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Pharmacologic management and treatment challenges in tumour-induced epilepsy: an observational study

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ABSTRACT

Patients with brain tumors, especially gliomas, frequently experience tumor-induced epilepsy (TIE), a neurological complication in which seizures frequently occur prior to diagnosis and continue throughout the course of the illness. The purpose of this study was to investigate clinical factors in choosing safe and effective antiepileptic drug (AED) therapy as well as the pharmacologic management of epilepsy among patients with brain tumors. Patients at a tertiary care hospital who were diagnosed with tumor-induced epilepsy participated in a retrospective observational study. Clinical information was gathered and examined, including demographic information, tumor features, prescribed antiepileptic drugs, treatment results, and adverse drug responses. The findings highlight that enzyme-inducing AEDs such as phenytoin and carbamazepine may reduce the efficacy of chemotherapy by accelerating drug metabolism, whereas non–enzyme-inducing agents like levetiracetam and valproate demonstrated better tolerability and fewer drug–drug interactions. Despite these advantages, adverse effects such as sedation, behavioural changes, and hepatotoxicity remain significant limitations. Optimal management of TIE requires individualised pharmacotherapy, close multidisciplinary collaboration, and therapeutic drug monitoring to ensure efficacy and safety. A personalised and cautious approach emphasising drug safety and seizure control can substantially improve patient outcomes. Further research is warranted to develop tumor-specific epilepsy management strategies and strengthen evidence-based clinical practice.

Keywords: Tumor-induced epilepsy, Antiseizure medications, Brain tumors, Glioma, Levetiracetam, Drug-drug interactions, Pharmacologic challenge.

INTRODUCTION

The connection between brain tumors and epilepsy has been observed since the 19th century [1]. Tumor-induced epilepsy, sometimes referred to as brain tumor-related epilepsy (BTRE) or tumor- related epilepsy (TRE), is the term used to describe epileptic seizures brought on by a brain tumor. These seizures may appear later in the course of the disease or may be the initial indication of a brain tumor [2]. The kind of tumor, its location, and other variables can affect the frequency and nature of seizures [3]. In fact, the most prevalent symptom among individuals with brain tumours is epilepsy [4].

Brain tumour-related epileptogenesis has been demonstrated to be significantly influenced by tumour location in addition to growth rate. Frontal, temporal, and parietal cortex cancers are more epileptogenic, and tumours in the grey matter of the cortical structure, particularly those in the eloquent regions, are more likely to cause seizures [5]. There are also established correlations between specific seizure types and tumor locations. Lesions affecting different parts of the brain are linked to distinct seizure patterns in individuals with low-grade gliomas, according to Wang et al. and others.

Among brain tumours, gliomas are most frequently associated with tumor-related epilepsy. Gliomas are classified I through IV by the World Health Organization (WHO) based on their histological and genetic features [6]. Seizures can occur in as many as 80-90% of instances of low-grade gliomas (Grade II), including diffuse astrocytomas and oligodendrogliomas [6]. These tumours are especially epileptogenic. Conversely, high-grade gliomas (Grades III and IV), like glioblastoma multiforme and anaplastic astrocytoma, usually develop more aggressively but initially show fewer seizures. This variance is caused by tumor growth patterns, infiltration into cortical areas, and the degree of peritumoral inflammation. Customising antiepileptic oncologic therapy plans requires an understanding of the kind of glioma [7].

The prevalence of brain tumour-related epilepsy (BTRE) varies significantly depending on the type of tumour; it can range from 10–15% in brain metastases to over 80% in low-grade gliomas. Additionally, the incidence of BTRE is a typical complication of cerebral tumours. Histology of the tumour has a significant role in determining the likelihood of developing brain tumor- related epilepsy (BTRE). More than 80% of patients with diffuse low-grade gliomas experience BTRE, whereas 40–47% of patients with meningiomas and 62–68% of patients with glioblastomas experience seizures. More than 80% of patients with diffuse low-grade gliomas experience BTRE, whereas 40–47% of patients with meningiomas and 62–68% of patients with glioblastomas experience seizures. This study aims to analyse real-world clinical data from patients with tumour-induced epilepsy treated at a tertiary care hospital.

