Original Research Article

Clinico-social profile of adult patients with uncontrolled seizures attending a neurology OPD at a tertiary care hospital in Goa

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ABSTRACT

Background: Of the 70 million persons with epilepsy (PWE) worldwide, nearly 12 million PWE are expected to reside in India. Nearly one-third of the patients with newly diagnosed epilepsy on long-term follow-up will have their seizures unsatisfactorily controlled by treatment with available anti-epileptic drugs (AEDs). Objective of this study was to study the clinico-social profile of adult patients with uncontrolled seizures.
Methods: A cross-sectional study was conducted over a period of 3 months among 106 patients with uncontrolled seizures. Universal sampling was used to select the participants, and a semi-structured questionnaire was used to collect the data.
Results: Poor compliance to medication was the most common cause for uncontrolled seizures (51.8%) and was significantly associated with those who were prescribed <3 AEDs (OR=2.532, p=0.041). Focal with impaired awareness (34.9%) and generalised tonic clonic seizures (GTCS) (34.9%) were the most commonly seen.
Conclusions: Patient compliance is of utmost importance in maintaining good seizure control.

Keywords: Epilepsy, Seizures, AEDs, Poor-compliance, Goa

INTRODUCTION

According to the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE), epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neuro-biologic, cognitive, psychological, and social consequences of this condition.

Seizures may be either provoked or unprovoked. Provoked seizures, also known as acute symptomatic seizures, may result from electrolyte disorders, toxins, head injury, infectious processes, vascular anomalies, tumours or other mass lesions, and many other causes.[1]

Uncontrolled seizures

Studies suggest that epilepsy fails to come quickly under control with medicines in about one-third of adults.[2]

Seizures can be uncontrolled for four broad reasons.[2]

The diagnosis is wrong (mis-classified epilepsy). The treatment is wrong (wrong medication, sub-optimal doses). Despite the best treatment, triggers or lifestyle factors may affect seizure control. Poor compliance with medicine or factors such as severe sleep deprivation, alcohol consumption, stress may limit how well medication works. Properly diagnosed seizures sometimes

do not respond even to the best medical treatment (medically refractory epilepsy).

Magnitude of the problem

The estimated burden of epilepsy using the disability-adjusted life years (DALYs) accounts for 1% of the total burden of disease in the world, excluding that due to social stigma and isolation, which further add to the disease burden.[3] Of the 70 million persons with epilepsy (PWE) worldwide, nearly 12 million PWE are expected to reside in India; which contributes to nearly one-sixth of the global burden.[4] Nearly one-third of the patients with newly diagnosed epilepsy on long-term follow-up will have their seizures unsatisfactorily controlled by treatment with available AEDs.[5] The risk of premature death in people with epilepsy is up to three times higher than for the general population.[6]

Need for the study

People with epilepsy tend to have physical (such as fractures and bruising from injuries related to seizures), as well as psychological conditions, including anxiety and depression. Seizures not only affect the individual but hidden and unpredictable nature of epilepsy makes it even harder for families. Moreover, the stigma related to having epilepsy can be the biggest struggle of the patient's journey. Hence this research was carried out to study the clinico-social profile of adult patients with uncontrolled seizures in order to help improve their quality of life.

METHODS

Study setting

Out-patient department (OPD) of Neurology at Goa Medical College.

Study design and duration

A cross-sectional study was conducted over a period of 3 months from May to July 2024.

Sampling and sample size

All patients attending the Neurology OPD at Goa Medical College with uncontrolled seizures within the 3 months of the study period were universally included in the study and the sample size at the end of the 3 months was 106.

Study participants

The study included all patients 18 years and above, with first seizure occurring minimum 6 months prior to the date of interview, taking at least one Anti-Epileptic Drug (AED) since the diagnosis and having at least one seizure in the past 3 months (i.e., after three months of taking any AEDs).[7]

Patients less than 18 years, having seizure free period of 3 months or more, patients diagnosed to have epilepsy less than 6 months ago were excluded from the study.

Data collection tool

The interviewer administered questionnaire contained four components:

Sociodemographic data, seizure related data, treatment data, EEG and MRI reports. The cause for uncontrolled seizures was arbitrarily considered to be one of these five categories: (i) poor drug compliance (missing more than one dose the week prior to the seizure). (ii) suboptimal doses of appropriate drug (iii) inadequate sleep (iv) medically refractory seizures (v) wrong medication (vi) triggers- menses, alcohol intake, sleep deprivation, febrile state.

