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"Clinical evaluation of classification of seizure, epilepsy and etiology with current concepts by using seizure semiology, Electro Encephalogram (EEG) and MRI of the brain in a tertiary care hospital - An observational study."

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Abstract

Introduction: The classification of seizures and epilepsies is needed to identify seizures that have both focal and generalized onset and simplify the terminologies for easy understanding for both patients and clinicians.
Aim of the study: This study aimed to evaluate the classification of seizures, epilepsy, and their etiology by analyzing semiology, EEG, and MRI data, emphasizing the differences between focal and generalized onset epilepsy.

Methods: This was a prospective cross-sectional observational study and was conducted in the epilepsy clinic, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, during the period from February 2021 to July 2022. We included 160 patients with epilepsy in our study.

Result: Among the 160 patients, 120 had focal onset epilepsy, and 40 had idiopathic generalized epilepsies (IGEs), which included 24 cases of Juvenile Myoclonic Epilepsy (JME) and 16 cases of Generalized Tonic-Clonic Seizures (GTCA). The majority of patients (68%)

were aged 18-30 years, with a higher prevalence in males (58%) compared to females (42%). The study found that most focal onset epilepsy cases were temporal lobe epilepsy (79.2%), followed by frontal (10%), occipital (5%), and parietal lobe epilepsy (5.8%). Among temporal lobe epilepsy patients, 25% had left mesial temporal sclerosis (MTS), while 20.8% had right MTS. Frontal lobe epilepsy was associated with meningiomas (5%) and arteriovenous malformations (2.5%). In patients with occipital and parietal lobe epilepsy, post-stroke epilepsy and hypoxic encephalomalacia due to cerebral palsy were noted. Regarding seizure types, 6.67% of patients had versive seizures, 11.67% had psychic aura, 7.5% experienced oro-elementary automatisms, and 12.5% had auditory aura. A focal to bilateral tonic-clonic seizure pattern was observed in all patients.

Conclusion: In conclusion, this study highlights the importance of evaluating the etiology and classification of focal and generalized onset epilepsies using semiology, EEG, and MRI, which has significant therapeutic and prognostic implications for patient management.

Key words: Epilepsy, Classification, Focal Onset, Generalized Onset**.**

Introduction

In the current classification by ILAE, the clinical features of epilepsy are categorized into three levels: seizures, epilepsies, and epilepsy syndromes. Emphasis has been placed on considering etiology and comorbidities at each level.[1] This new classification is better organized with a clear elucidation of terminologies and lists some new seizure types.[2] Seizures are classified into focal onset (seizures arising in one hemisphere of the brain), generalized onset (seizures originating in both hemispheres simultaneously), and unknown onset.[3] The starting point of the epilepsy classification framework is the seizure type.[4] The epilepsy type includes a new category of "Combined Generalized and Focal Epilepsy" in addition to the well-established Generalized Epilepsy and Focal Epilepsies. It also includes an unknown category. Many epilepsies will include multiple types of seizures.[5] Epilepsy syndrome refers to a cluster of features incorporating seizure types and having distinctive co-morbidities such as intellectual and psychiatric dysfunction, together with specific findings from EEG and imaging studies.[6,7] Pharmacologically, this classification has great relevance, as focal seizures, regardless of the part of the brain involved, were shown to respond to a specific set of anticonvulsants. In contrast, drugs for generalized seizures depend on their specific type.[8] In the Fiest et al., the overall lifetime prevalence of epilepsy was 7.60 per 1,000 people.[9] The most common type of focal seizure is a focal impaired awareness seizure which accounts for approximately 36% of all people with seizures.[10] IGE is a common group of epilepsy, accounting for 15%-20% of persons with epilepsy.[2] Juvenile myoclonic epilepsy (JME) is a common, well-defined, age-related epileptic syndrome with a prevalence of 4–11% of all epilepsies and an incidence of 0.4 -0.9%.[11-13] JME is common, with a prevalence ranging from one to three per 10,000 persons in population-based studies.[14,15] GTCA accounted for one-third of all adolescent-onset IGEs.[16,17] The five etiological groups are genetic, infectious, metabolic, and immune, as well as an unknown group (Figure 1). Neuroimaging is carried out first to recognize the etiological groups, ideally by MRI where available.[3]

Therefore, in this study, we aimed to evaluate the classification of seizures, epilepsy, and etiology by analyzing the semiology, EEG, and MRI of the brain.

