] and adults[3] recommend that an EEG be obtained after a single unprovoked seizure. Epileptiform abnormalities are related to seizure disorders and have been shown to predict recurrent unprovoked seizures. Thus, the identification of epileptiform abnormalities after a single unprovoked seizure can inform treatment options. The purpose of our study is to evaluate the clinical, radiological and electrophysiological profile in patients presenting with first unprovoked seizures.

MATERIALS AND METHODS

Study Design

This is a single centre descriptive study conducted at a tertiary care hospital from January 2021 to June 2022.

Methodology

Inpatients or outpatients who had experienced a single first unprovoked seizure were included. Trained and experienced Neurologists and epileptologists identified patients who presented with history of first paroxysmal event and decided whether to include these patients based on the seizure description of by standers. The diagnostic criteria for seizure were according to those formulated by the ILAE in 2005. All seizure types were categorized as generalized or partial.

In our study, first unprovoked seizures were categorised as partial seizures (simple, complex and secondarily generalized tonic-clonic seizures) and generalized seizures (generalized tonic-clonic seizures, tonic seizures and clonic seizures). Patients presenting with status epilepticus and two or more seizures that had occurred within 24 h (cluster seizures) were also included. Patients were excluded from our study if their first paroxysmal events were non-epileptic seizures, acute symptomatic seizures (associated with acute factors such as acute stroke, traumatic brain injury, Acute CNS infections, abrupt withdrawal of alcohol, acute intoxication, hypoglycaemia, Diabetic Ketoacidosis, Uraemia and other metabolic derangements), other seizure types (absence, myoclonic seizures and unclassified epileptic seizures) and children less than 13 years of age.

After enrolment, relevant clinical information and demographic data were acquired, including, sex, age, birth and development , family history of seizures, significant antecedent history(febrile seizures, meningoencephalitis, head trauma or surgery), alcohol , tobacco or substance use, comorbid medical conditions(Diabetes, hypertension, hyperlipidaemia, previous stroke), seizure type, presence/absence of nocturnal seizure. Patients then underwent general and complete neurological examination followed by standard blood investigations(complete blood counts, renal and liver function tests, random blood sugars, serum electrolytes, serum calcium) , Overnight Video EEG, MRI Brain under epilepsy protocol(3D FLAIR, SPGR).

Video EEG

Overnight Video EEG recordings were carried out on a 32-channel digital EEG acquisition system, with the scalp electrodes placed according to the International 10–20 system with bipolar and average referential montages from 8pm to 8am. First hour of the record included activation procedures like intermittent photic stimulation and Hyperventilation. Epileptologist blinded to the study reported the overnight records. The VEEG recordings were classified as either normal or abnormal. An abnormal

VEEG was further categorized as either (a) non-epileptiform discharges (e.g., increased slow waves, bilateral asymmetry or absence of normal sleep patterns) or (b) epileptiform discharges (e.g., spikes or sharp waves, or spike and wave discharges) that were generalized, focal or focal discharges with secondary generalisation.

MRI

1.5 Tesla MRI brain done in standard protocol and were reviewed by radiologists and Neurologists, divided into normal and abnormal according to whether any observed foci could be responsible for seizure onset or not.

The Institutional Ethics Committee was obtained for our study. Each patient had given informed consent prior to the study. The Study subjects were not started on anti-epileptic drugs (AEDs) treatment and were kept on close follow up.

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

The one-way analysis of variance (ANOVA) is employed to determine whether there are any statistically significant differences between the means of three or more independent (unrelated) groups. The one-way ANOVA compares the means between the groups you are interested in and determines whether any of those means are statistically significantly different from each other. Specifically, it tests the null hypothesis:

$$H_0: \mu_1 = \mu_2 = \mu_3 = \cdots = \mu_k$$

Where μ = group mean and k = number of groups. If, however, the one-way ANOVA returns a statistically significant result, we accept the alternative hypothesis (H_A), which is that there are at least two group means that are statistically significantly different from each other.