Ethical clearance

Approval was obtained from the Institutional Ethics Committee of GMC (Reg No; ECR/83/Inst/GOA/2013/RR-20; Ref Code: GMCIEC/2013/310).

Statistical analysis

Data was entered and analysed using Microsoft Excel. Descriptive statistics for continuous data with normal distribution were expressed as mean and standard deviation. Frequency distribution was estimated for categorical data and expressed in percentages. Chi square test was used to find the association of categorical variables with compliance to medication and all variables with $p<0.05$ were considered statistically significant.

RESULTS

The socio-demographic characteristics of the participants are shown in Table 1. The mean age of the participants was 35.1±14.6 years. A little more than half of the patients, i.e. 60 (56.6%) were male. Almost equal number were married (48.1%) and single (51.9) i.e. unmarried, widows, widowers or divorcees. A large majority i.e.75 (70.8%) of the participants were Hindus. Although more than half of the participants, 62 (58.4%) were educated up to high school, 15 (14.2%) of the participants were illiterate. Majority, 80 (75.5%) of the participants lived in nuclear families. Most of the participants belonged to middle class families as per the Updated BG Prasad classification of April 2024.[8]

Table 2 shows that 43, (40.5%) of the participants had an onset of seizures in adulthood. 12, (11.3%) of the individuals had their first seizure during infancy. Almost half i.e. 46 (43.4) of the participants were on dual anti-epileptic drugs (AEDs). levetiracetam (53.8%) and carbamazepine (49.1%) were the most commonly used drugs. A small proportion of the participants had

comorbidities like diabetes mellitus (DM), hypertension (HTN), bronchial asthma (BA) and HIV.

Table 1: Socio-demographic characteristics of the participants (n=106).

| Characteristic	Frequency (%)
Sex	
Male	60 (56.6)
Female	46 (43.4)
Marital status	
Unmarried	52 (49.1)
Married	51 (48.1)
Widow/widower/divorced	3 (2.8)
Religion	
Hindu	75 (70.8)
Christian	15 (14.2)
Muslim	16 (15.1)
Education	
Illiterate	15 (14.14)
Up to high school	62 (58.4)
Above high school	29 (27.4)
Type of family	
Nuclear	80 (75.5)
Joint	18 (17.0)
Three-generation	05 (4.7)
Broken	03 (2.8)
Socio-economic status	
Upper	29 (27.3)
Upper middle	10 (9.4)
Middle	43 (40.6)
Lower middle	07 (6.6)
Lower	17 (16)
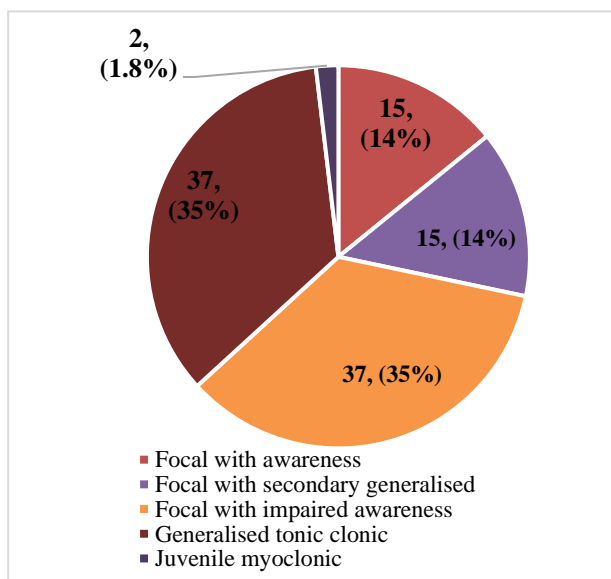
Figure 1: Types of seizures.

A total 58 (54.7%) of the patients had normal EEG findings as seen in Table 3. Abnormal EEG patterns like epileptiform discharges, slowing over temporal regions and spike and wave patterns were seen among 44 (41.5%) of the participants. Almost half, 46 (43.3%) of the patients also had MRI changes of which the most commonly seen change was gliosis followed by atrophy, sclerosis and encephalomalacia.

From Figure 1 it is evident that the most common type of seizure is GTCS (35%) and focal with impaired awareness (35%). Only 2 (1.8%) had Juvenile Myoclonic seizures.

Table 2: Seizure related characteristics.