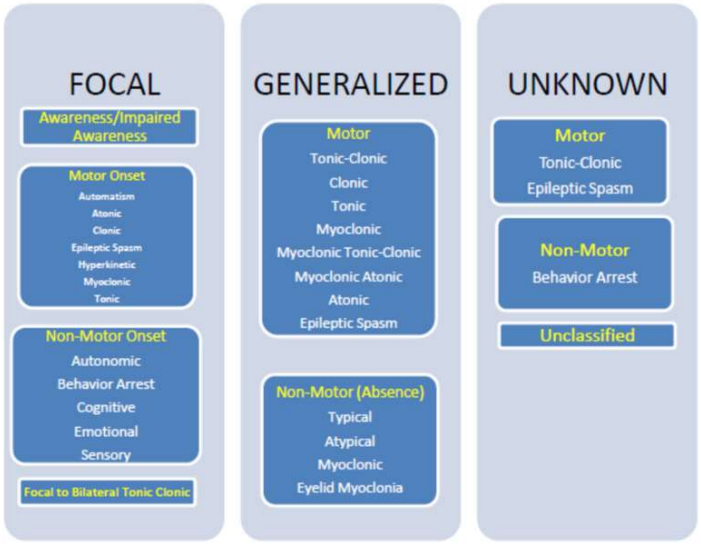


Figure 1: ILAE 2017 Classification of Seizure Types: Expanded Version [22]

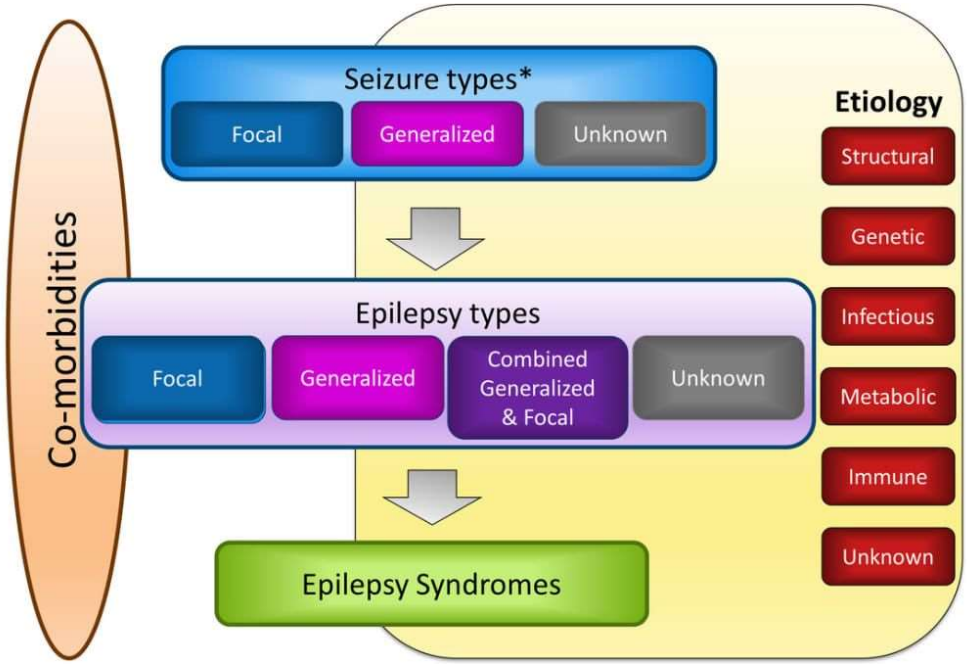


Figure 2: Framework for Classification of the Epilepsies [8]

Objective of the study

The main objective of the study was to evaluate the classification of seizure, epilepsy and etiology with current concepts by analyzing the semiology, EEG and MRI of the brain.

Methodology & Materials

This was a prospective observational study and was conducted in the Epilepsy clinic, Department of Neurology of Bangabandhu Sheikh Mujib Medical University, Dhaka,

Bangladesh during the period from February,2021 to July,2022. The sample size was 160. Among of these 160 patients, we found 120 patients with frontal epilepsy and 40 patients with IGEs (24 were JME patients and 16 were GTCA). Generally, the age onset for the patients with epilepsy is range 3-25 but as they can be occurred upto as late as 40 years. Typical age of onset for patients with focal epilepsy is range 3-20, age of onset of JME patients is 10-24 years (range = 8-40 years) and Epilepsy with GTCA age of onset is 10-25 years (range =5-40 years). In this study, it was provided the diagnostic criteria of focal and generalized epilepsy as their adult age of presentation in the clinic. We included only a) the patients with focal and generalized epilepsy aged more than 18.b) the patients should be evaluated by diagnostic seizure type, c) CT scan of the brain and MRI of the brain with Epilepsy protocol with normal imaging finding should be done from radiology department of BSMMU and outside of BSMMU d) Mandatory diagnostic interictal long duration routine EEG (3 hours) showing generalized spike -wave and Polyspike wave at 2.5-5.5 Hz and morphology were available for view. In this study, those patients with: (a) Age Below 18 (b)Acute Sympomatic seizures secondary to acute conditions like acute stroke, CNS infection, meningitis (c) Inadequate EEG Recording or Technical Artifacts (d) Progressive Neurological Disorders (e) Incomplete Diagnostic Workup such as 3-hour interictal EEG with generalized spike-wave or polyspike-wave discharges, were excluded from this study.

All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS (Statistical Package for So Sciences) for windows version 10. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance. Ethical review board of Bangabandhu Sheikh Mujib Medical University, Dhaka approved the study.

