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CROSS – SECTIONAL STUDY OF ADVERSE EVENTS ASSOCIATED WITH ANTIEPILEPTIC DRUG IN TERTIARY CARE SETTING

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ABSTRACT

Background: Antiepileptic drugs (AEDs) are essential for seizure control in epilepsy, yet they are frequently associated with adverse events (AEs) that can significantly affect patient adherence and quality of life. However, data on the prevalence and impact of AED- related AEs in tertiary care settings remain limited. **Objective:** To assess the prevalence, pattern, and predictors of adverse events associated with AEDs and evaluate their impact on quality of life among epilepsy patients in a tertiary care hospital. ***Methods:*** This cross-sectional study was conducted over three months at the Neurology Department of Government Medical College, Kozhikode. A total of 136 patients with epilepsy on AED therapy for at least six months were recruited. Data were collected using structured questionnaires and medical record reviews. Statistical analyses included chi-square tests and logistic regression using SPSS.

Results: Among 136 participants, 58.8% reported AEs, with aggression, somnolence, fatigue, and gastrointestinal disturbances being the most common. Levetiracetam and clobazam were the AEDs most frequently associated with behavioural AEs. Duration of AED therapy was the only variable significantly associated with AEs ($p = 0.045$). Quality of life was significantly lower in patients reporting AEs across all domains ($p < 0.001$). Despite AEs, 70% of affected patients did not consult healthcare providers, and only 30% received management interventions. ***Conclusion:*** A significant proportion of epilepsy patients on

AEDs experience adverse events, which negatively impact quality of life and adherence. Duration of therapy is a key predictor of AEs. Regular monitoring, patient education, and individualized treatment strategies are crucial for optimizing epilepsy care.

KEYWORDS: *Monotherapy, Polytherapy, Adverse events, Adverse events on Domain Specific, Quality of life Scores, Anti-epileptic therapy.*

1. INTRODUCTION

Epilepsy is a neurological disorder characterized by recurrent, unprovoked seizures. A seizure occurs when there is abnormal electrical activity in the brain. These electrical disturbances can result in various symptoms, ranging from mild staring episodes to severe convulsions.[1] Epilepsy is considered a chronic condition, meaning it persists over time, and it can affect people of all ages, races, and ethnic backgrounds. In a healthy brain, neurons (nerve cells) communicate with each other through electrical signals in a highly coordinated manner. However, in epilepsy, this electrical activity becomes abnormal, causing sudden surges of electrical impulses that can lead to seizures.

ETIOLOGY

Genetic factors: In some cases, epilepsy may be inherited, with certain genes making individuals more susceptible to seizures.

Brain injury: Head trauma, stroke, or brain infections can damage brain cells, leading to epilepsy.

Developmental brain disorders: Conditions like cerebral palsy or autism may increase the risk of epilepsy.[2]

Brain tumors: Growths or lesions in the brain may interfere with normal electrical activity.

Metabolic issues: Disorders related to metabolism can sometimes trigger seizures.

Infections: Infections such as meningitis or encephalitis can also damage the brain and result in epilepsy.

However, in many cases, the exact cause of epilepsy is unknown, and it is classified as idiopathic (without a known cause).

EPIDEMIOLOGY

Epilepsy is one of the most common neurological disorders globally. According to the World Health Organization (WHO) Approximately 50 million people worldwide are living with

epilepsy.[3]

1 in 100 people will experience epilepsy at some point in their life. The condition affects individuals across all ages, but it is most commonly diagnosed in childhood and in older adults.

Each year, nearly 2.4 million new cases are diagnosed worldwide.[4] Despite its prevalence, epilepsy remains under diagnosed and undertreated, particularly in low- and middle-income countries, where access to healthcare and medications can be limited.

TYPES OF SIEZURES[5]

Epileptic seizures are typically classified into two main categories: focal seizures and generalized seizures. Each category is further subdivided based on the type and pattern of seizure activity.

1. Focal Seizures (Partial Seizures)

Focal seizures originate in a specific part of the brain. They can be either focal onset aware seizures or focal onset impaired awareness seizures, depending on the individual's level of consciousness during the event.

Focal Onset Aware Seizures (Simple Partial Seizures): In these seizures, the person remains fully conscious and aware. The seizure may cause abnormal sensations, jerking movements, or unusual sensations like tingling or flashing lights.

Focal Onset Impaired Awareness Seizures (Complex Partial Seizures):[6] During these seizures, the person's awareness or consciousness is impaired, and they may appear confused, unresponsive, or disoriented. These seizures can involve strange movements, such as lip-smacking, hand wringing, or repetitive actions.

Focal seizures may or may not progress into generalized seizures, and they are often preceded by an aura, which is a sensory experience such as a smell, sound, or visual disturbance that signals the onset of a seizure.

2. Generalized Seizure

Generalized seizures involve the entire brain from the onset, affecting both hemispheres of the brain. These seizures are typically associated with a loss of consciousness. There are

several types of generalized seizures.

Tonic-Clonic Seizures (Grand Mal Seizures): These are the most well-known type of seizure, often depicted in popular media. The individual experiences two phases: a tonic phase (stiffening of the muscles) followed by a clonic phase (jerking or rhythmic movements). There is a loss of consciousness, and the person may also bite their tongue, lose bladder control, or experience confusion afterward (postictal state).

Absence Seizures (Petit Mal Seizures): These seizures cause brief lapses in awareness or staring spells. They are most common in children and can occur many times a day, lasting only a few seconds. The individual may seem to "zone out" and not respond to stimuli.

Atonic Seizures (Drop Attacks): This type causes a sudden loss of muscle strength, leading to the person collapsing or falling without warning. The person may not lose consciousness, but they are at risk of injury due to the fall.

Myoclonic Seizures: These are characterized by sudden, brief jerks or twitches of muscles, often in the arms or legs. They can occur in clusters and may or may not affect consciousness.

Tonic Seizures: These seizures involve sudden muscle stiffening or rigidity, often affecting the muscles of the back, arms, or legs. The individual may fall if the leg muscles become stiff.

Clonic Seizures: These involve rhythmic, jerking movements and typically affect the face, arms, and legs. They may follow a tonic phase or occur on their own.

3. Unknown Onset Seizures

In some cases, it is not immediately clear whether a seizure is focal or generalized. These seizures are categorized as having an unknown onset until further diagnostic testing can determine the origin of the seizure activity.

TREATMENT

For 70%of patients with epilepsy, drugs can control seizures. However, they can't cure epilepsy, and most people will need to continue taking medications.[7]

An accurate diagnosis of the type of epilepsy, a person has is very important in choosing the

best treatment.

Treatments include

- medicines called anti-epileptic drugs (AEDs)
- surgery to remove a small part of the brain that's causing the seizures
- a procedure to put a small electrical device inside the body that can help control seizures
- a special diet (ketogenic diet) that can help control seizures.