Assumptions for ANOVA test

1. The dependent variable is normally distributed in each group that is being compared in the one-way ANOVA
2. There is homogeneity of variances. This means that the population variances in each group are equal.
3. Independence of observations.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher exact test used when cell samples are very small.

Significant Figures

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value: 0.01<P ≤ 0.05)

** Strongly significant (P value: P≤0.01)

Statistical software: The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

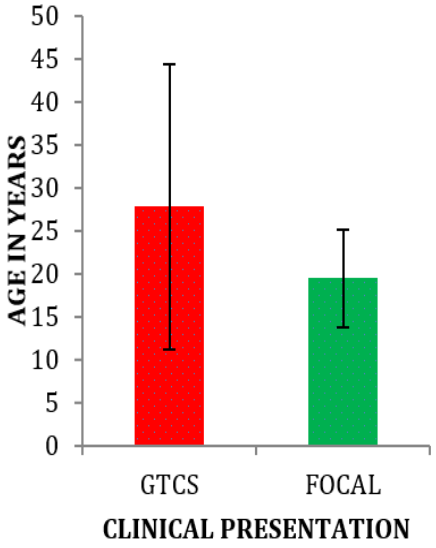
RESULTS

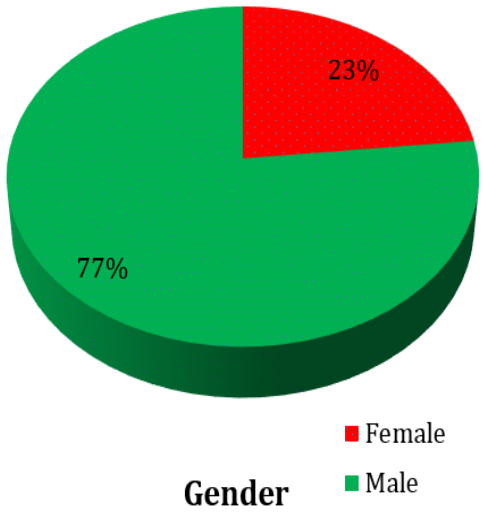
Our study included 30 patients, of whom 23(76.7%) were male and 7(23.3%) were female. Age of the patients ranged from 13 to 74 years, with mean age 24.5 +/- 13.76. 4(13.3%) patients had significant past history ie, Febrile seizures in 3(10%), Migraine in 1 (3.3%). There were 6(20%) patients with family history of seizures in immediate family. The number of patients who presented with more than 1 episode of seizure within 24hrs period was 3. The number of patients presenting with generalized or partial onset seizures (including secondary generalization), were 18(60%) and 12(40%) respectively.

The Laboratory parameters of all the patients i.e, CBC, Blood sugars Renal Profile, Liver Profile and Electrolytes (Sodium, Potassium, Calcium) were within normal limits.

MRI Brain of 24(80%) patients was normal while abnormalities were noted in 6(20%) patients. The abnormalities noted were mesial temporal sclerosis and volume loss in 2 patients (6.6%), Focal cortical dysplasia in 2 patients (6.6%) and granulomatous lesions in 2 patients(6.6%).