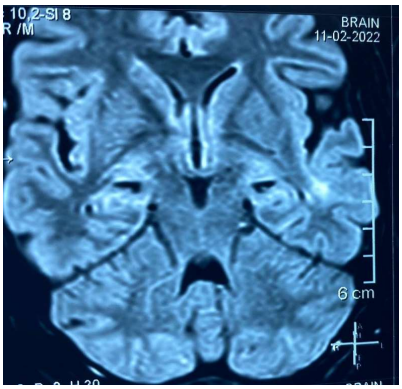
EEG recordings:

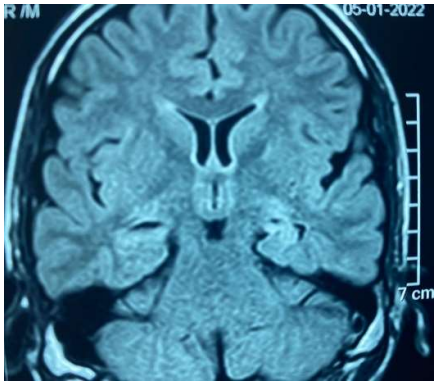
In this study, EEG recordings were performed on patients at the Neurology Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) using long-duration interictal EEGs (lasting 3 hours). The EEG was done after evaluating the seizure type for both Juvenile Myoclonic Epilepsy (JME) and Epilepsy with Generalized Tonic-Clonic Seizures (GTCA) patients in the Epilepsy Clinic. Sleep deprivation was applied before the EEG, and the recordings were done with a 21-channel digital system using different electrode montages: common average reference, average reference, and bipolar longitudinal and transverse montages, with standard 10-20 electrode placements. During the 3-hour recording, both awake and sleep states were assessed, including tests like hyperventilation and intermittent photic stimulation at frequencies of 1â€“20 Hz, both with the eyes open and closed. The last 30 minutes of the EEG session also included intermittent photic stimulation and hyperventilation.

Evaluation of EEG:

The EEG was analyzed to identify any focal epileptiform or non-epileptiform abnormalities. The study specifically focused on the evaluation of background rhythm, symmetry, regularity, amplitude, and focal sharp & slow waves for patients with focal onset epilepsy. For generalized onset epilepsy, it examined generalized spikewaves and polyspike-wave complexes, looking at their frequency and duration. In the case of JME, more than one-third of patients exhibited a photoparoxysmal response to intermittent photic stimulation. For diagnosis, the presence of generalized spike-wave or polyspike-wave complexes at a frequency of 3-5.5 Hz was required, and an ictal recording was not necessary. Similarly, interictal EEG in patients with GTCA also required the presence of generalized spike-wave or polyspike-wave at 3-5.5 Hz for a definitive diagnosis.

Results

A) 

B) 

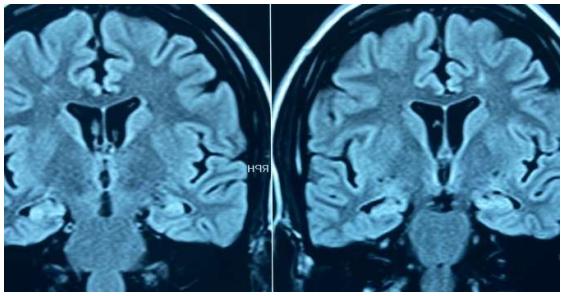
C) 

Figure 1. Coronal fluid-attenuated inversion-recovery (FLAIR) image of MRI with epilepsy protocol showing A) right mesial temporal sclerosis, B)left mesial temporal sclerosis; C) Bilateral mesial temporal sclerosis respectively.

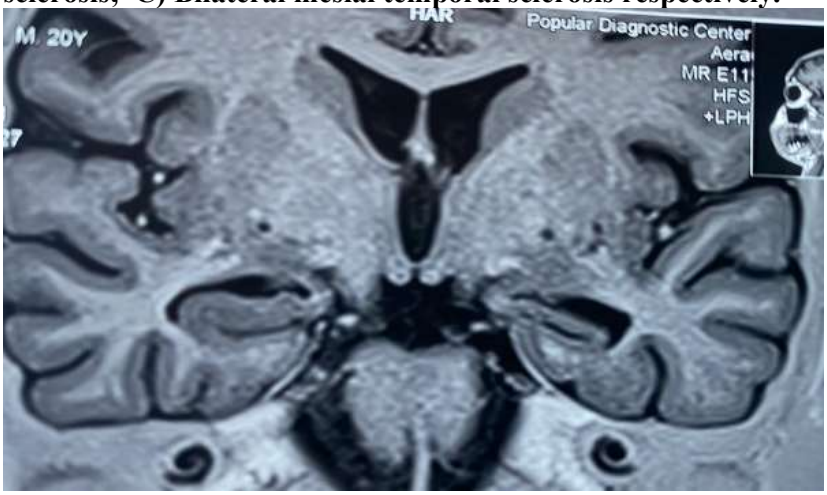


Figure 2 : Coronal fluid-attenuated inversion-recovery (FLAIR) image of MRI with epilepsy protocol showing bilateral hippocampal atrophy.