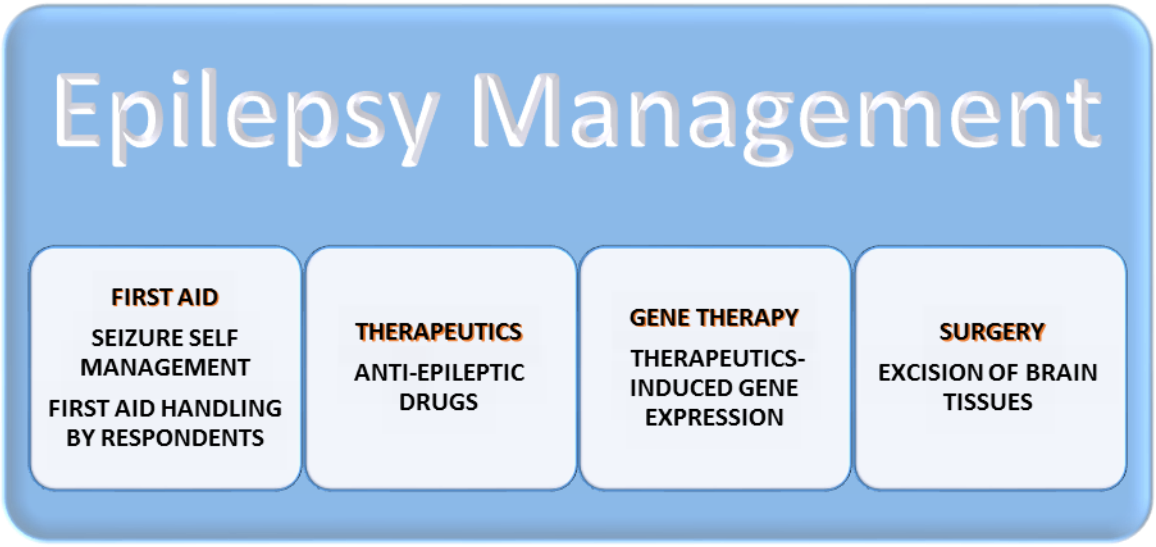

Figure 1: Epilepsy management.

For people with drug-resistant epilepsy, neuromodulation is an alternate treatment to antiseizure medications and surgery. Neuromodulation may prevent or stop ictal episodes by disrupting the neural system in different ways. Neuromodulation techniques include non-invasive techniques like transcutaneous VNS and transcranial stimulation, as well as invasive therapies that need an implanted device and electrodes, like vagus nerve stimulation (VNS), deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS), and responsive neurostimulation (RNS) of the epileptogenic zone or zones. As of right now, the only authorised treatments for refractory focal epilepsy are VNS, ANT-DBS, and RNS.[8]

Table 1: Type of seizures and anti-epileptic drugs Used.[9]

Type of siezures	First-line antiepileptic drugs
eneralised tonic-clonic	Carbamazepine Lamotrigine Oxcarbamazepine Sodium valproate Levetiracetam Topiramate

Focal	Topiramate Carbamazepine Levetiracetam Oxcarbamazepine Sodium valproate Phenytoin Zonisamide
Abscesses	Ethosuximide Sodium valproate Lamotrigine
Myoclonic	Levetiracetam Sodium valproate Topiramate
Focal siezures in older patients	Lamotrigine Gabapentine Levetiracetam

Epilepsy is commonly treated with anticonvulsant or antiepileptic drugs to manage seizure. If administered at the earliest stage of the illness, AEDs have been shown to totally treat about 65% of youngsters. Many people require alternate treatment since they are resistant to AEDs. Extra care must be used when taking AEDs to prevent potentially dangerous medication interactions. Some of the most widely prescribed Anti-epileptic drugs include phenytoin, which stabilizes neural membranes to prevent seizure activity, and valproate (valproic acid), which increases the levels of neurotransmitters like GABA to reduce excitability in the brain.[10] Lamotrigine works by inhibiting sodium channels, thus stabilizing electrical activity in the brain, while levetiracetam modulates synaptic neurotransmitter release.[11] Carbamazepine is often used for focal seizures as it reduces the frequency and severity by blocking sodium channels.[12] Topiramate and gabapentin are also used for various seizure types, with topiramate influencing neurotransmitter activity and gabapentin affecting calcium channels.[13] Brivaracetam is used for treatment of partial onset seizures in patients age 16years and older.[14] The choice of drug depends on the type of epilepsy, the patient's age, comorbid conditions, and response to previous treatments, which side effects can be tolerated, other illness etc.[15] Managing epilepsy often requires adjusting medications to minimize side effects and optimize seizure control.

ADVERSE EVENTS

Antiepileptic medication (AED) side effects are frequent, can significantly affect quality of life, and can lead to treatment failure in as many as 40% of patients.[16] Although the majority of AEDs exhibit similar efficacy rates, their side effect profiles vary widely and are

frequently a deciding factor in treatment selection.[17] The most frequent side effects are temporary and dose dependent. Particularly concerning is cognitive impairment, particularly for people who study or work. Chronic side effects like weight gain and idiosyncratic ones like skin rashes can make clinical management more difficult and increase therapy termination rates.[18] When used during pregnancy, almost all conventional AEDs raise the risk of congenital abnormalities. Every drug carries the risk of adverse effects. The side effects of antiepileptic drugs fall into three categories.

When beginning antiepileptic drugs, certain mild side effects are typical, especially if the dosage is increased quickly. These include mood swings, anxiety, irritability, nausea, dizziness, and tiredness. Although they are typically not significant, some people may find them concerning, so you should talk to your doctor or pharmacist about them. Your doctor may reduce the dosage of another antiepileptic drug that the medicine may be reacting with, or they may modify the rate at which the medication is administered.

Table 2: Characteristics of several anti-epileptic drugs.