Pathophysiology

The presence of a tumour in the brain causes intricate structural and metabolic changes that result in tumour-induced epilepsy (TIE). The type, location, and interaction of the tumor with the surrounding brain tissue all have an impact on the intricate pathophysiological system. Tumors in or near the cerebral cortex are particularly epileptogenic due to their ability to interfere with or penetrate neuronal networks. This stimulation often results in the formation of epileptogenic foci, areas of hyperexcitable neurons capable of producing abnormal electrical discharges [7]. Further impairing neural stability, peritumoral oedema also raises intracranial pressure and causes local inflammation.

The neurotransmitter imbalance is another important element. In order to promote a hyperexcitable state, tumor cells may decrease GABAergic inhibitory transmission and enhance the release of glutamate, the primary excitatory neurotransmitter [8]. Brain tumors also frequently cause the blood-brain barrier (BBB) to break down, which lowers the seizure threshold by allowing toxins and inflammatory mediators to penetrate the neuronal environment [9].

Tumor type and grade additionally affect seizure frequency and risk. Because of their sluggish growth and cortical involvement, low-grade gliomas are more frequently linked to chronic seizures. On the other hand, high-grade tumours may result in fewer seizures, because of their aggressive invasion and tissue destruction, they result in rapid neurological impairment.

Diagnosis

According to the 2017 International League Against Epilepsy (ILAE) standards, seizure type should be categorised to help direct treatment [10]. Magnetic resonance imaging (MRI) and electroencephalogram (EEG) tests should be performed on patients who are suspected of having GRE [11]. The clinical data and imaging results should both be used to make the GRE diagnosis. Glioma is mostly diagnosed by MRI, which includes FLAIR, DWI, PWI, T2-weighed, and contrast – enhanced T1- weighted sequences. Differential diagnosis may benefit from the use of CT, MRS, and PET. The gold standard is still histopathological examination, which includes molecular testing according to the 2016 WHO classification [11].