A) B)

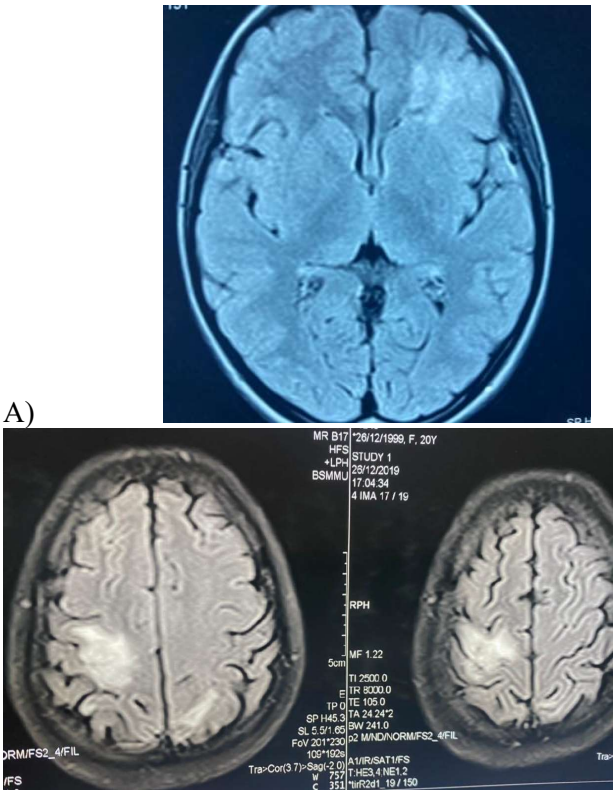


Figure 3: Axial T1 weighted MRI shows features of encephalitis (A and B)

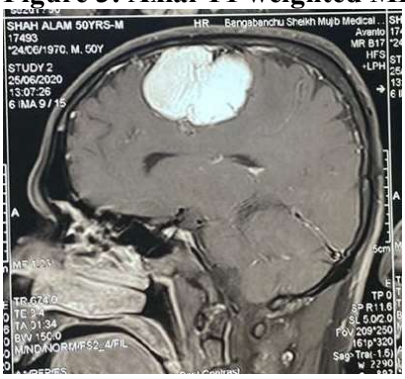


Figure 4: Sagital T1 weighted MRI shows right frontal lobe meningioma.

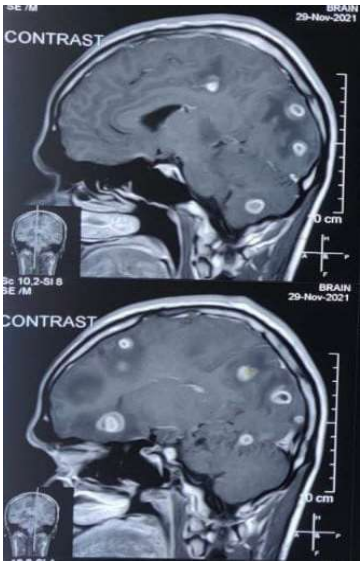


Figure 5: Sagital T1 weighted MRI of the brain shows multiple tubercolema.

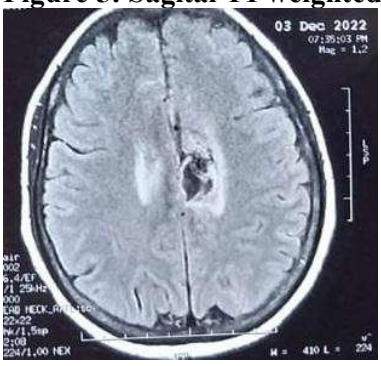


Figure 6: Axial T1 weighted MRI of the brain shows arteria venus malformation in late frontal lobe.

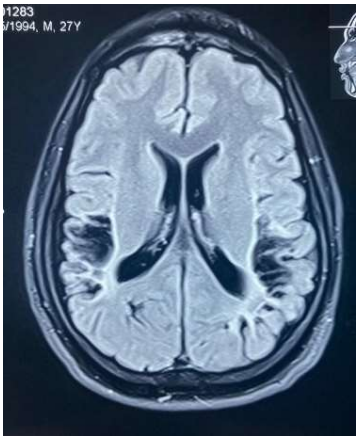


Figure 7: Axial FLAIR image of MRI showing bilateral parietal post hypoxic enchaphalomalacia.

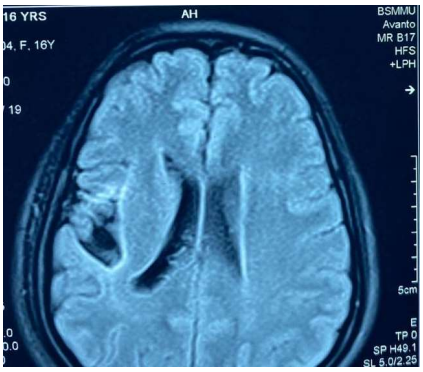


Figure 8: Axial FLAIR image of MRI showing right parietal post hypoxic enchaphalomalacia