Variable	Frequency (%)
Age at onset (n=106)	
Infancy	12 (11.3)
Childhood	28 (26.4)
Adolescence	21 (19.8)
Adulthood	43 (40.5)
Elderly	02 (1.8)
Past history (n=106)	
Foetal insult#	27 (25.4)
Organic cause*	33 (31.1)
No significant past history	46 (43.3)
Number of AEDs (n=106)	
Monotherapy	34 (32.1)
Dual therapy	46 (43.4)
Poly therapy	26 (24.5)
Type of AEDs	
Levetiracetam	57 (53.8)
Carbamazepine	52 (49.1)
Clobazam	39 (36.8)
Valproate	25 (23.6)
Phenytoin	08 (7.5)
Phenobarbitone	07 (6.6)
Lacosamide	07 (6.6)
Lamotrigine	03 (2.8)
Topiramate	03 (2.8)
Brivaracetam	01 (0.9)
Gabapentin	01 (0.9)
Co-morbidity other than epilepsy	
No comorbidity	94 (88.6)
DM	05 (4.7)
HTN	05 (4.7)
BA	01 (0.9)
Dementia	01 (0.9)
HIV	01 (0.9)

#Foetal causes- Prematurity, Low Birth Weight (LBW), Birth asphyxia; *Organic causes include- Tuberculoma, Encephalitis, Neurocysticercosis, Head injury, Cerebral Venous Thrombosis, Brain Tumour and Angioma.

Figure 2 shows that poor compliance to medication was the most common antecedent event for the uncontrolled seizure (51.8%). This was followed by inadequate sleep (15.1%) and suboptimal doses (9.4%). 2 (1.9%) of the individuals were found to have been prescribed wrong medication which was then corrected after the interview.

Since poor compliance with medication was the most common antecedent event for uncontrolled seizures, a univariate analysis was performed with sex, mean age, marital status, literacy, type of family, socio-economic status, mean duration of treatment and number of AEDs. Table 4 shows a significant association between poor compliance and ≤ 2 AEDs (OR = 2.532, p = 0.041).

Table 3: Results of EEG study and MRI of participants.

| Diagnosis	EEG Study (n=106)			MRI (n=106)		
	Normal N (%)	Abnormal N (%)	Not done N (%)	Normal N (%)	Abnormal N (%)	Not done N (%)
Focal with awareness (n=15)	09 (60)	05 (33.3)	01 (6.7)	05 (33.3)	10 (66.7)	00
Focal with secondary generalised (n=15)	09 (60)	04 (27.6)	02 (13.3)	04 (26.7)	10 (66.7)	01 (6.7)
Focal with impaired awareness (n=37)	18 (48.6)	18 (48.6)	01 (2.7)	20 (54.1)	15 (40.5)	02 (5.4)
Generalised tonic clonic (n=37)	21 (56.8)	16 (43.2)	00	24 (64.9)	11 (29.7)	02 (5.4)
Juvenile myoclonic epilepsy (n=2)	01 (50)	01 (50)	00	01 (50)	00	01 (50)
Total	58 (54.7)	44 (41.5)	04 (3.7)	54 (50.9)	46 (43.3)	06 (5.6)
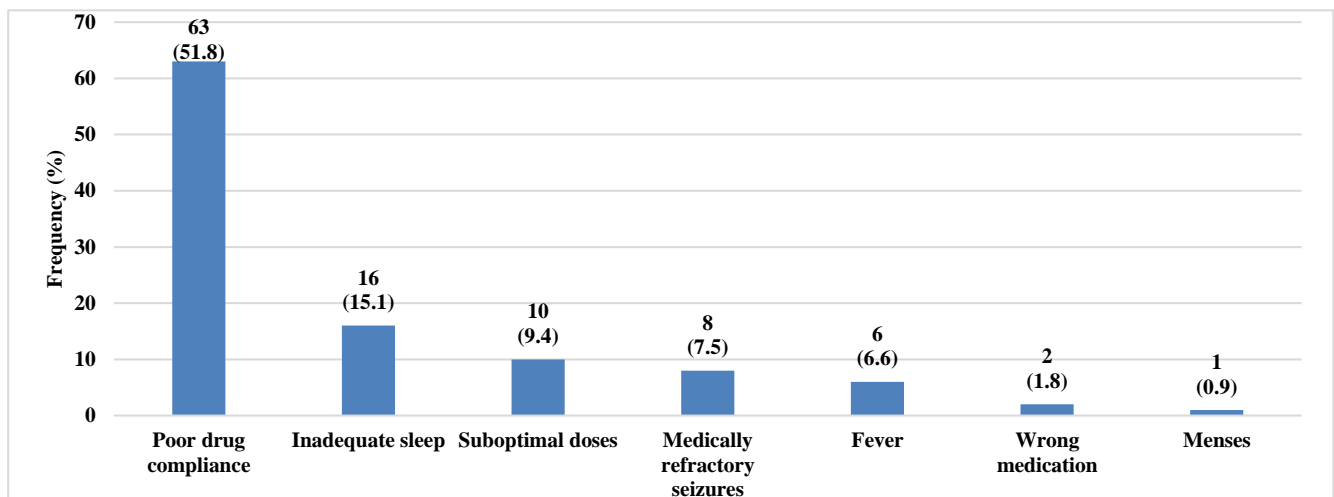
Figure 2: Antecedent events to seizure (n=106).

