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A STUDY OF CLINICAL AND IMAGING FEATURES OF REFRACTORY EPILEPSY IN PATIENTS ATTENDING A TERTIARY CARE HOSPITAL

Neurology

Dr Sudarshan Reddy* Post Graduate Resident, Department of Neurology, Osmania Medical College *Corresponding Author

Dr Vineela Post Graduate Resident, Department of Neurology, Osmania Medical College

Dr K. Sreelekha Intern, Maheswara Medical College

Dr G. Sree Ranga lakshmi Head Of the Department, Department of Neurology, Osmania Medical College

Dr B. Archana Associate Professor, Department of Neurology, Osmania Medical College

ABSTRACT

Background & objectives Epilepsy is a chronic noncommunicable disease of the brain that affects people of all ages. It is estimated that 70% of people living with epilepsy could live seizure free if properly diagnosed and treated. The exact magnitude of medically intractable epilepsy in India is unknown. The factors that determine the outcome of epilepsy are age of onset and the type of seizure. The aim of our study was to identify the causes of refractory epilepsy **Objectives:** To identify the clinical and imaging features in refractoriness. To determine the importance of early and proper evaluation of seizures in refractory epilepsy. **Methods:** It was an observational study in patients of refractory epilepsy. After taking informed consent, detailed history was taken and examination was done. **Results:** 105 Patients with refractory epilepsy were included in the study. Majority were between 21-30 years age group. 44% of the patients had the onset of seizures below 10 years. Focal seizure type (68 patients) was the most frequent type. Status epilepticus was found in 41.9% of the patients. Engel's seizure score showed the association of high seizure score with RE. **Interpretation & Conclusions:** The most common cause for refractoriness was found to be congenital anomalies in children and calcification in adults.

KEYWORDS

Anti-Epileptic Drugs, Engel's seizure score, Refractory epilepsy, Status epilepticus.

INTRODUCTION:

Epilepsy is a condition in which the patient is prone to recurrent unprovoked seizures. This definition is clinically applied as having 'two unprovoked seizures more than 24 hours apart.' Epilepsy is considered as active when an epileptic patient has had seizures in the last 5 years.[1] International League Against Epilepsy defined drug resistant epilepsy as failure to achieve sustained seizure freedom for a sufficiently long period of time after an adequate trial of two tolerated and appropriately chosen AEDs. A sufficiently long period of time is operationally defined for an individual patient as three times the longest inter-seizure interval for that patient, or 1 year, whichever is longer[2]

There is limited data available specifically addressing the risk factors and predictors associated with refractoriness. Besides, predictors of intractable epilepsy in an Indian population may be different in view of different aetiologies. Early identification of patients who are at high risk of developing intractable epilepsy would be essential in parental counselling and selecting patients for more intensive investigations and treatment.

AIM AND OBJECTIVES

AIM

- To identify the aetiological factors of refractory epilepsy.

OBJECTIVES

- To identify the association of clinical and imaging features in refractoriness.
- To determine the importance of early and proper evaluation of seizures in refractory epilepsy

MATERIALS AND METHODS

It was an observational study conducted in the Department of Neurology over a 2 year period from January 2021 to January 2023. Institutional ethics committee approval and consent from the patients were obtained.

Selection Of Subjects

Inclusion Criteria:

Patients above 1 year of age and on adequate treatment with two AEDs either alone or in combination, with proper dosage and compliance and had uncontrolled seizures.

Exclusion Criteria

Patients with pseudo seizures and patients with poor compliance in the form of irregular medication or inadequate dosing were excluded.

Study Design

Detailed history of seizure was taken which included the following:Age of onset, type of seizure and semiology of seizures, frequency, response to antiepileptic drugs, longest seizure free interval, history of status epilepticus (SE) before or as a part of presentation.

Details of birth, developmental mile stones, history of febrile convulsions and head trauma were noted. A note also was made regarding family history of seizure disorder and history of scholastic performance, behavioural abnormality and focal motor deficits. Semiology of seizure including auras, autonomic symptoms, motor phenomenon including generalization, focal seizures, tonic posturing, clonic jerks, Jacksonian march, versive head turning, tonic-clonic movements, myoclonic jerks, infantile spasms, drop attacks, post ictal phenomenon were collected. Details regarding precipitating and triggering factors, time of occurrence of seizure were also noted.