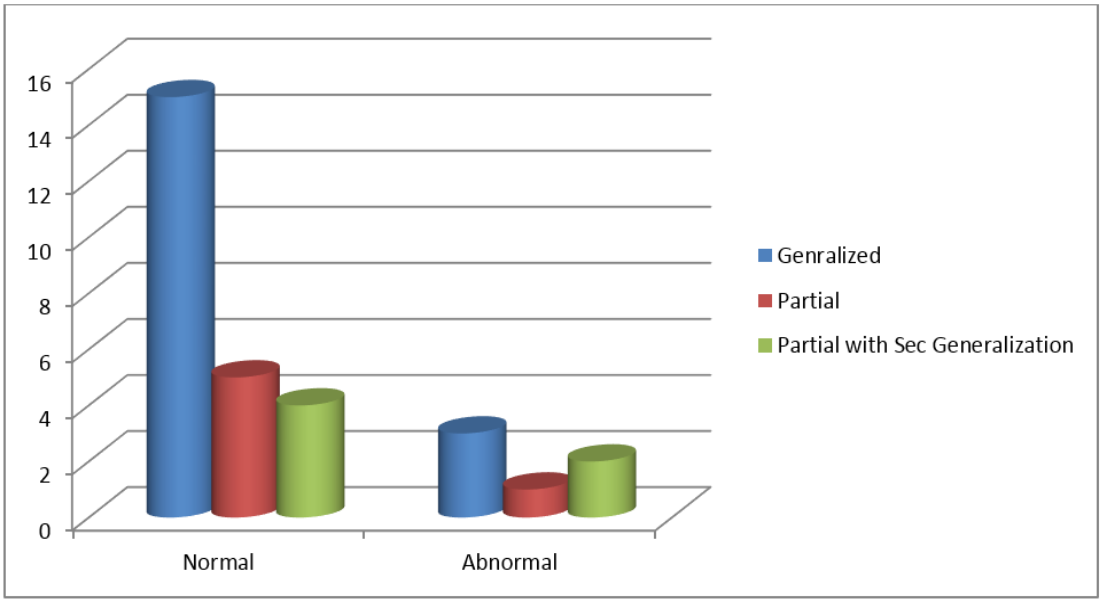
2(6.6%) patients had seizure recurrence during the overnight Video EEG recording. Both were focal seizures with secondary generalization. Interictal VEEG was normal in 27(90%) patients during the first hour of record with activation procedures while it was normal in 20(66.7%) patients during overnight recording. Interictal EEG abnormalities were found in 3(10%) patients, with focal IEDs in 1(3.3%) and bilateral IEDs in 2(6.6%) of them during first hour of recording. During overnight recording epileptiform abnormalities were noted in 10(33.3%) patients, with focal IEDs in 5(16.6%), bilateral IEDs in 3(10%) and focal with secondary generalization in 2(6.6%) patients.