Table 4: Univariate analysis of factors associated with poor compliance to AEDs.

Variable	Compliance N (%)		P value	Crude OR	95% CI
	Poor (n=63)	Good (n=43)			
Sex					
Male	33 (55)	27 (45)	0.288	0.652	0.295-1.439
Female	30 (65.2)	16 (34.8)			
Mean age in years (SD)	35.3 (14.7)	34.8 (14.6)	0.880	-	-
Marital status					
Married	39 (58.8)	21 (41.2)	0.902	0.952	0.438-2.096
Single (unmarried, divorced, widow, widower)	33 (60)	22 (40)			
Literacy					
Illiterate	06 (40)	09 (60)	0.098	0.398	0.130-1.215
Literate	57 (62.6)	34 (37.4)			
Type of family					
Nuclear	48 (60)	32 (40)	0.835	1.100	0.448-2.699
Others (joint/broken/problem)	15 (57.7)	11 (42.3)			

Continued.

Variable	Compliance N (%)		P value	Crude OR	95% CI
	Poor (n=63)	Good (n=43)			
Socio-economic status*					
Upper	20 (69)	09 (31)	0.332	-	-
Middle	35 (58.3)	25 (41.7)			
Lower	08 (47)	09 (53)			
Mean years of duration of treatment (SD)	15.3 (13.8)	16 (12.5)	0.792	-	-
Number of AEDs					
≤2	52 (65)	28 (35)	0.041	2.532	1.026-6.251
>2	11 (42.3)	15 (57.7)			

AEDs: anti-epileptic drugs; *As per Modified BG Prasad Classification of April 2024

DISCUSSION

Almost half, 40.5% of our participants with uncontrolled epilepsy had an adult onset. Similar results were seen in a study on adult-onset seizures by Kaur et al in Punjab.[9]

However, Chauhan et all in their study mentioned that about 75% of epilepsy occurs during childhood.[10]

Although most patients (43.3%) did not have any significant past history, of those who did, central nervous system infections (tuberculoma, neurocysticercosis), cerebral venous thrombosis (CVT) and stroke were some of the most commonly seen antecedent causes. 25.4% of our participants had a history of foetal insult in the form of prematurity, perinatal asphyxia and birth trauma. Rao et al in their study said that preterm infants are at a high risk for central nervous system injury, with seizures occurring in 6% to 48% of this population.[11]

GTCS and Focal with impaired awareness each were seen in 35% of the participants with uncontrolled seizures. These findings were similar to that in a study conducted by Asadi-Pooya et al.[7] The first step towards the correct diagnosis of epilepsies is to establish whether a paroxysmal clinical event was actually an epileptic seizure or something else.[12] Accurate diagnosis of seizures depends on taking a careful medical history and use of brain imaging and other tests to assess abnormal patterns of electrical activity in the brain. Adequate assessments by neuropsychologists, speech and cognitive experts help complete the clinical picture of a person's seizures and indicate what course of treatment may be most beneficial.

Uncontrolled seizures can have many short-term and long-term consequences hence the cause of the uncontrolled seizure needs to be identified and corrected.

Among our study participants, 63 (59.4%) had poor compliance to medication, which was unlike that seen in the study by Asadi-Pooya et al where poor compliance to medication was least common (1%) cause for having uncontrolled seizures.[7] Similar findings were seen in a study by Kafle et al where 87% of the participants showed a good compliance to medication.[13] During data collection it was noted that many patients were not forthcoming with the details of non-compliance to medication, and only revealed the same on repeated questioning. Proper history taking is a must in patients with uncontrolled seizures to avoid unnecessary increase or change in the medication which adds to healthcare cost and pill burden.