Drug	Mechanism of action	Metabolism	Possible adverse effects	Characteristics
Topiramate	Blocks voltage dependent sodium ions. Inhibit GABA	70% excreted and 30% metabolized	Weight loss, cognitive problems, metabolic acidosis	Never withdraw drug promptly, but gradually
Vigabatrin	Inhibits GABA transaminase	Renal	Insomnia, visual field defects, weight gain	Has been also used for infantile spasms
Stiripentol	Increases GABA release	Metabolized in liver	Minor central nervous system (CNS) effects	Not frequently prescribed
Zonisamide	Acts on sodium channels and voltage dependent calcium channels	Metabolized in liver	Weight loss, CNS side effects, ataxia	Have drug interactions
Rufinamide	Prolongs inactive state of sodium channels	Metabolized in liver	CNS side effects	Not given to patients of familial short QT syndrome
Levetiracetam	Inhibits calcium	Renal and enzymatic	Behavioral disturbances,	Favorable safety profile,

	channels, also lessens the calcium release from intraneuronal stores		headache, anorexia	safe for liver disease patients
Carbamazepine	Shows anticonvulsive action when solubilised with chemically modified cyclodextrins	Metabolized in liver	Confusion, agitation, aggression	Iv administration is efficient against seizures
Lacosamide	Increases fraction of sodium channels for depolarization	Metabolized in liver	Nausea, Diplopia, CNS affected	Hypothesized to produce a neuroprotective effect
Lamotrigine	Inhibits voltage gated sodium channels	Metabolized in liver	Allergic reactions,	Can cause myoclonic seizures
Oxcarbazepine	Inhibits voltage gated sodium channels	Metabolized in liver to active metabolite	Dizziness, CNS side effects, hyponatremia	Can make myoclonia worse

Antiepileptic drugs frequently cause adverse symptoms that are similar to being "drunk" when used in excess, such as tremor, vomiting, double vision, unsteadiness, poor concentration, and tiredness. If you experience any of these adverse effects, you should notify your doctor right once.

Certain adverse effects, such as rash, blood or liver issues, severe behavioural disturbances, or worsening seizure control, are specific to each medicine and only happen to certain people. Certain persons or circumstances may be more susceptible to these adverse effects when using a particular drug.

There have been numerous attempts over the last 20 years to lessen the burden of antiepileptic medication toxicity. Numerous techniques have been developed to screen for and measure negative effects. Advances in the fields of pharmacogenomics and epidemiology have revealed patient profiles linked to an elevated risk of particular side effects. The therapeutic arsenal now includes a number of new-generation antiepileptic medications with

better tolerability profiles and lower risk of drug interactions. All things considered, these developments have increased the potential to customise antiepileptic medication treatment in order to maximise efficacy and reduce the possibility of harmful side effects. Although side effects have been documented since the beginning of antiepileptic medication therapy, only in recent years has there been a concerted attempt to characterise, measure, and address their therapeutic importance. The Veterans Administration Cooperative I study, conducted in 1985, examined carbamazepine, phenobarbital, phenytoin, and primidone. Systematic research into new chemicals, tailored antiepileptic treatment regimens, and ways for assessing toxic effects in everyday practice has resulted in more effective tactics for dealing with side effects. Advances in epidemiology and pharmacogenetics have enhanced our understanding of the various features of antiepileptic medication toxic effects, allowing us to identify distinct patient profiles that are more likely to have specific side effects.

The goal of this study is to analyse not only the severity of the adverse events on AEDs, demographic factors and epileptic characteristics, but also evaluates impact of adverse events on quality of life in patients on AED therapy. This is not a systematic study; rather, it is based on our evaluation of the literature in this field as well as our own experience caring for epileptic patients in specialist clinics.

Limited data on AED-related AEs in tertiary care hospital. Need to identify factors associated with AED-related AEs. Importance of informing clinicians and patients about potential risks and benefits of AED therapy. Although AEDs are indispensable for seizure management, their potential to cause adverse events presents a double-edged sword in clinical practice. A significant proportion of patients experience drug-related side effects that impair daily functioning and quality of life, leading to non-adherence, suboptimal seizure control, and increased healthcare costs. While multiple studies have examined the efficacy of AEDs, limited data are available regarding their adverse effect profiles, especially in the Indian context and more specifically in tertiary care hospitals. Additionally, the frequency, severity, and nature of these adverse events may differ based on genetic, environmental, and healthcare access factors unique to regional populations.

This study is therefore essential to

- Fill the knowledge gap concerning AED-related adverse events in a tertiary care setting.
- Identify patient and treatment-related predictors of adverse drug events.
- Help clinicians make more informed, individualized decisions in AED prescribing.

- Provide evidence-based insights to enhance patient counseling, monitoring, and follow-up practices.
- Inform policy makers about the need for robust pharmacovigilance systems and patient education programs.

By contributing to a deeper understanding of the adverse effects associated with AEDs, this study aims to support the development of safer and more effective epilepsy care models that can be implemented in similar clinical settings.

2. MATERIALS AND METHODS

Participants in this cross-sectional study were chosen from among patients with epilator epilepsy who were seen in the Government Medical College Kozhikode, India, Neurology outpatient department Research was conducted from December 2024 to March 2025.

2.2. SELECTION CRITERIA

In this study we considered various criteria for inclusion and exclusion of epileptic patients for getting accurate result.

2.2.1. INCLUSION CRITERIA:

- Patients of both sex
- Patients aged 5 -70 years.
- Patients diagnosed with epilepsy as per the International League Against Epilepsy (ILAE) criteria.
- Currently taking antiepileptic drugs (AEDs) for at least 6 months.
- Able to provide informed consent.
- Willing to participate in the study.

2.2.2. EXCLUSION CRITERIA

1. Patients with a history of pseudo seizures or psychogenic non-epileptic seizures.
2. Those with severe cognitive impairment or dementia.
3. Patients with a history of substance abuse or dependence.
4. Individuals with significant hearing or visual impairment.
3. Those who have undergone epilepsy surgery.
4. Patients with a diagnosis of status epilepticus within the past 6 months.
5. Individuals with a known hypersensitivity to AEDs.

6. Patients with significant comorbid medical conditions (e.g., cancer, kidney disease).
7. Patients with a history of psychiatric illness.
8. Those who have participated in another epilepsy-related study within the past year.

2.3. Sample Size Calculation

The sample size for this study was determined using the formula: $N = Z^2$ X Pq /d2 and found to be 136.Thus, a minimum of 136 participants was determined to be necessary for this study.

2.4. DATA ENTRY FORMAT

A specially designed data entry format was used to enter all patients details like name, age, sex, duration of therapy, past medical history, medical history, comorbities, drugs prescribed and drug adverse events involved.

2.4.1. Sampling Procedure: A cross- sectional study were carried out for a period of 3 months with the primary objective of determination of Adverse events among epileptic patients receiving antiepileptic drug therapy from the Govt. Medical College, Kozhikode. On the basis of inclusion criteria, patients receiving antiepileptic drugs for controlled seizures were selected. Data was collected through a cross-sectional study using patient questionnaires. Random sampling (Prescription analysis and personal interview). The data was tabulated and statistically analysed using SPSS Software based upon normal/ non-normal distribution of data obtained.

2.4.1. Sampling Frame

The sampling frame consists of patients with epilepsy attending the neurology department of a tertiary care hospital.

2.4.2. Sampling Technique

A prospective observational study was conducted using a consecutive sampling technique. All patients diagnosed with epilepsy who attended the neurology department during the study period were considered eligible for inclusion based on the predefined inclusion criteria (mentioned separately). A total sample size of 136 patients was recruited for the study.