Seizure Scoring System

Engels seizure burden score gives clue about the seizure frequency and disability. The score is a longitudinal scale from 0-12. (Table 1) Score less than 5 is associated with no disability and usually without the loss of consciousness and loss of muscle tone. Score of 6-12 is associated with disability and Intractability.[3]

Seizure Frequency Scoring System

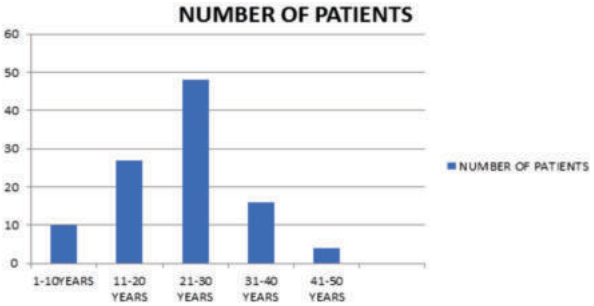
Seizure frequency	Score
Seizure-free, off antiepileptic drug	0
Seizure-free, need for antiepileptic drug unknown	1
Seizure-free, requires antiepileptic drugs to remain so	2
Nondisabling simple partial seizures	3
Nondisabling nocturnal seizures only	4
1–3 per year	5
4–11 per year	6
1–3 per month	7
1–6 per week	8
1–3 per day	9
4–10 per day	10
>10 per day but not status epilepticus	11
Status epilepticus without barbiturate coma	12

Neurological Examination
Detailed neurological examination was done for all patients

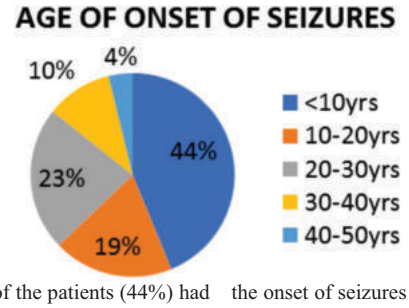
Electro Encephalogram
EEG and MR imaging of brain were done in all patients.

RESULTS
Total 105 patients with refractory epilepsy were included in the study.

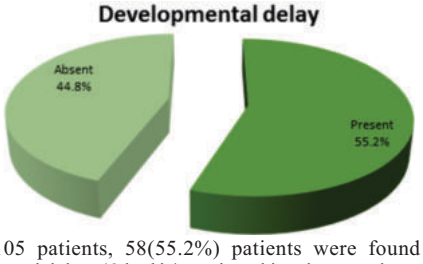
Age Distribution



Majority of patients with refractory epilepsy were between 21 and 30 years of age. Males were 70 and females were 35. Majority of the patients (44%) have the onset of seizures below 10 years. Focal seizures were seen in 68 patients followed by generalised seizures in 37 patients. Sixteen (15.2%) patients had nocturnal seizures and 17 (16.1%) patients had seizures only in awake state. Remaining 72(68.5%) patients had seizures irrespective of the time of the day.



Majority of the patients (44%) had the onset of seizures below 10 years.



Among 105 patients, 58(55.2%) patients were found to have developmental delay, 42 had h/o perinatal insult, mental retardation in 30 patients and family history of seizures was present in 10 patients. Febrile seizures were seen in 25 patients.

Status epilepticus was found in 44(41.9%) patients. Out of these 44 patients, 10 patients had status epilepticus at onset of illness and 34 patients had status during the course. Engel's seizure score questionnaire showed the association of high seizure score with RE. Seizure score of 6 and 8 were observed in majority of the patients.

30 patients had aphasia/dysarthria, 30 patients had cognitive decline, visual defects seen in 20 patients, hemiparesis seen 22 patients.

In our study, EEG was abnormal in 76% of the patients, bilateral epileptiform discharges were seen in majority of patients.

MRI Brain: MRI was abnormal in all patients

Etiology	Number of Patients
Congenital anomalies	22
Mesial temporal sclerosis	10
Hypoxic ischemic encephalopathy	18
Rasmussen encephalitis	4
Calcifications	35
Infarction	8
Trauma	5
Tumors	3

Congenital Anomalies

Pathology	Number of Patients
Tuberous sclerosis	4
Focal cortical dysplasias	6
Heterotopias	4
Schizencephaly	6
Hemiatrophy	2

In childhood onset RE , the most common aetiology was congenital malformations, seen in 22 patients followed by HIE in 18 patients. In adults most common abnormalities were calcifications (35 patients) followed by gliosis (5 patients).

Aetiology for calcifications were Neurocysticercosis (20) followed by Tuberculosis (10), 2 had AVMs(2), unknown(3).