Figure 1: Mechanisms underlying tumor-induced epilepsy

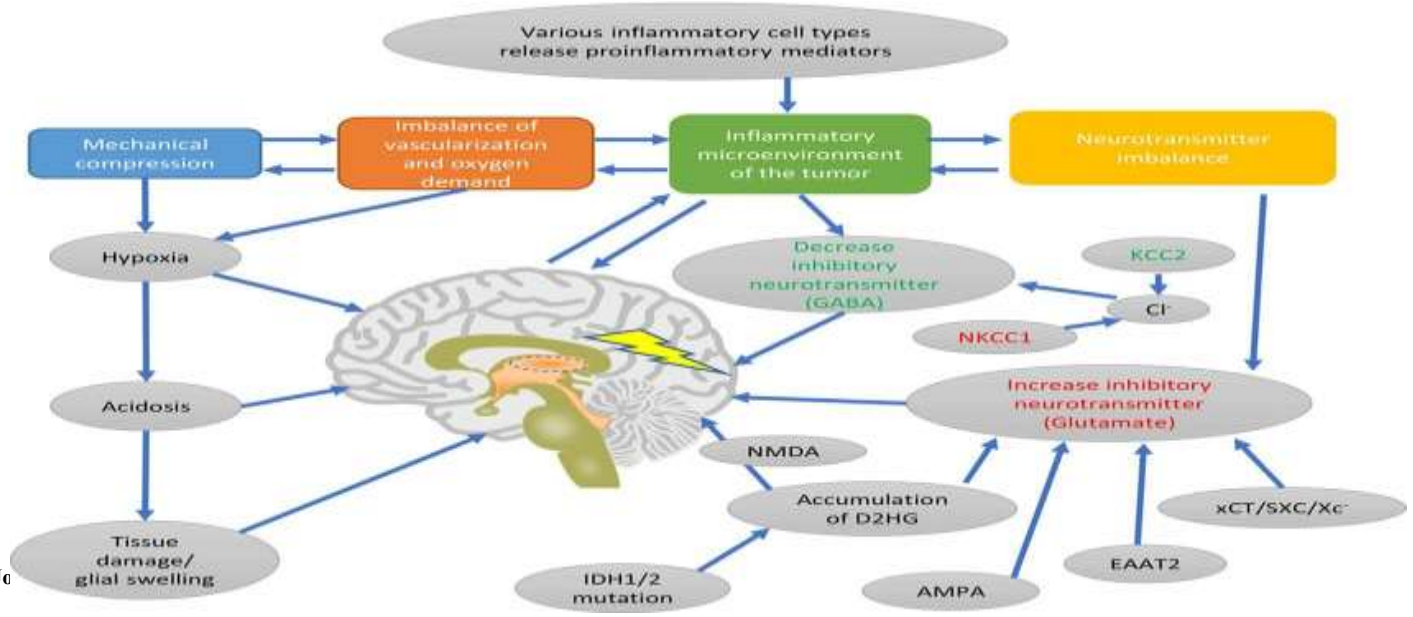


Figure 2: Diagnostic algorithm for tumor-related epilepsy [15]

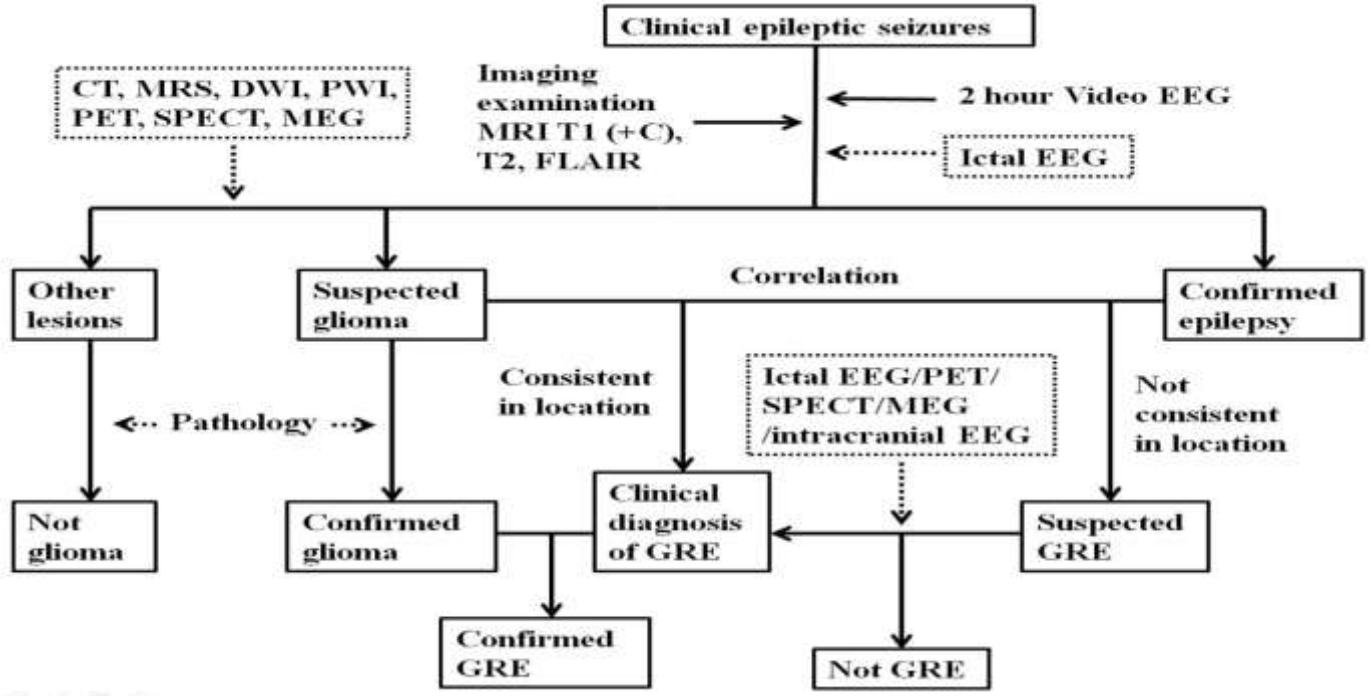


Table:1 Commonly used anti-seizure medications in TRE [17,18]