2.4.3. Sampling Procedure

Patients visiting the neurology department were screened for eligibility by the research team. Those who met the eligibility criteria were approached and provided with detailed information regarding the study. Patients who expressed willingness to participate were asked

to provide written informed consent. After obtaining consent, eligible patients were enrolled in the study, and their data was collected using a structured data collection form.

2.4.4. Data Collection

Data collection focused on key variables, including patient demographics, epilepsy diagnosis, antiepileptic drug (AED) therapy, and adverse drug events. The structured data collection form was designed to capture relevant information in the following sections

1. Patient demographics
2. Epilepsy diagnosis
3. AED therapy
4. Adverse drug events

Data were collected at baseline and during follow-up visits conducted after a 3-month period.

2.4.5. Instruments for Data Collection: A structured and standardized data collection tool was used to gather information on patient demographics, epilepsy diagnosis, antiepileptic drug therapy, and any adverse drug events. A validated questionnaire, developed to meet the objectives of the study, was utilized. Additionally, medical records were reviewed to obtain relevant clinical information.

2.4.6. Data Management Strategy

1. **Data Collection:** Information was gathered using a structured form that included demographic data, epilepsy diagnosis, details of AED therapy, and adverse drug reactions.
2. **Data Entry:** The data were entered into a secure, password-protected electronic database.
3. **Data Cleaning:** The dataset was reviewed and cleaned to address any errors, inconsistencies, or missing values.
4. **Data Storage:** All data were stored securely in an electronic database with password protection and regular backups.
5. **Data Sharing:** The data were not shared with individuals outside the research team without prior approval from the Institutional Review Board (IRB).

Data Analysis Plan

Data were analysed by using descriptive statistics to summarize patient demographics, epilepsy diagnoses, antiepileptic drug regimens, and the occurrence of adverse drug reactions. chi-square tests and logistic regression, were conducted to explore factors associated with

adverse drug events and to assess the relationships between antiepileptic drug use and these events.

3. RESULTS

A total of 1 36 patients on antiepileptic drug (AED) therapy were included in this cross-sectional study. The findings are categorized under sociodemographic characteristics, clinical variables, adverse event profile, and quality of life (QoL) analysis.

3.1. Sociodemographic Characteristics

The study population demonstrated a wide range of socio-demographic characteristics, which appeared to influence the pattern of reported adverse effects.Table-3 Participants aged 15 years or below formed the largest age group (44.1%), followed by those aged 16–30 years (30.1%). Fewer participants belonged to the 31–45 years (11.8%) and above 46 years (14.0%) age brackets. Preliminary analysis suggested that younger individuals, particularly those under 30, reported a higher frequency of adverse effects, possibly due to metabolic differences or increased sensitivity to medication. Gender distribution was nearly equal, with males (52.2%) slightly outnumbering females (47.8%). However, females were observed to report a greater number of subjective adverse events, such as dizziness and nausea. Regarding marital status, most participants were single (68.4%), followed by married individuals (27.9%). Emotional and social factors linked to marital status may have influenced the perception or reporting of adverse effects. Educational level also varied, with the majority having completed only primary education (43.4%), while 27.2% had secondary education and 17.6% were graduates. A small proportion (11.8%) had no formal education. Notably, participants with lower educational attainment appeared to report fewer adverse effects, which may reflect underreporting due to lack of awareness or difficulty in recognizing symptoms.

Table 3: Socio demographic variables.

Socio demographic variables	*Categories*	*Frequency (n)*	*Percent (%)*
Age	<=15	60	44.1
	16-30	41	30.1
	31-45	16	11.8
	>=46	19	14.0
Gender	Female	65	47.8
	Male	71	52.2
Marital Status	Single	93	68.4

	Married	38	27.9
	Divorced	2	1.5
	Widowed	3	2.2
Educational level	No formal education	16	11.8
	Primary	59	43.4
	Secondary	37	27.2
	Graduate	24	17.6

5.2. Clinical Characteristics

Among the study participants, 58.8% reported experiencing adverse events (AEs) due to antiepileptic drugs (AEDs), while 41.2% did not. Of those affected, most described the severity as mild (58.8%), followed by moderate (31.3%) and severe (10%). Daily life was impacted in 45% of those experiencing AEs. Although 55% discussed these side effects with healthcare providers, only 30% received specific management strategies. Among those, dose adjustments were the most common intervention (45.8%), followed by switching to another drug and adding supportive treatments (each 20.8%). Table -2.

Satisfaction with the management of side effects varied, with 37.5% expressing satisfaction and only 16.7% being very satisfied. About 29% of patients were hospitalized at least once due to seizures or AE management, and 57.3% required more than two outpatient visits per year for related issues. Notably, 11% of participants considered stopping or skipping medication due to AEs, with forgetfulness (5.1%), side effects (3.7%), and allergy (0.7%) cited as the main reasons.

The occurrence of adverse events in patients undergoing antiepileptic treatment appears to be influenced by several clinical parameters. The type of epilepsy plays a notable role, with a majority of individuals diagnosed with idiopathic epilepsy, who may exhibit differing susceptibility to drug-related side effects compared to those with symptomatic or cryptogenic types. Seizure frequency also seems relevant, as those experiencing more frequent seizures—especially daily or weekly—could be on higher doses or more complex regimens, potentially elevating the risk of adverse outcomes. The duration of antiepileptic drug (AED) use is another factor; prolonged exposure, particularly beyond one year, may increase cumulative toxicity or tolerance, thereby affecting side effect profiles. Furthermore, patients on polytherapy are often exposed to multiple pharmacologic agents, raising the likelihood of drug interactions and associated adverse reactions. The presence of comorbid conditions such as diabetes, stroke, or chronic illnesses like asthma, CKD, or thyroid disorders could also compound vulnerability to adverse events due to altered pharmacodynamics or

pharmacokinetics. Overall, these clinical variables collectively shape the safety profile of AEDs and should be considered in therapeutic planning.

Table-4: Clinical variables associated with Adverse events.

Clinical variables	*Description/Category*	*Frequency (%)*
Type of Epilepsy	Idiopathic	82(60.2)
	Symptomatic	48(35.3)
	Cryptogenic	6(4.4)
Seizure frequency	Rarely	103(75.7)
	Monthly	18(13.2)
	Weekly	10(7.4)
	Daily	5(3.7)
Duration of AEDs	<0.5 months	23(16.9)
	0.5-1 yr	15(11.0)
	1-5 yr	49(36.0)
	>5 yr	49(36.0)
Type of AED	Monotherapy	81(59.5)
	Polytherapy	55(40.4)
Comorbidities		9(6.6)
Type of Comorbidity	Diabetes	3(2.2)
	Stroke	3(2.2)
	asthma/CKD/thyroid	1(0.7)

5.3. Associations of various factors with AEs

The present study investigated the relationship between several demographic and clinical variables and the occurrence of adverse events (AEs) among patients receiving antiepileptic drugs (AEDs), using the Chi-square test for statistical analysis. The variables examined included age, gender, type of epilepsy (idiopathic vs. symptomatic/cryptogenic), seizure frequency, duration of AED therapy, type of AED regimen (monotherapy vs. polytherapy), and the presence of comorbid conditions. Table-4.