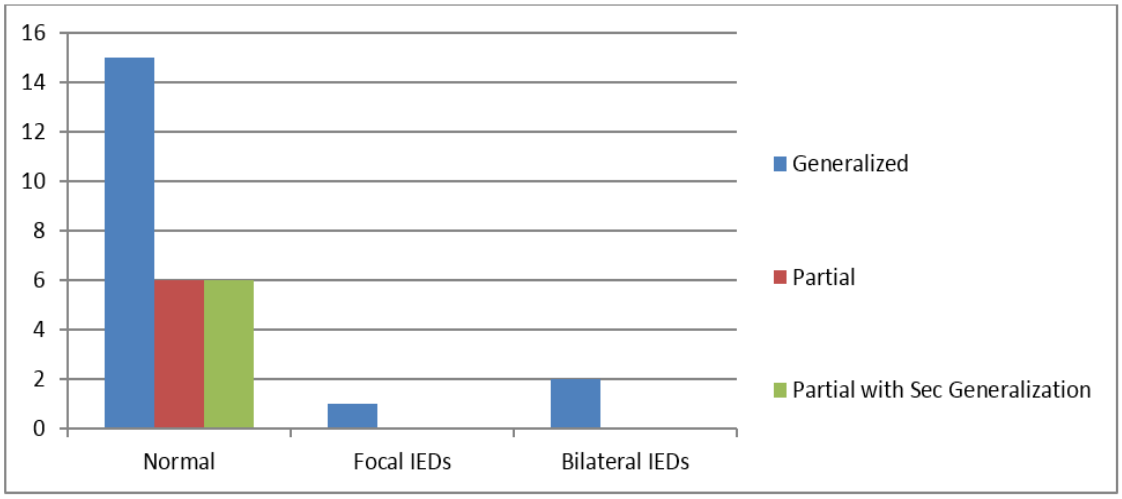




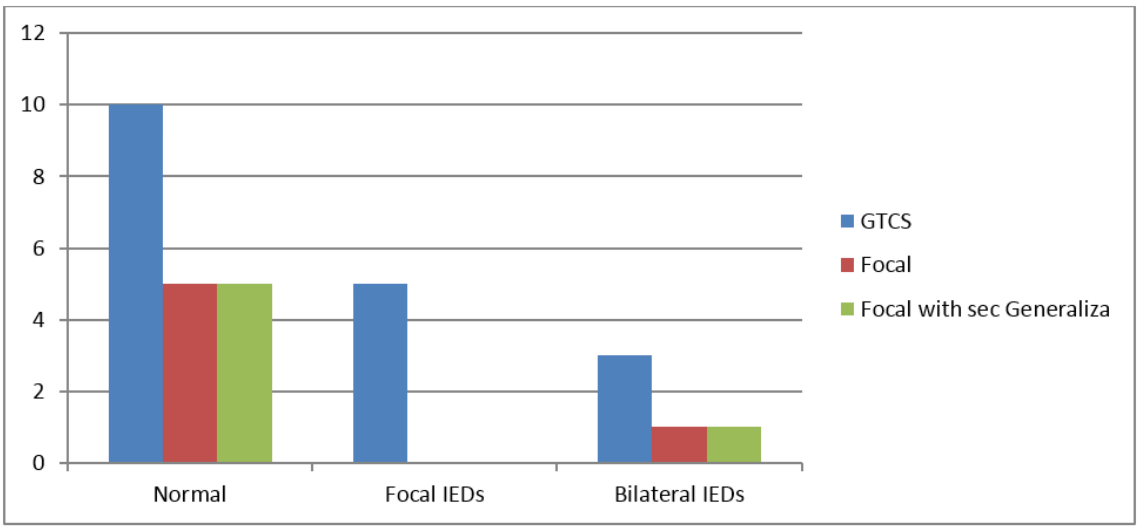
Variables	CLINICAL PRESENTATION				P Value
	Generalized	Partial	Partial with Secondary Generalization	Total	
AGE IN YEARS	27.78±16.52	20.17±7.47	18.83±3.76	24.47±13.76	0.276
WBC	9683.33±3070.78	8938.33±1165	8366.67±1864.05	9271±2580.4	0.539
HB	20.02±29.23	12.75±1.78	12.93±1.39	17.15±22.69	0.712
PLT	2.97±0.84	2.66±0.33	2.85±0.75	2.88±0.74	0.680
BUN	24.61±14.63	23.67±11.18	24.33±15.2	24.37±13.68	0.990
CREATININE	0.99±0.38	0.87±0.18	0.87±0.16	0.94±0.32	0.571
CALCIUM	9.49±1.07	9.65±0.83	9.22±1.37	9.47±1.07	0.783
NA	139.78±3.25	141±3.69	138.33±2.25	139.73±3.18	0.360
K	3.99±0.52	3.9±0.3	3.9±0.37	3.96±0.45	0.860

Variables	CLINICAL				P Value
	Generalized (n=18)	Partial (n=6)	Partial with Secondary Generalization (n=6)	Total (n=30)	
MRI BRAIN					
• Normal	15(50%)	5(16.6%)	4(13.3%)	24(80%)	0.690
• Abnormal	3(10%)	1(3.3%)	2(6.6%)	6(20%)	
FIRST HOUR VEEG					
• NORMAL	15(50%)	6(20%)	6(20%)	27(90%)	0.306
• ABNORMAL	3(10%)	0(0%)	0(0%)	3(10%)	
1.FOCAL IEDS	1(3.3%)	0(0%)	0(0%)	1(3.3%)	
2.BILATERAL IEDS	2(6.7%)	0(0%)	0(0%)	2(6.7%)	
OVERNIGHT VEEG					
• NORMAL	10(33.3%)	5(16.6%)	5(16.6%)	20(66.6%)	0.350
• ABNORMAL	8(26.6%)	1(3.3%)	1(3.3%)	10(33.3%)	
1)FOCAL IEDS	5(16.6%)	0(0%)	0(0%)	5(16.6%)	
2)BILATERAL IEDS	3(10%)	1(3.3%)	1(3.3%)	5(16.6%)	