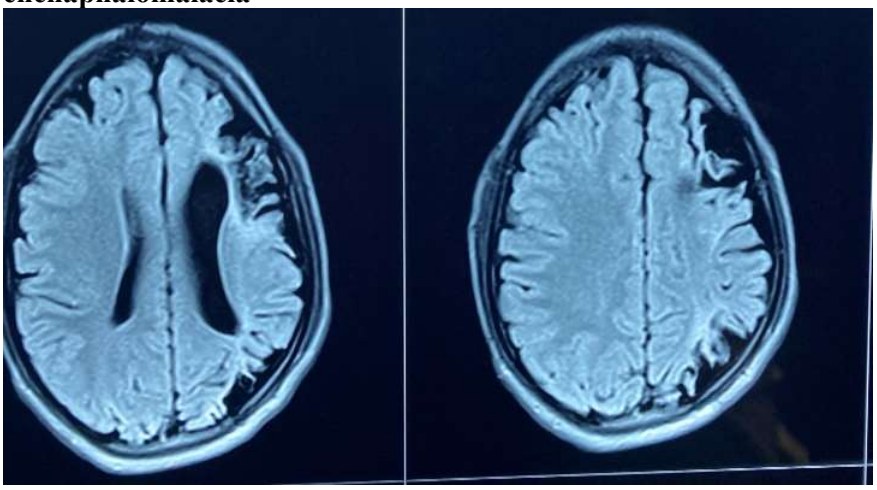


Figure 9: Axial FLAIR image of MRI showing post hypoxic left parietal occipital enchaphalomalacia

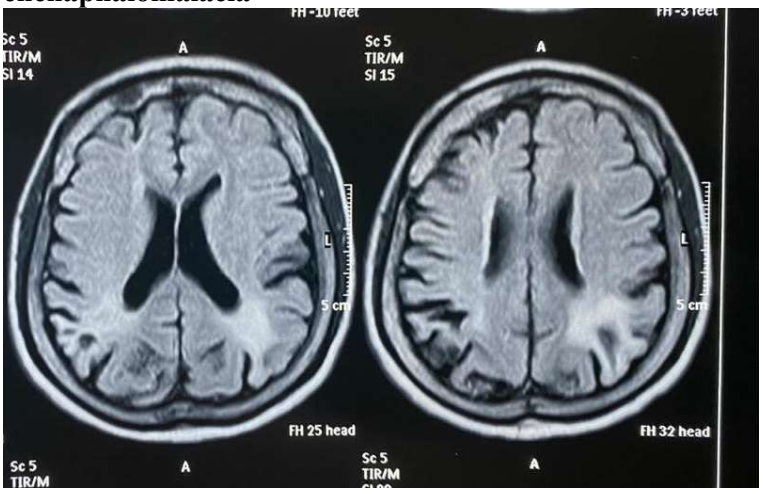


Figure 10: Axial FLAIR image of MRI showing post hypoxic left occipital enchaphalomalacia

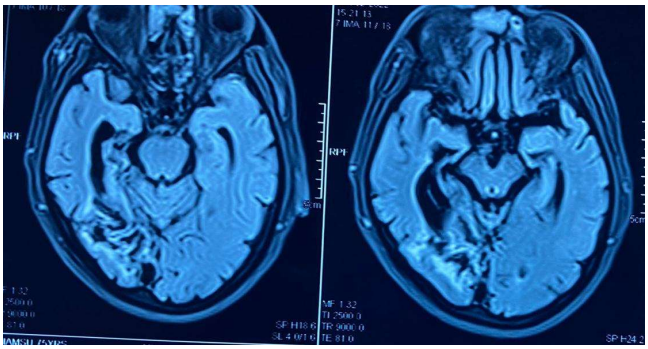


Figure 11: Axial FLAIR image of MRI showing post hypoxic right occipital enchaphalomalacia