Among all the factors analyzed, only the duration of AED therapy demonstrated a statistically significant association with the occurrence of adverse events, with a p-value of 0.045. This finding suggests that the length of time a patient remains on antiepileptic treatment may influence their risk of developing adverse effects. Specifically, patients who had been on AEDs for more than one year appeared more likely to report adverse events compared to those on treatment for shorter durations. Figure- 1. In contrast, variables such as age group, gender, type of epilepsy, seizure frequency, type of therapy, and comorbidities did not show a significant association with the incidence of adverse effects, indicating that these factors may not play a major role in influencing AED-related tolerability in this study population.

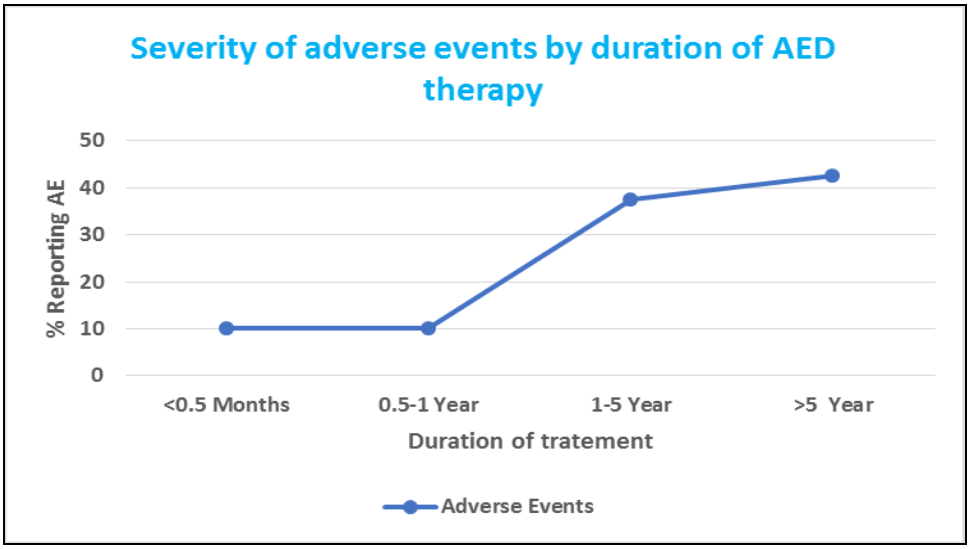

Figure -2: Severity of adverse events by duration of AED therapy.

These results highlight the importance of closely monitoring patients, especially those undergoing long-term antiepileptic therapy, for the emergence of potential adverse effects. Regular follow-up and timely dose adjustments may be necessary to minimize the risk and ensure optimal therapeutic outcomes.

Table -5: Factors associated with Adverse events.

Variables		***Adverse events***		***P Value***
		Yes	No	
Age	<=15	33(41.3)	27(48.2)	0.762
	16-30	24(30.0)	17(30.4)	
	31-45	11(13.8)	5(8.9)	
	>=46	12(15.0)	7(12.5)	
Gender	Female	41(51.2)	24(42.9)	0.335
	Male	39(48.8)	32(57.1)	
Type	Idiopathic	45(56.3)	37(66.1)	0.249
	Symptomatic/crptogenic	35(43.8)	19(33.9)	
Seizure frequency	Rarely	58(72.5)	45(80.4)	0.293
	Frequently	22(27.5)	11(19.6)	
Duration of AEDs	<0.5 months	8(10.0)	15(26.8)	0.045
	0.5-1 yr	8(10.0)	7(12.5)	
	1-5yr	30(37.5)	19(33.9)	
	>5 yr	34(42.5)	15(26.8)	
Type of AEDs	Monotherapy	44(55.0)	37(66.1)	0.195
	Polytherapy	36(45.0)	19(33.9)	
Comorbidities	Yes	7(8.8)	3(5.4)	0.456
	No	73(91.3)	53(94.6)	

5.4.Major adverse events associated with common drugs

Among the various antiepileptic drugs assessed, Levetiracetam was most frequently associated with aggression and somnolence, each reported by 14 patients. Valproate and Clobazam were also linked to aggression in 11 patients each. Fatigue appeared as a common adverse event across all medications, with Clobazam (12 cases), Valproate (10), and Carbamazepine (10) showing notably high occurrences.

Weight gain was reported most commonly with Clobazam (7) and Valproate (5), whereas gastrointestinal disturbances were noted predominantly with Clobazam (6) and Carbamazepine (5). Drowsiness was less frequently reported but still present, especially with Levetiracetam (4). Hair loss was relatively uncommon, with the highest incidence seen with Valproate (4).

Loss of appetite was most reported with Carbamazepine (2) and Clobazam (2), while skin reactions were observed in low numbers, mostly in Carbamazepine, Clobazam, and Levetiracetam. Memory loss was chiefly associated with Clobazam (3 cases), and liver-related issues appeared in a small proportion of patients taking various drugs. Weight loss was noted occasionally, with Clobazam having the highest count (4).

Overall, Clobazam and Levetiracetam presented with a broader range of adverse effects compared to the other drugs, while Phenobarbital and Oxcarbazepine were linked to fewer reported events. Table-5.

Drugs most associated with behavioural AEs included levetiracetam, clobazam, andcarbamazepine. Fatigue and GI issues were widespread across multiple drugs, indicating ageneralized side effect profile for several AEDs.

Table-6: Major adverse events associated with common drugs.

Adverse events	*Levetiracetam*	*Valproate*	*Clobazam*	*Carbamazepine*	*Phenobarbital*	*Oxcarbazepine*
Aggression	14	11	11	8	1	2
Somnlence	14	5	11	8		4
Fatigue	9	10	12	10	2	3
Weight Gain	4	5	7	2	1	2
GI problem	5	3	6	5	Nil	3
Drowsiness	4		2	1	2	
Hair Loss	1	4	2	1	Nil	Nil
Anorexia	3	1	2	2	Nil	
Skin reaction	2	1	2	2	1	1

Memory loss	2	Nil	3	1	1	Nil
Liver problem	2	1	1	1	Nil	Nil
Weight loss	2	3	4	Nil	Nil	1

4.5. Adverse Event Profile

Out of the total participants, 58.8% reported experiencing adverse events (AEs), while 41.2% did not. Among those who reported AEs (n=80), 58.8% described them as mild, 31.3% as moderate, and 10% as severe. Nearly half (45%) stated that AEs interfered with their daily life. Despite this, only 30% of participants had discussed these side effects with healthcare professionals.