Drug Name	Class	Mechanism of Action	Clinical Relevance in TRE
Levetiracetam	SV2A modulator	Modulates synaptic vesicle protein 2A	Fewer interactions, well tolerated in brain tumors
Phenytoin	Sodium channel blocker	Inhibits receptor firing by blocking Na+ channel	Older drug, more interactions
Lacosamide	Sodium channel modulator	Enhances the slow inactivation of the Na+ channel	Useful in refractory epilepsy
Valproic acid	Broad spectrum	Increases GABA, blocks Na+ and T-type Ca^{2+} channel	Use with caution due to hepatotoxicity and thrombocytopenia
Lamotrigine	Sodium channel blocker	Inhibit glutamate release	Good for cognitive safety
Topiramate	Mixed	Blocks Na+ channels, enhances GABA, inhibits AMPA/kainite receptors	Caution with cognitive side effects

A video EEG lasting at least two hours is advised for the diagnosis of epilepsy. The epileptogenic zone can be located with the aid of ictal EEG, PET, SPECT, and MEG. It is necessary to prove a link between the tumour and seizures to validate GRE [12]. Although intracranial EEG is rarely utilised due to the expense and risk, it may be considered in ambiguous cases [13]. Clinical characteristics, EEG, and MRI are usually used to diagnose GRE, and pathological evaluation is then used to confirm the diagnosis [14].

Treatment

Treatments for tumour-related epilepsy (TRE), in which Seizures are caused by brain tumours, require a combination of therapeutic approaches. These include antiepileptic drugs (AEDs), tumour-directed therapies, and occasionally surgery. In addition to tumour-specific therapies including radiation, chemotherapy, and surgery, AEDs are the first line of defence for controlling seizures [15]. Antiseizure drugs must be safe, effective, and compatible with other treatments, such as tumour-directed therapies like radiation, chemotherapy, and surgery.

Anti -seizure drugs (ASMs)

In patients with TRE, antiseizure medications are the cornerstone of seizure management. Newer-generation ASMs, such as levetiracetam, lamotrigine, lacosamide, topiramate and pregabalin, are generally preferred due to their favourable interaction profile and tolerability [16] (Table 1).

The choice of ASM depends on several factors

Tumour type and grade

Neurological symptoms

Drug -Drug interactions (especially with chemotherapeutic agents)

Patient's prognosis and comorbidities

For drug-resistant epilepsy, additional ASMs or combination therapies may be considered if monotherapy proves ineffective.

Tumor – Targeted Therapies

Surgical Resection: When the tumor is clearly linked to seizure onset and is surgically accessible, gross total resection (GTR) is often the preferred approach, aiming to reduce both tumor burden and seizure frequency [19,20].

Chemotherapy and Radiotherapy: These modalities are used to reduce tumor progression and may help indirectly control seizures. The type, grade, and location of the tumor influence the treatment plan [21,22].

Targeted Therapy and Immunotherapy: Though still under research, molecular-targeted therapies are being explored to target gliomas and related tumor causing seizures.

Treatment data summary

In this observational study (cohort) involving 49 patients

diagnosed with tumor-induced epilepsy:

All patients (100%**)** received antiepileptic drug (AED) therapy as the first-line approach for seizure management.

Chemotherapy was administered to 69.3% of patients, based on tumor type, grade, and progression.

A combination of AEDs and chemotherapy was utilised in 57.1% of cases, reflecting the need for integrated seizure and tumor control.

Corticosteroids, primarily dexamethasone, were prescribed in 32.6% of patients to manage peritumoral oedema and associated symptoms.