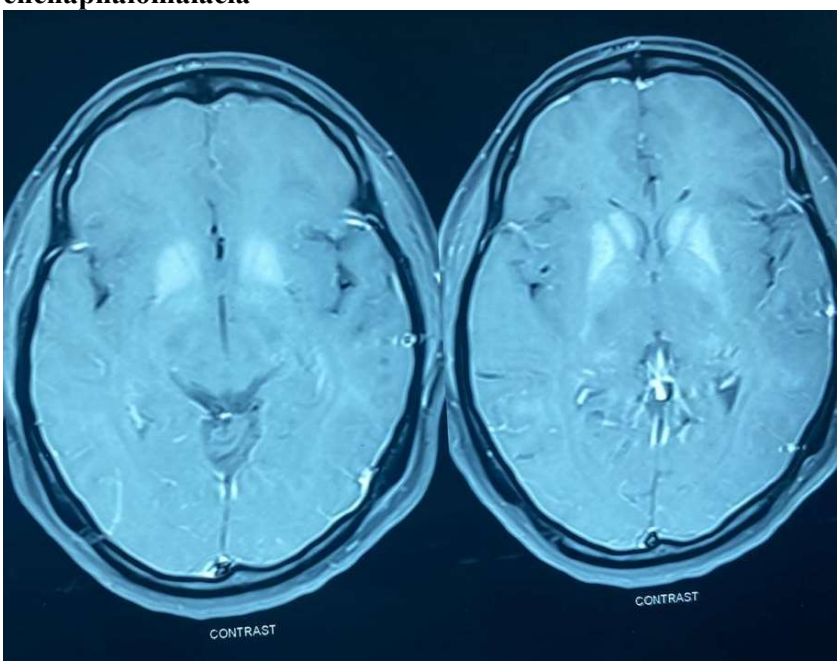


Figure 12: Axial FLAIR image of MRI shows bilateral basal Ganglaia calcification

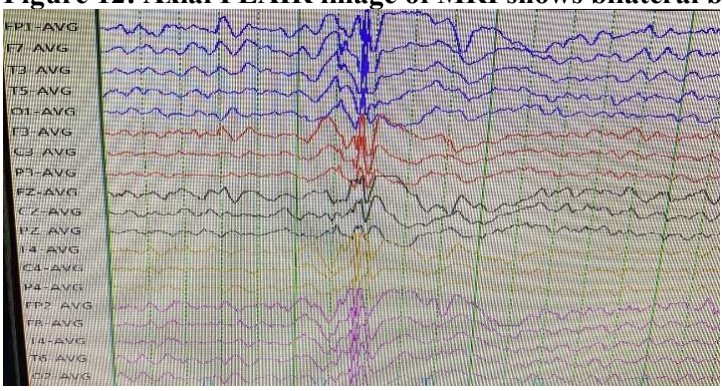


Figure 13 : An interictal electroencephalogram (EEG) of a young man aged 18 years old with JME showing his generalized poly spike wave pattern on a normal awake background.

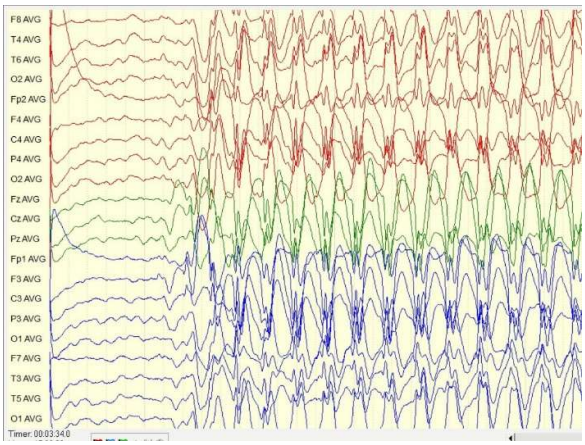
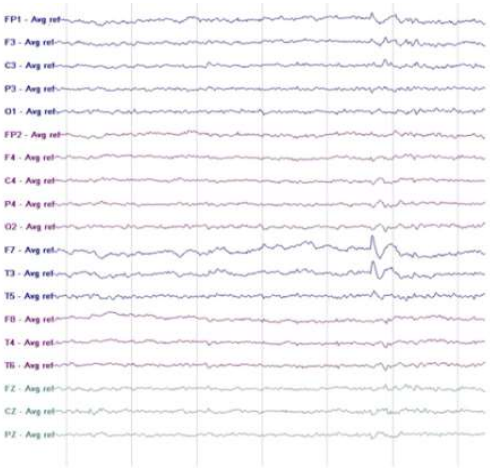


Figure 14: An interictal electroencephalogram (EEG) of a young man aged 21 years old with epilepsy with GTCA, showing his generalized spike wave pattern on awakening from sleep on a normal awake background.

A 

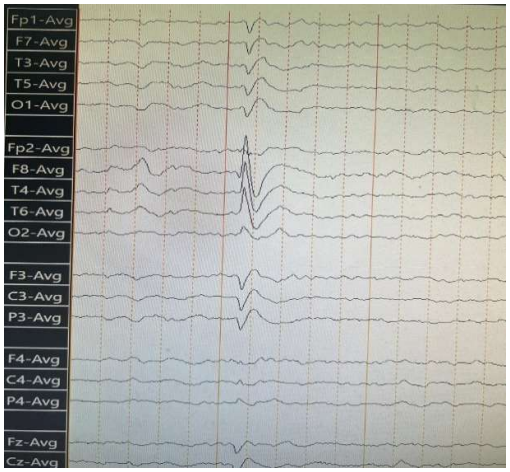
B 

Figure 15: A) Electroencephalogram in a 53- year- old patient with mesial temporal lobe epilepsy with hippocampal sclerosis (left- sided hippocampal sclerosis) and B) This EEG shows interictal right anterior temporal sharp and slow discharge recorded from a 28 year-old boy with right temporal lobe epilepsy due to mesial temporal sclerosis.

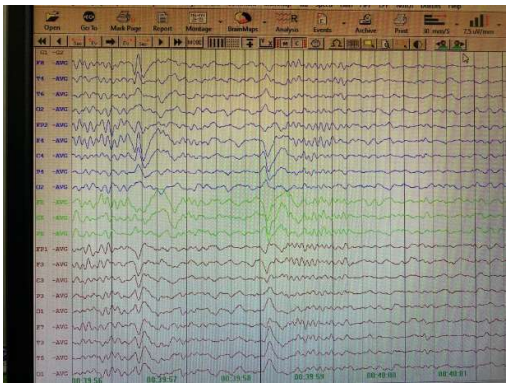


Figure 16: This EEG shows interictal right frontal sharp and slow wave discharge

recorded from a 32 year-old boy with right frontal lobe epilepsy due to encephalitis .