Among the 24 individuals who discussed side effects with providers, 45.8% underwent dose adjustments, 20.8% were switched to a different drug, 20.8% received supportive treatment, and 12.5% experienced no change in therapy. Regarding satisfaction with AE management, 37.5% were satisfied, 16.7% were very satisfied, while 27.5% remained neutral and 8.3% were dissatisfied.

In terms of healthcare utilization, 29 participants (21.3%) were hospitalized once due to seizures or AEs, while 5.9% had two hospitalizations and 2.2% had more than two. Most participants (70.5%) reported no hospitalizations. For outpatient visits, 40.4% visited the hospital up to two times per year, while 57.3% reported more than two visits annually. Notably, 11% of participants considered discontinuing or skipping their medication due to AEs. The primary reasons cited for skipping antiepileptic drugs (AEDs) included forgetfulness (5.1%), side effects (3.7%), and allergies (0.7%). Monotherapy was used in 59.5% of patients, while 40.4% were on polytherapy. Comorbidities were reported in 6.6% of patients, the most common being diabetes and stroke (each 2.2%).

Table -7: Adverse events profile.

***Adverse** events*	***Description/Category***	***Frequency(n) (%)***
Adverse events	Yes	80(58.8)
	No	56(41.2)
Severity of Adverse events (% out of 80)	Mild	47(58.8)
	Moderate	25(31.3)
	Severe	8(10.0)
AE s effected daily life (% out of 80)	Yes	36(45)
	No	44(55.0)
Discussed side effects with HC providers	Yes	24(30)
	No	56(70)

(% out of 80)		
If yes, measures of management (% out of 24)	No change	3(12.5)
	Dose adjustment	11(45.8)
	Switch to another drug	5(20.8)
	Addition of supportive treatment	5(20.8)
Satisfaction in side effects managed (% out of 24)	Dissatisfied	2(8.3)
	Neutral	9(27.5)
	Satisfied	9(37.5)
	Very satisfied	4(16.7)
No: of hospitalization due to seizure/AE management	0	96(70.5)
	1	29(21.3)
	2	8(5.9)
	>2	3(2.2)
No: of OP visits due to seizure/AE management per year	0	3(2.2)
	<=2	55(40.4)
	>2	78(57.3)
Did you think of stopping/skipping medication due to AE's	Yes	15(11.0)
	No	121(89.0)
Reasons for skipping AED's	Forgetfulness	7(5.1)
	Side effects	5(3.7)
	Allergy	1(0.7)

A comparative analysis of adverse events between monotherapy and polytherapy groups was conducted. As illustrated in the grouped bar chart, aggression and somnolence were the most frequently reported adverse events in both groups, with a slightly higher proportion in the monotherapy group (43.1% and 38.6%, respectively) compared to polytherapy (30.5% and 27.7%, respectively), Table 6. Fatigue, however, was more prominent in the polytherapy group (44.4%) than in monotherapy (25%). Other notable adverse events included gastrointestinal problems, weight gain, and drowsiness, with variable patterns across the two treatment types. Overall, the chart highlights a broader distribution and higher intensity of adverse events in polytherapy, despite the lack of statistically significant difference in incidence ($p > 0.05$). This visual comparison underscores the need for cautious use of polytherapy, particularly in patients prone to fatigue and metabolic issues. Figure 3

Table -6: Distribution of common adverse events by therapy type.

Adverse events	*Monotherapy (44) n(%)*	*Polytherapy (36) n(%)*
Aggression	19(43.1)	11(30.5)
Somnolence	17(38.6)	10(27.7)
Drowsiness	8(18.2)	0
Fatigue	11(25.0)	16(44.4)
Hair Loss	4(9.1)	2(5.5)

Depression	0	1(2.7)
Memory Problem	2(4.5)	3(8.3)
Ataxia	2(4.5)	1(2.7)
Tremor	2(4.5)	1(2.7)
GI Problem	5(11.3)	8(2.2)
Allergy	1(2.3)	0
Liver Problem	1(2.3)	2(5.5)
Loss of Appetite	2(4.5)	2(5.5)
Weight gain	6(13.6)	6(16.7)
Mood changes	2(4.5)	0
Skin rxn	2(4.5)	3(8.3)
Weight loss	2(4.5)	3(8.3)
Irritability	0	2(5.5)
Loss of vision	0	1(2.8)

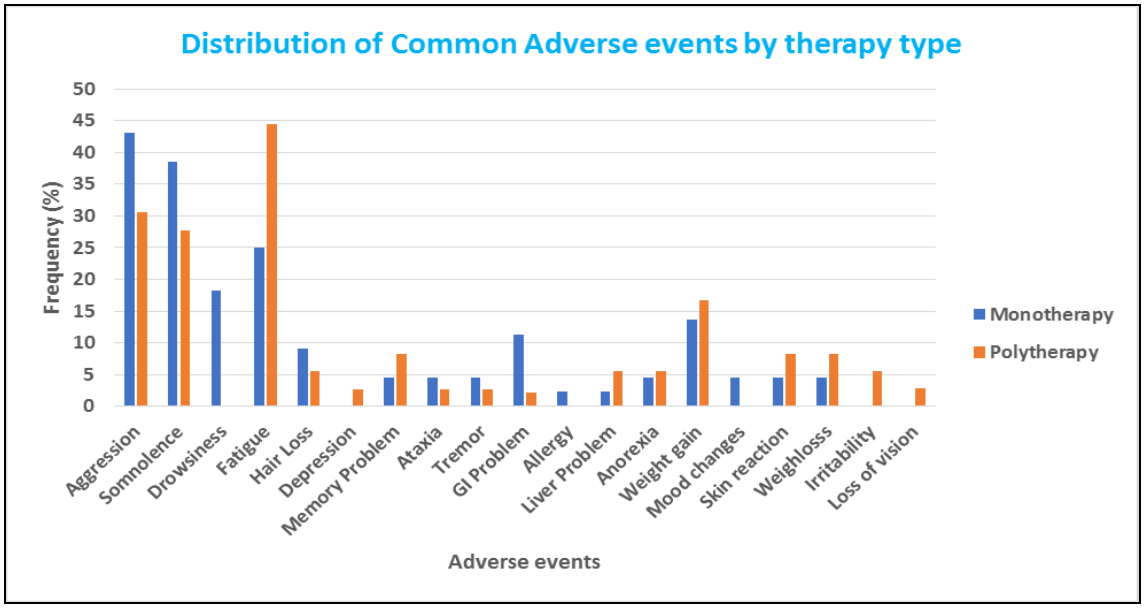

Figure 3: Distribution of Common Adverse events by therapy type.