Treatment regimens were individualised, with choices tailored to the patient's tumour characteristics, seizure frequency, and risk of pharmacologic interactions.

This data underscores the complexity of managing tumour-induced epilepsy, highlighting the importance of a multidisciplinary approach in optimising both oncological and neurological outcomes.

METHODOLOGY

Study design

This retrospective observational cohort study was conducted at GSL General Hospital to evaluate the pharmacologic management and treatment challenges in patients with tumor-induced epilepsy. The study was carried out over three months from January 2025 to March 2025. Ethical considerations were maintained, and patient confidentiality was ensured during data collection and analysis.

Study population

A total of 49 patients diagnosed with brain tumours and associated seizures were included in the study. All patients were treated at the neurology and oncology departments during the study period.

Inclusive criteria

Patients of either gender, aged ≥18 years.

Patients with a radiologically and histologically confirmed diagnosis of a primary or secondary brain tumor.

Patients with at least one documented seizure episode after tumour diagnosis.

Patients who received antiepileptic drug (AED) therapy.

Patients who underwent tumour-directed treatment (surgery, chemotherapy, or radiotherapy).

Exclusive criteria:

Patients with pre-existing epilepsy or seizure disorder before tumor diagnosis.

Patients with incomplete or missing medical records.

Patients with metabolic, infectious, or traumatic causes of seizures unrelated to tumor.

Data collection

Data were collected from medical records using a structured data sheet in Excel. The variables included:

Demographics: Age, gender.

Tumour details: Type, grade, and treatment received (surgery, chemotherapy, radiotherapy).

Seizure profile: Presence of seizures before and after AED initiation.

Antiepileptic drugs: AEDs prescribed, dosage, route, duration, and side effects.

Drug interactions: Documented interactions between AEDs and chemotherapeutic agents.

Outcomes: Seizure control, side effects, and overall patient response.

The study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Institutional Ethics Committee of GSL General Hospital.

Statistical analysis

Data were entered into Microsoft Excel and analysed using descriptive statistics**.**

Continuous variables like age were expressed as mean ± standard deviation (SD)**.**

Categorical variables such as gender, type of AED, chemotherapy received, and outcomes were summarised using frequencies and percentages**.**

Graphs such as bar charts and pie charts were used to visualize key trends.

Interactions and treatment outcomes were explored using cross-tabulations to observe patterns.

Further statistical analysis using SPSS can be performed as needed to compare subgroups (e.g., seizure control vs. uncontrolled groups)

Inferential statistics (Chi-square test) were used to assess the association between variables.

RESULTS

A total of 49 patients diagnosed with tumor-induced epilepsy were included in this study. The mean age was 45.2 ± 12.8 years, with a slight male predominance (53% male, 47% female) (Table 2).

Table 2: Demographic characteristics of study participants

Varible	n (%) or Mean ± SD
Total patients	49
Age (years)	45.2 ± 12.8
Gender	
-Male	26 (53.0
-Female	23(47.0)

The most common tumor type was Anaplastic Astrocytoma (42.9%), followed by Glioblastoma Multiforme (GBM) (36.7%) and other gliomas (20.4%). Regarding tumor grade, the majority were WHO Grade III (44.9%) and Grade IV (34.7%), with a smaller proportion classified as Grade II (20.4%).

Anti-Seizure Medication (ASMs) and Seizure Outcomes

Among ASMs prescribed, Levetiracetam (40.8%) was the most frequently used, followed by Phenytoin (30.6%)**,** and other ASMs such as Valproate and Carbamazepine (28.6%). Chemotherapy

was administered in 69.3% of patients, while the remainder received surgery and/or radiotherapy.

Seizure control rates varied significantly across ASM groups. Patients on Levetiracetam achieved the highest seizure control (73%), while those on Phenytoin had poorer outcomes, with 58% experiencing uncontrolled seizures. Other ASMs demonstrated intermediate results (Table 4).