A small proportion of our participants (15.1%) reported having inadequate sleep. Sleep disorders are said to disrupt seizure control and in turn sleep and vigilance problems can be exacerbated by seizures and by antiepileptic treatments.[14] This factor should also be addressed for by doctors in order to get adequate seizure control and better quality of life.

A total 10 (9.4%) of our study population were taking suboptimal doses of the appropriate drug. Possible reasons for the same may be, AED dosage is weight based therefore an increase in patient's weight may have caused the dose of the drug to be insufficient. Sometime, physicians reduce the dose of the AEDs if patients experience side effects. In patients who remain seizure free for 3 years, down titration and subsequent omission of AED may be attempted which results in suboptimal levels of AEDs. Polypharmacy also can lead to drug interactions that limit how well the drug may work. Patients often may develop tolerance to the AED, especially in benzodiazepines such as clobazam which is often used an add on drug. Certain individuals are far more likely than others to have a decrease in the effectiveness of medication over time due to differences in their body types, the type of their epilepsy, or its underlying causes.

Sometimes despite trials of maximal dosage of two appropriate AEDs patients continue to have seizures. Our study showed that 8 (7.5%) of the individuals had medically refractory seizures. Marouf et al in their study showed that 25.5% of their participants had drug resistant epilepsy.[15]

Neuroimaging and electroencephalography (EEG) are two widely used techniques to differentiate, verify, or exclude the diagnosis of epilepsy and characterize the underlying

pathology. Experts say that an EEG study is crucial to determining the seizure type and to diagnose and differentiate epilepsy syndromes. The role of neuroimaging on the other hand is to detect underlying cerebral lesions that may be causally related to the seizure disorder, provide a prognosis, and plan appropriate care.[16] In our study most of the study participants had normal EEG and MRI findings. Similar results were seen in the study in Iran.[7]

Hakami et al in their study documented potentially epileptogenic lesions in a minority of patients with seizures.[17] According to Winston et al despite advances in imaging technology, around 20-30% of patients with refractory focal epilepsy have normal MRI scans.[18]

A normal EEG does not rule out a seizure. Approximately one-half of all EEGs done for patients with seizures are interpreted as normal because the EEG only shows brain activity during the time of the test. Once the seizure is over, the brain rapidly returns to normal in most individuals.[19]

Since poor compliance to medication was found to be the most common antecedent event for uncontrolled seizures, a univariate analysis of factors associated with poor compliance was performed. Poor compliance to medication was seen among those who were prescribed ≤2 AEDs (p=0.041). We observed that patients who are prescribed >2 AEDs tend to be those who have followed up for a longer duration, have more frequent follow ups and are more aware of the importance of compliance to their treatment.

Poor compliance to AEDs is associated with increased risk of mortality, and a higher incidence of emergency department visits, hospital admissions, injuries, and fractures.[20]

Only 2 (1.8%) of the individuals were prescribed wrong medication for their seizure type. This may be due to both insufficient histories taking as well as inadequate history giving by the patient or relative. Many seizure medications have useful actions against a number of different seizure types. But some medicines are not right for certain types of seizures. Carbamazepine, for example is usually good for treating focal seizures, but not absence and myoclonic seizures.[21]

Medically refractory seizures were seen in 8 (7.5%) of the patients. Mean age of these patients was 18.125 years. One third of patients with epilepsy are said to have medically refractory seizures, which means that medicines don't work well, or at all, to control the seizures.[22]

Limitations

The reasons for non-compliance to medications was not asked for. That may be taken up in a separate study, as the knowledge of the reasons to non-compliance is important so that it can be corrected, and seizures can be controlled.

CONCLUSION

Poor compliance to medication was found to be the most common antecedent event of uncontrolled seizures. This not only increases morbidity and mortality but also increases the cost of healthcare. Medication adherence being the mainstay of treatment, regular patient education is a must.

Recommendations

Health education of the patients regarding the importance of compliance to medication should be stressed upon during each visit. Training and education of primary caregivers should also be done to assist in the treatment. Behavioural interventions can also be part of the holistic treatment. Frequent provision of tertiary level of care may be arduous for both the patient as well as the doctor hence the capacity building of primary healthcare team should be considered.

Implications for further research

Qualitative research in patients with epilepsy is required to understand the reasons behind poor compliance and to develop interventions to improve adherence.

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