4.6. Quality of Life (QoL)

4.6.1. Assessment of Quality of Life Among Study Participants

On assessing the normality of the data, it was found that the Quality of Life (QOL) scores, both overall and across individual domains, were not normally distributed. Therefore, the non-parametric Mann-Whitney U test was employed to compare QOL between patients with and without adverse events. The Quality of Life (QoL) of patients on antiepileptic drugs (AEDs) was assessed using a standardized scale covering six domains: physical health, emotional wellbeing, social functioning, cognitive functioning, energy, and daily activity. Both the overall and domain-wise QoL scores were examined. Table 8 presents the descriptive statistics of Quality of Life (QoL) across various domains among the study

participants. The overall mean QoL score was **4.18 ± 0.81**, and the median score was 4 (IQR: 4–4.5), indicating a moderately high perception of QoL among participants. Among the individual domains.

- The highest mean score was observed in *social functioning* (4.21 ± 0.82), suggesting relatively preserved social engagement despite chronic illness.
- This was followed by *daily activity* (4.19 ± 0.88), *cognitive functioning* (4.18 ± 0.87), and *physical health* (4.13 ± 0.86).
- The lowest mean scores were noted in *emotional wellbeing* (4.11 ± 0.86) and *energy* (4.15 ± 0.93), suggesting that emotional state and fatigue may be areas where patients face more challenges.

This overall pattern suggests that while basic functioning and social participation are relatively well-maintained, psychological and energy-related aspects of QoL may require more attention.

Table -8: Overall Quality of life statistics.

	Mean ±SD	Median(Q1,Q3)
Overall QOL	4.18±.81	4(4,5)
QOL in physical health	4.13±.86	4(4,5)
QOL in emotional wellbeing	4.11±.86	4(3,5)
QOL in social functioning	4.21±.82	4(4,5)
QOL in cognitive functioning	4.18±.87	4(4,5)
QOL in energy	4.15±.93	4(3,5)
QOL in daily activity	4.19±.88	4(4,5)

4.6.1. Comparing adverse events and its effect on quality of life

Table 9 presents a detailed comparison of mean QoL scores. A statically significant reduction in QoL scores was observed across all domains in participants who experienced adverse events (P<0.001). Patients without AEs consistently reported higher median scores, typically 5 (IQR: 5–5) across domains, indicating minimal QoL impairment. In contrast, those with AEs had lower scores, with medians ranging from 3 to 4, clearly suggesting a negative impact of AEs on their quality of life.

For instance, the overall QoL score in patients without adverse events was 4.95±3.65, While

it was significantly lower in those with adverse events (3.65±0.64). Similar trends were noted on physical health (4.82±.38 vs. 3.65±0.76) and cognitive functioning (4.73±3.80 vs. 3.80±0.87) Figure 4.

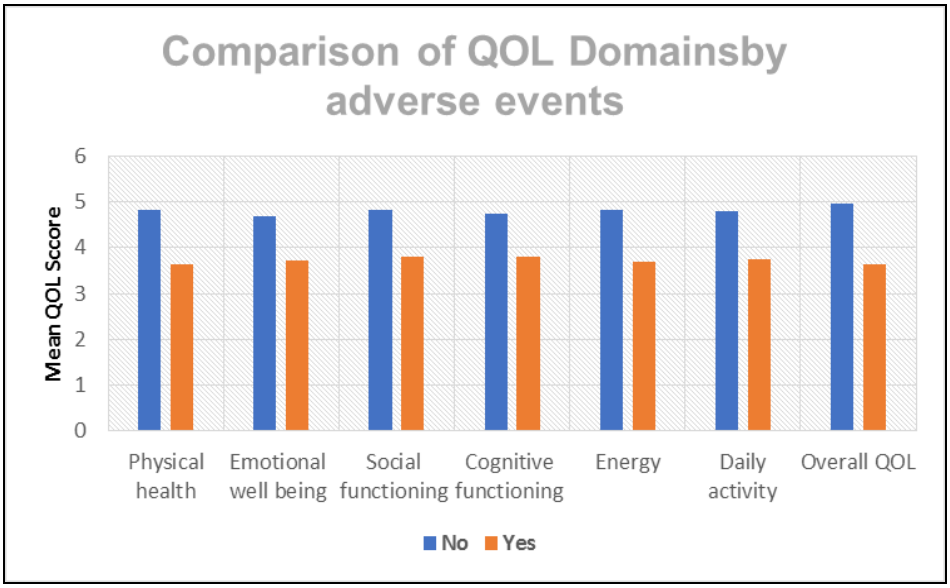

Figure 4: Impact of Adverse events on Domain-Specific Quality of life Scores Among Patients.

These differences reflect a consistent and substantial decline in patient-reported QoL in the presence of AEs. Particularly notable are

- A 1.17-point drop in physical health scores between the two groups.
- A marked decline in energy and emotional wellbeing, underscoring the psychological and physiological burden of AED-related side effects.
- Even cognitive functioning, often a critical aspect of epilepsy management, was adversely affected.

Table – 9: Impact of Adverse Events on Quality of Life.

QOL (Mean±SD)	Adverse events		P value
	No	Yes	
Physical health	4.82±.38	3.65±.76	<0.001
Emotional well being	4.68±.51	3.71±.84	<0.001
Social functioning	4.82±3.79	3.79±.76	<0.001
Cognitive functioning	4.73±3.80	3.80±.87	<0.001
Energy	4.82±3.69	3.69±.89	<0.001
Daily activity	4.80±3.76	3.76±.87	<0.001
Overall QOL	4.95±3.65	3.65±.64	<0.001

4.6.3. Patient behaviour and Medication Adherence

Notably, approximately 11% of patients reported having considered discontinuing or skipping their medications due to AE**s**. This behaviour could have serious implications for seizure control, long-term outcomes, and overall disease management.

5. DISCUSSIONS

This cross-sectional study was conducted to assess the prevalence and profile of adverse events (AEs) associated with antiepileptic drugs (AEDs), and to evaluate their impact on the quality of life (QoL) of patients attending a tertiary care hospital. Our findings revealed that a significant proportion of patients (58.8%) experienced at least one AE while on AED therapy. This is consistent with previous reports indicating that up to 80% of individuals with epilepsy may encounter side effects during treatment, which can range from mild to severe [Perucca & Gilliam, 2012; Kanner et al., 2022].

Among the reported AEs, behavioral symptoms such as aggression and somnolence were most prevalent. These were particularly associated with levetiracetam and clobazam, findings that mirror existing literature on the neuropsychiatric effects of certain AEDs [*Thisayakorn* Paul et al., 2021]. Fatigue, gastrointestinal disturbances, and weight changes were also commonly observed, with drugs like valproate and carbamazepine being notable contributors. These side effects can have a cumulative impact on the patient's physical and emotional well-being, emphasizing the importance of individualized AED selection.