First Hour EEG Record



Overnight EEG Record

DISCUSSION

An epileptic seizure can be provoked or unprovoked. Provoked seizure is defined as an event which is caused by an acute CNS insult like Stroke, trauma , infections and neoplasms and Toxins(poisoning and withdrawal). And an unprovoked seizure is of unknown cause. The risk of a single seizure occurring during the lifespan in the general population is 5–10% and approximately 3% of these cases may develop into epilepsy. Patients presenting with ≥2 unprovoked seizures are readily diagnosed with epilepsy, and virtually all are prescribed antiepileptic drug (AED) therapy. In contrast, starting vs withholding AED treatment after a single unprovoked seizure has been a long-standing topic of debate.

According to Hauser et al[4], among patients presented with First unprovoked seizure, 66% were of generalized type and 33% focal, while our study found generalized seizures in 60% and focal seizures in 40% of patients. Detrimental past history was noted in 21.6% patients in Chen et al.[5], while in our study, such history was noted in 13.7% patients. According to Chen et al.[5], MRI Brain abnormalities were noted in 26% patients while in the present study MRI abnormalities were noted in 20% patients. Our study found that the rate of EEG abnormalities was 33.3% in first unprovoked seizure patients, similar to Allen Hauser W et al., that reported a rate of EEG abnormalities ranging from 45% to 84% in all first seizure patients, depending on the time to EEG after the episode. The risk of seizure recurrence is greatest within the first 1-2 years (21-45%) after a single unprovoked seizure in adults[6]. The risk increases to 60-90% after a second unprovoked seizure[4,7], at which point it is felt that the traditional definition of epilepsy is fulfilled. According to Bouma, H. K., et al.[8], an adult with Epileptiform discharges on routine EEG after a first unprovoked seizure has a 77% probability of having a second seizure, whilst a child with similar findings has a 66% probability. Fisch et al.[9],determined that a prolonged video-EEG (approximately 18 hours in duration) provided an additional yield of 30% after a normal standard EEG in patients. Burkholder, David B., et al[10], compared yield of 30 mins vs more than 45 mins EEG recording, 23.6% had IEDs at any time during their EEG. 4.5% had IEDs occur late. There was a relative increased yield of 19%, while our study showed IEDs in 3(10%) patients during first hour of record compared to 10(33.3%) patients during overnight record which showed an increased yield of 30% which was statistically significant.

CONCLUSION

EEG is a fundamental test to diagnose the presence or absence of epilepsy after a first seizure. . Ideally, it should be performed as early as possible after the event, if possible within 24 hours. The protocol should include activation procedures like eye opening and closure, photic stimulation, Hyperventilation and sleep record, preferably in a sleep deprived state. The recording duration should be prolonged preferably overnight recording

Proper and correct diagnosis of the type of epilepsy is fundamental in order to offer optimal treatment and prognostic information regarding seizure relapse. It is self-evident that such information is of utmost importance for the medical and socio-professional wellbeing of each patient.

LIMITATIONS

Due to a small sample size, the findings of the study cannot be applied to the population at risk.The rate of EEG abnormalities in highest in EEG studies done in less than 24hrs after the event, which was not the case in our study where the study was done after a period of 48hrs to 2 weeks. The recurrence risk could not be calculated due to lack of followup.

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