Chi-square analysis confirmed a statistically significant association between ASM choice and seizure control (χ^2=12.87, p=0.045), with a Cramér's V of 0.36 (strong association). Tumor type showed a moderate association with seizure outcomes (χ^2=9.22, p=0.056, V=0.31). Importantly, a very strong association was observed between ASM use and drug–drug interactions (χ^2=22.44, p<0.001, V=0.68) (Table 5).

Drug–drug interactions were observed in 44.9% of the total cohort, predominantly among patients on enzyme-inducing ASMs (Phenytoin, Carbamazepine) receiving concurrent chemotherapy. Tumor type showed a moderate association with seizure control, with GBM patients having poorer outcomes compared to those with anaplastic astrocytoma.

Table 3: Distribution of tumor types and grades

Tumor type	n (%)
Anaplastic Astrocytoma	21 (42.9)
Glioblastoma Multiforme (GBM)	18 (36.7)
Other Gliomas	10 (20.4)
Tumor Grade	
Grade II	10 (20.4)
Grade III	22 (44.9)
Grade IV	17 (34.7)

Figure 3: Distribution of tumor types and grades in the study population

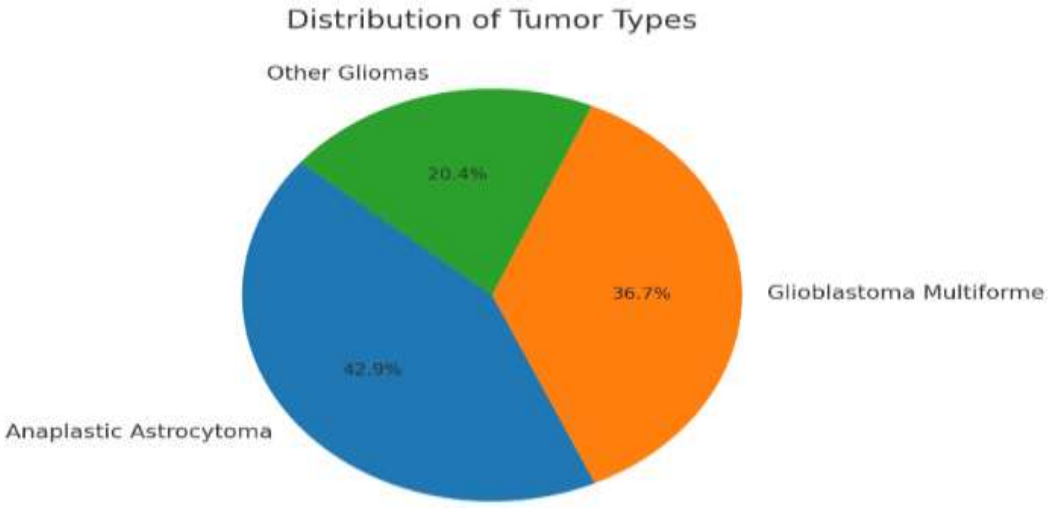


Table 4: Anti-seizure medications used and seizure outcomes

ASM Used	Controlled n (%)	Improved n (%)	Uncontrolled n (%)	Worsened n (%)	Total n (%)
Levetiracetam	15 (73.0)	4 (19.5)	1 (4.8)	0	20 (40.8)
Phenytoin	4 (26.7)	3 (20.0)	7 (46.6)	1 (6.7)	15 (30.6)
Others (Valproate, Carbamazepine)	6 (42.9)	3 (21.4)	4 (28.6)	1 (7.1)	14 (28.6)