Interestingly, although polytherapy was not statistically associated with a higher incidence of AEs, patients on multiple AEDs tended to experience a broader spectrum and greater intensity of symptoms. This observation highlights a well-documented concern in epilepsy management: while polytherapy may be necessary for patients with refractory seizures, it carries a heightened risk of drug-drug interactions, compounded toxicity, and reduced tolerability [Kwan & Brodie, 2006]. Clinicians must carefully evaluate the need for polytherapy and consider stepping down to monotherapy whenever possible, without compromising seizure control.

One of the most striking findings in this study is the significant association between the **duration of AED therapy and the occurrence of adverse events** ($p = 0.045$). Patients with longer treatment durations (>1 year) reported more AEs, suggesting the potential role of cumulative exposure and chronic drug toxicity. This aligns with previous studies that various

approaches should be implemented in order to reduce the adverse events especially monotherapy and dose adjustments, use of newer antiepileptic drugs the need for periodic review and dose optimization in long-term AED users to minimize risk [St Louis EK. l., 2019].

Furthermore, the study highlighted a crucial gap in **communication and clinical follow-up**. Despite experiencing AEs, 70% of patients did not discuss these symptoms with their healthcare providers. Among those who did, management strategies included dose adjustments, drug switching, and the use of supportive therapies. However, satisfaction with these interventions remained suboptimal, indicating a need to enhance patient counseling and shared decision-making practices. Encouraging open dialogue about side effects during routine consultations can play a pivotal role in improving adherence and therapeutic outcomes.

Quality of life assessments revealed a **statistically significant reduction in all domains**—physical, emotional, social, cognitive, energy levels, and daily activities—among patients experiencing AEs ($p < 0.001$). These findings reaffirm previous research indicating that AEs, not just seizure frequency, are a strong determinant of QoL in people with epilepsy [Baker et al., 1997, Ioannis Karakis etal, 2023]. Given that epilepsy is a chronic condition often requiring lifelong therapy, the burden of AEs must be addressed proactively to enhance overall patient satisfaction and long-term treatment success.

Moreover, 11% of patients in this study reported contemplating skipping or stopping AED therapy due to AEs. This is a concerning statistic, as non-adherence to medication can result in increased seizure frequency, emergency visits, and even life-threatening complications. Educating patients about the importance of adherence, while also validating and managing their experiences with side effects, is essential in promoting consistent treatment engagement.

This study contributes valuable real-world evidence to the growing body of research on AED safety, particularly in the Indian context, where limited pharmacovigilance data is available from tertiary care settings. Our findings emphasize the need for implementing robust monitoring systems to identify and manage AEs early, especially in patients requiring complex or long-term treatment regimens.

The findings from this study demonstrate that adverse events associated with antiepileptic

drugs significantly impact the quality of life in patients The study findings indicate that overall QoL among participants was moderately high, with higher scores in domains such as social functioning and daily activities. The study revealed a statistically significant reduction in all QoL domains among patients who experienced AEs. This suggests that AEs—independent of seizure control—substantially impair quality of life, supporting previous findings by Baker et al. (1997) and Karakis et al. (2023). Given that epilepsy is a lifelong condition, proactively managing AEs is essential to optimize patient satisfaction and adherence. This may reflect a supportive environment or relatively effective disease management. However, the relatively lower scores in emotional wellbeing and energy suggest areas where patients might need additional support, such as psychological counselling or fatigue management.

Furthermore, adverse events significantly compromised QoL across all domains. These results highlight the critical need for better monitoring and management of side effects associated with treatment, as they have a direct impact on patients' wellbeing. The large differences in mean scores and the statistically significant p-values underscore the clinical relevance of minimizing adverse events to improve overall treatment outcomes and patient satisfaction.

These findings are consistent with previous studies that have shown a negative correlation between treatment-related side effects and QoL. Early identification and intervention for adverse events may help maintain a better QoL in patients undergoing long-term treatment**.**

LIMITATIONS

There are some limitations to this study. First, the cross-sectional design limits the ability to infer causality between AED use and AEs. Second, the reliance on self-reported data introduces the possibility of recall bias. Third, the study was conducted at a single tertiary care center, which may limit the generalizability of the results to other healthcare settings. Despite these limitations, the study has strengths, including a well-defined sample, use of validated tools for QoL assessment, and a focus on a real-world population that often presents with complex treatment challenges.

Implications for Practice and Future Research

The findings of this study underscore the importance of **patient-centered care** in epilepsy management. Regular monitoring, patient education, and adverse event reporting systems

should be integral components of epilepsy treatment protocols. Future studies should explore **longitudinal patterns** of AEs and their long-term impact on QoL, as well as investigate potential genetic, metabolic, or psychosocial factors that may predispose certain individuals to a higher AE burden.

In conclusion, the adverse effects of AEDs are not only common but also significantly impair quality of life and treatment adherence. A balanced approach that weighs seizure control against tolerability and patient well-being is essential for effective and sustainable epilepsy care.

4. CONCLUSION

Implications for Practice and Future Research

The findings revealed that 58.8% of the participants experienced one or more AEs, with the majority being mild in severity. Commonly reported adverse events included aggression, somnolence, fatigue, gastrointestinal disturbances, and weight changes. Levetiracetam and clobazam were frequently associated with behavioural and cognitive side effects, aligning with existing evidence on the neuropsychiatric risks of these drugs.

Although polytherapy was not significantly associated with a higher incidence of AEs, patients on multiple AEDs reported a broader spectrum and greater severity of adverse effects. This highlights the importance of cautious drug selection, especially in patients requiring long-term therapy or combination regimens. Notably, the duration of AED therapy was the only factor significantly associated with AEs, suggesting that longer exposure may elevate the risk of drug-related complications.

Substantial communication gap was identified, with 70% of participants not reporting their side effects to healthcare providers. Even among those who did, a considerable proportion expressed dissatisfaction with the management strategies offered. This emphasizes the need for better patient-provider communication, routine monitoring, and personalized care approaches.

Quality of life analysis showed statistically significant reductions in all QoL domains among those who experienced AEs. Physical health, emotional well-being, cognitive functioning, and social interactions were notably affected, underlining how side effects can negatively influence daily living beyond seizure control. Furthermore, a concerning 11% of patients had

considered discontinuing or skipping medication due to AEs, which could compromise seizure control and overall treatment success.

In conclusion, the study underscores that while AEDs are essential for epilepsy management, their adverse effects can significantly burden patients' well-being and adherence to therapy. Regular follow-up, active surveillance of AEs, patient education, and individualized treatment plans are crucial to improve clinical outcomes and ensure sustained quality of life in people living with epilepsy.

Conflicts of Interest: None

Ethical approval and consent to participate

Approval for the study was granted by the Institutional Ethical committee and Institutional Research Committee of the Government Medical College, Kozhikode, India. The approval was issued under the reference number GMCKKD/RP 2024/IEC/340, and IRC-2024/Protocol/362, dated 29/11/2024 respectively. Participants were clearly informed about the study and verbal and written consent was obtained from them prior to their involvement.

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