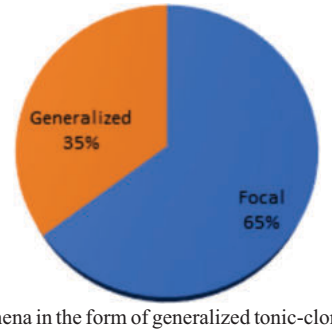
Summary

	N=105	Percentage
Male sex	70	66.66
Age of onset <30years	90	85.7
Type of seizures		
Generalised	37	35.2
Focal / focal with secondary generalised	68	64.7
Developmental delay	58	55.2
Perinatal injury	42	40
Febrile seizures	25	23.8
Status epilepticus	44	41.9
Seizure score 1-3/wk	50	47.6
1-3/day	20	19
Neurological abnormality	67	63.8
EEG abnormality	80	76
MRI imaging		
Congenital anomalies	22	20.9
Mesial temporal sclerosis	10	9.5
HIE	18	17.1
Calcifications	35	33.33

DISCUSSION:
The various aetiological factors of Refractory Epilepsy have been evaluated in this study. The basic factor that determines the prognosis is the underlying aetiology, identification of these factors helps in proper management and prognostication.

In our study, males were more affected than females similar to the study done by Akhondian etal[4]. The age of onset of seizures was below 10 years in majority of patients and similar to the data of Roy PL et al [5] and Wassenaaretal[6].

The commonest seizure types included focal seizures or focal with secondary generalization seen in 68 patients and generalised seizures in 37 patients. History of aura was present in 29 patients.



Motor phenomena in the form of generalized tonic-clonic seizures was documented in 37 patients, tonic, clonic movements involving one side of body seen in 24 patients, complex partial seizures seen in19 patients, myoclonic seizures were present in 22, jacksonian march was documented in 3 patients.

Generalized seizure type had the worst prognosis that was more refractory to medication which was similar to a study done by Walczak et al[7]

In our study developmental delay was seen in 58(55%) patients. The causative factors were hypoxic ischemic encephalopathy, congenital anomalies and vascular insults. These results were similar to studies by Udani et al [8](Mumbai), Singhvi et al[9]

Perinatal insult was seen in 42 patients, early onset seizures were associated with RE, similar to the study of Tripathi et al [10] and Berg et al. [11]

Febrile seizures were present in 25 patients (23.8 %) in this study. Among 25 patients 10 patients had complex febrile seizures and 15 patients had simple febrile seizures. The association of febrile seizures with refractoriness is controversial. Tripathy et al[10] observed febrile seizures as independent factor.

Kwong et al[12] showed it as significant on multivariate analysis but not on univariate analysis. Berg et al[13] observed a slightly protective association between febrile seizures and intractability. Camfield et al[14] study found association of RE with prolonged febrile seizures.

In our study, Engel's seizure score was also taken as a parameter, to study the burden of RE. All the patients presented with high seizure score; out of which majority have seizure score >1-3/day to 1-3/week and were associated with worst prognosis. This was similar to the study of So EL et al. [15]

Status epilepticus was found in 44 patients (41.9%). Among 44 patients 10 patients had status epilepticus at the onset of epilepsy. 34 patients had during illness, these patients had structural pathology like focal cortical dysplasia, HIE, heterotopias and tuberous sclerosis. Patients who had status were more refractory to medical management. Thus, presence of status epilepticus found to be associated with refractory epilepsy. This is identical with most of the studies.

Abnormal EEG was seen in 80 patients who constituted 76.1%, similar to many other studies. Abnormalities included were generalised epileptic discharges in 50 patients, focal epileptiform activity in 15 patients, hypsarrhythmia seen in 3 patients, hemispheric dysfunction seen in 4 patients, bihemispheric dysfunction seen in 8 patients. An abnormal EEG was associated with poor outcome.

In this study congenital malformations were seen in 22 patients. These are tuberous sclerosis 4 patients, FCD in 6, schizencephaly in 6, heterotopia in 4 and hemi atrophy in 2 patients. Malformations of cortical development (MCDs) were common causes of medically refractory epilepsy, particularly in children, this is similar to a study by Barkovich et al[16]

In this study focal cortical dysplasia were present in 6 patients and 4 of them s had h/o status epilepticus.

In our study calcifications were found in 35 patients, majority of patients with NCC had multiple calcifications and significantly higher seizure frequency and treatment refractoriness similar to the Atulagarwal et al[17]

CONCLUSION:

We concluded that the following factors are associated with refractoriness to medical treatment

1. Childhood onset of seizures,
2. Focal onset seizures,
3. Multiple seizure types,
4. Myoclonic seizures,
5. Developmental delay,
6. Congenital anomalies
7. Structural abnormality on imaging,
8. Abnormal EEG,
9. High seizure score

In children most common cause was found to be congenital anomalies and in adult age most common cause found to be calcifications.

In patients with epilepsy, thorough evaluation should be done which includes detailed seizure semiology, imaging and selection of appropriate AED. Proper counselling should be given about the need for continuation of the drugs and appropriate management of associated comorbid conditions.

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