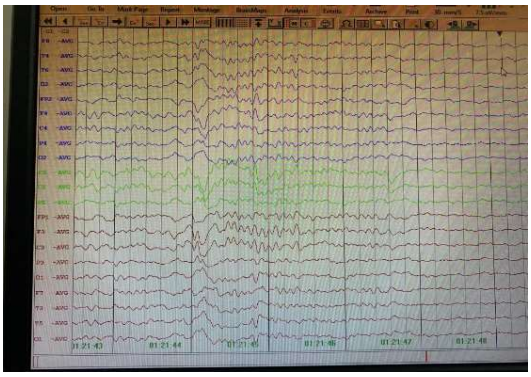


Figure 17: This EEG shows interictal left centro parietal sharp and slow pattern recorded from a 38 year-old boy with left fronto-parital lobe epilepsy due to post stroke hypoxic enchaphalomasic change .

Figure 18: Age distribution of our study people

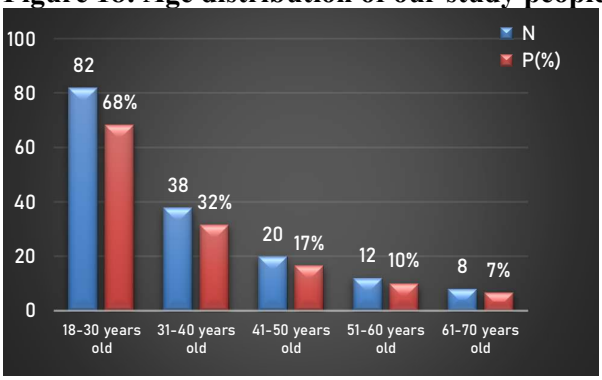


Figure 19: Distribution of our study people based on their gender

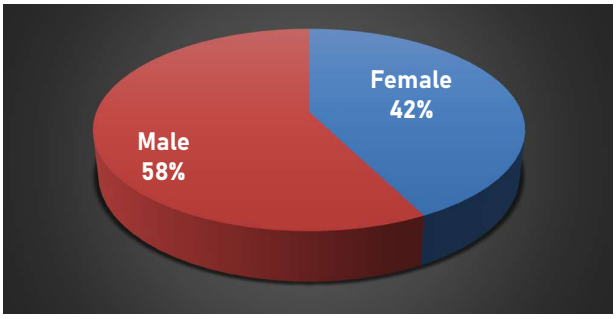


Table 1: Distribution of our study patients based on EEG & MRI (n=160)

Classification	N	P (%)	P-value
Focal onset Epilepsy (N=120)			
Temporal lobe Epilepsy	95	79.2%	0.002
Frontal lobe Epilepsy	12	10%	
Parietal lobe Epilepsy	6	5%	

Occipital lobe Epilepsy	7	5.8%	
Generalized Epilepsy (N=40)			
Juvenile Myoclonic Epilepsy (JME)	24	60%	0.002
Generalized tonic-clonic Seizures (GTCS)	16	40%	

Table 2: Distribution of the study patients based on incidence of focal onset epilepsy (n=120)

Focal onset Epilepsy	***N***	***P(%)***	***P-value***
Temporal lobe Epilepsy			
MTS left	*30*	*25.0*	*0.002*
MTS right	*25*	*20.8*	
Bilateral Hippocampucal atrophy	*20*	*16.7*	
Bilateral MTS	*7*	*5.8*	
Post stroke epilepsy	*5*	*4.2*	
Viral encephalitis	*8*	*6.7*	
Frontal lobe Epilepsy			
Meningioma	*6*	*5.0*	*0.001*
Viral encephalitis	*2*	*1.7*	
Arteriovenous malformation	*3*	*2.5*	
Tuberculoma	*1*	*0.8*	
Parietal lobe Epilepsy			
Enchaphalomalacia due to cerebral palsy	*3*	*2.5*	*0.001*
Post stroke epilepsy	*3*	*2.5*	
Occipital lobe Epilepsy			
Enchaphalomalacia due to Cerebral palsy	*4*	*3.3*	*0.002*
Post stroke epilepsy	*3*	*2.5*	

Table 3: Distribution of our study subjects by seizure semiology classification

Semiology	**Number**	**Percentage**
Frontal lobe epilepsy		
Versive seizure	12	10.00
Temporal lobe epilepsy		
Olfactory aura	18	15.00
Gustatory aura	12	10.00
Psychic aura	19	15.83
Abdominal aura	21	17.50
Auditory aura	16	13.33
Autonomic aura	17	14.17
Parietal lobe epilepsy		
Somatosensory aura	6	5.00
Occipital lobe epilepsy		
Visual aura	7	5.83
Focal to bilateral tonic clonic seizure	120	100
Juvenile Myoclonic Epilepsy (JME)		