Figure 4: Bar chart showing frequency of ASM use

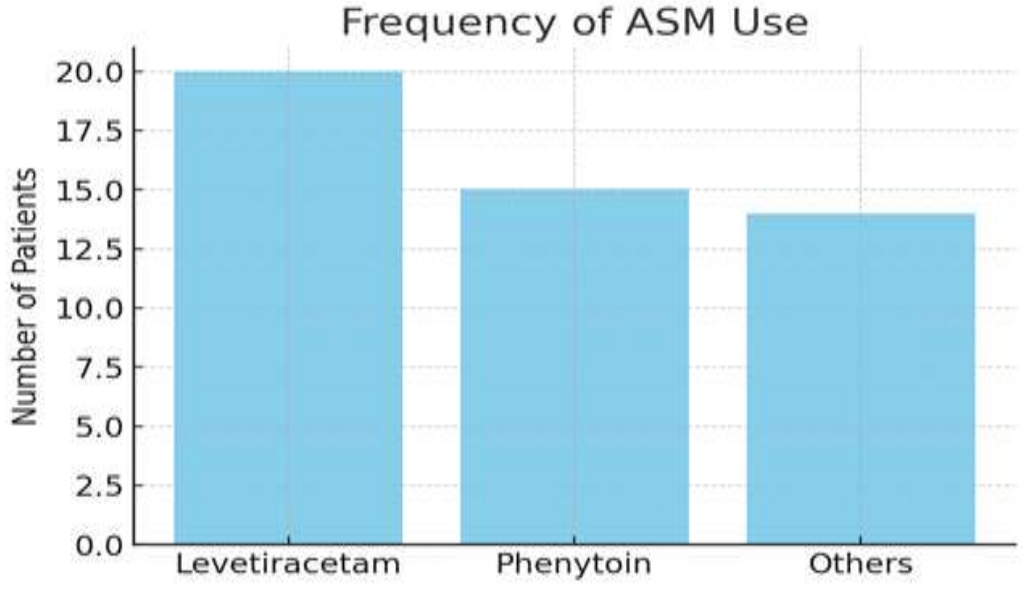


Figure 5: Stacked bar chart comparing seizure outcomes by ASM type

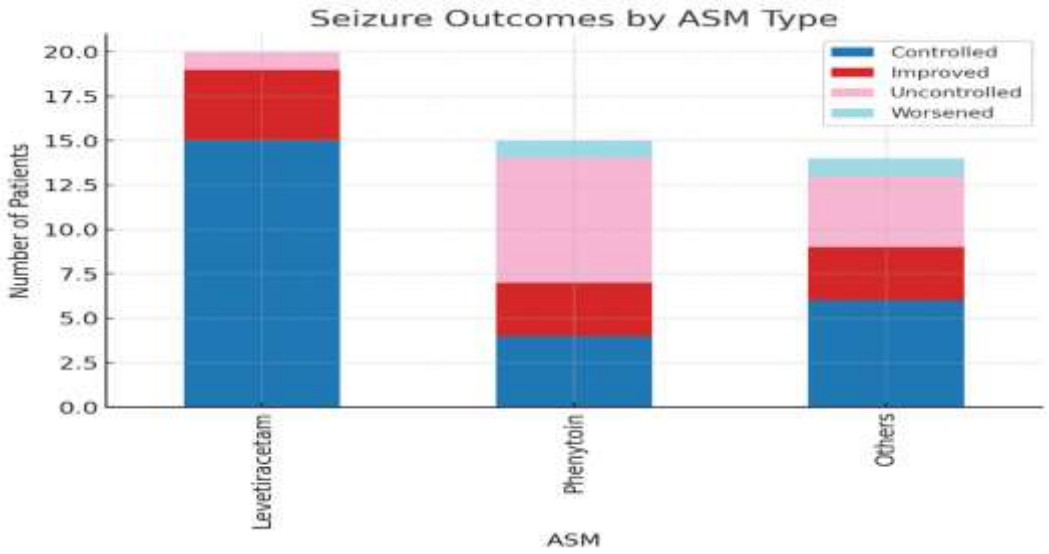


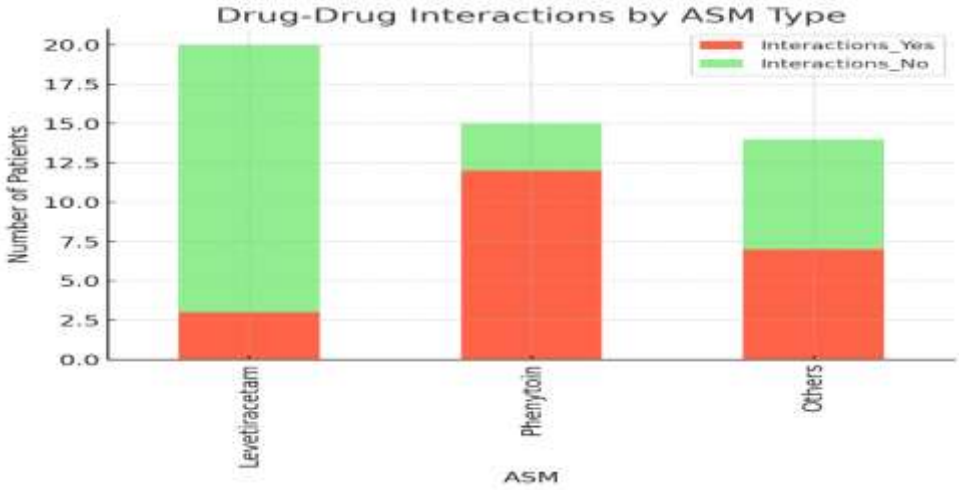
Table 5: Chi-square analysis results and effect size (Cramér's V)

Variable Comparison	Chi-square ()	df	p-value	Cramér's V	Strength of Association
ASM Used × Seizure Outcome	12.87	6	0.045	0.36	Strong
Tumor type × Seizure Outcome	9.22	4	0.056	0.31	Moderate
ASM Used × Interactions	22.44	2	<0.001	0.68	Very Strong

Table 6: Frequency of drug-drug interactions by ASM type

ASM Used	Interactions Yes n (%)	Interaction No n (%)	Total n (%)
Levetiracetam	3 (15.0)	17 (85.0)	20 (40.8)
Phenytoin	12 (80.0)	3 (20.0)	15 (30.6)
Others	7 (50.0)	7 (50.0)	14 (28.6)

Figure 6: Bar chart showing frequency of drug–drug interactions across different ASM types



DISCUSSION

The clinical complexity of treating tumor-induced epilepsy is highlighted by this observational study, especially when choosing the right ASMs for patients receiving multimodal oncologic treatment. Our results show a robust, statistically significant correlation between seizure control outcomes and ASM selection. Levetiracetam's limited drug-drug interaction profile, favorable pharmacokinetics, and absence of enzyme-inducing characteristics may be the reason for its excellent seizure management. Phenytoin, on the other hand, was linked to increased incidence of uncontrollable seizures, most likely as a result of its ability to induce enzymes. significant interaction with chemotherapeutic drugs, resulting in decreased efficacy and changed plasma concentrations.

The type of tumor was found to be a moderate predictor of seizure control. Because GBM is more aggressive, progresses more quickly, and is more likely to be resistant to treatment, patients with GBM had worse seizure control than those with anaplastic astrocytoma. These results are consistent with earlier research showing that tumor biology affects ASM responsiveness and seizure pathogenesis.

One significant clinical problem was drug-drug interactions. Interactions occurred in over half of the patients,

particularly those receiving chemotherapy in addition to enzyme-inducing ASMs. This confirms previous findings that concomitant oncologic therapy can worsen pharmacokinetic variability, requiring therapeutic medication monitoring and modifications to the ASM regimen.

Our findings highlight the necessity of individualized treatment plans for tumor-induced epilepsy. When choosing ASMs, seizure control, minimizing medication interactions, and compatibility with concurrent oncologic regimens should be given first priority. Additionally, to maximize treatment results, interdisciplinary collaboration between neurologists, oncologists, and clinical pharmacists is crucial.

CONCLUSION

control in tumor-induced epilepsy. Tumor type and drug–drug interactions also contribute to treatment outcomes. These results advocate for evidence-based ASM selection tailored to tumor pathology and concurrent treatments, thereby improving both seizure control and overall patient prognosis.

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