Myoclonic	12	30.00
Absence + Myoclonic	8	20.00
Myoclonic + GTCS	4	10.00
Generalized tonic-clonic Seizures (GTCS)		
GTCS	16	40.00

In figure 18 we showed the age distribution of our study people. Majority (68%) of our patients were aged between 18-30 years old, followed by 32% & 17% were 31-40 & 41-50 years old respectively. The least prevalence 7% & 10% was found among 61-70 & 51-60 years old respectively.
In figure 19 we distributed our patients based on their gender. Majority of our patients were male (58%) compared to female(42%).
In table 1 we showed the distribution of our study people based on EEG & MRI. Majority (120) of our patients were from focal onset group and 40 patients were from generalized onset group respectively. Among of focal onset epilepsy we found the majority was temporal lobe (79.2%), 10% were frontal, 5.8% & 5 % were occipital & parietal lobe epilepsy. Among of idiopathic generalized onset epilepsy, we found 60% had JME & 40% had epilepsy with GTCA respectively.
In table 2 we showed the distribution of the study people based on incidence of focal onset epilepsy. Among the patients with temporal lobe epilepsy 25% had MTS left, 20.8 % & 16.7% had MTS right & bilateral hippocampucal atrophy respectively. Among the patients with frontal lobe epilepsy 5% had meningioma, 2.5% had arteriovenous malformation respectively. Among the patients with parietal lobe epilepsy 2.5% had both stroke & enchaphalomalacia . Among the patients with occipital lobe epilepsy 3.3% had Enchaphalomalacia & 2.5% had stroke respectively.
Table 3 shows the seizure semiology classification of our patients. Most of our patients had semiology of temporal lobe epilepsy. Among all patients 6.67% had versive seizure, 11.67% had psychic aura, 7.50% had abdominal aura & 12.50% had auditory aura**.** Focal to bilateral tonic clonic seizure was found in all patients.

Discussion

A study done by Scheffer and colleagues extensively discussed the revised classification of epilepsy and epilepsy syndromes, emphasizing etiology, and associated comorbidities.[18] In this revised classification, epilepsy is classified into three levels: seizure type, epilepsy, and epilepsy syndrome.[5] In our study, we found the majority (68%) of our patients were aged between 18-30 years old. Other literature found the mean age was 15 to 35 years.[19,20] Also noteworthy is the age range of spell onset from 3 to 60 years in our population.
In our study, we found the majority of our patients were male (58%) compared to female (42%). Hudak et al. found that 47% of the patients were male and 53% were female.[21] In this study, the majority (120) of our patients were from the focal onset group, and 40 patients were from the generalized onset group, respectively. Among focal onset epilepsy, we found the majority was temporal lobe (79.2%), 10% were frontal, 5.8%, and 5% were occipital and parietal lobe epilepsy. Among idiopathic generalized onset epilepsy, we found 60% had JME and 40% had epilepsy with GTCA, respectively. Hudak et al. found in their study that generalized onset was 9% and focal onset was 91%. Among patients with focal onset, 56% were temporal, 36% were frontal, and 3% and 5% had occipital and parietal lobe epilepsy, respectively.[21]

Hudak et al. and other studies found that temporal lobe epilepsy is the most common cause of focal-onset seizures. Frontal lobe seizures are also common, whereas onsets of parietal and occipital lobe seizures are relatively rare. When the MRI data were evaluated in conjunction with the seizure semiology and ictal EEG pattern, 53% of patients with temporal lobe seizures had the mTLE. The most common identified cause of mTLE is febrile seizures early in life.[22-24] IGE is a common group of epilepsies, accounting for approximately 15%-20% of persons with epilepsy. JME has a prevalence of 4-11% of all epilepsies and an incidence of 0.4-0.9%. Epidemiological data are limited, although, in one study, GTCA accounted for one-third of all adolescent-onset IGEs. In this study, most of our patients had semiology of temporal lobe epilepsy. Among all patients, 6.67% had versive seizure, 11.67% had psychic aura, 7.50% had abdominal aura, and 12.50% had auditory aura. In our study, we used semiology, EEG, and MRI of the brain to classify the seizure type, epilepsy, and diagnose the etiology of epilepsy and epilepsy syndrome.

Limitations of the study

Our study was a single centre study. We showed the classification of focal onset and generalized epilepsy because of our limited resource and short study period. There are more classifications of epilepsy that needs to be identified and evaluated. After evaluating once those patients we did not follow-up for a long term and have not known other possible interference that may happen in the long term with these patients.

Conclusion and recommendations

In our study, we tried to evaluate the classification of focal onset and generalized onset epilepsy by semiology, EEG and MRI of the brain. We found patients with temporal, frontal, parietal & occipital lobe epilepsy among the focal onset epilepsy group. Among the idiopathic generalized epilepsy, we found that JME & Epilepsy with GTCA was present in our patients. So further study with a prospective and longitudinal study design including larger sample size needs to be done to identify and evaluate more classifications of epilepsy by health professionals to prevent the adverse effects of epilepsy.

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