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Beneath the Seizures: A Closer look at Epilepsy's Demographic and Clinical Landscape in India- The REMAP study

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Abstract

Background: Epilepsy, a chronic neurological disorder, poses a significant burden globally—especially in low- and middle-income countries like India, where challenges such as underdiagnosis, limited care access, poor treatment adherence, and social stigma persist. This study explores the demographic, clinical, and treatment profiles, along with comorbidities, in a large Indian epilepsy cohort

Methods: This retrospective, multicenter cross-sectional study across Indian healthcare settings collected data on demographics, seizure characteristics, lifestyle factors, treatment patterns, and comorbidities. Statistical analysis was conducted using SPSS, with significance set at $p < 0.05$.

Results: The study analyzed 9,201 patients aged 18–80 years (mean age 43.3 ± 11.2 years). The mean age of epilepsy onset was 11 years, indicating early manifestation. Generalized tonic-clinic seizures were the most prevalent (61.9%), followed by focal seizures (38.1%). A positive family history was observed in 20% of cases. Comorbid psychiatric conditions were prominent, with depression reported in 34% of patients, followed by sleep disturbances (11.5%) and psychotic disorders (8.5%). Levetiracetam was the most frequently prescribed AED, with 78.9% of patients managed on monotherapy.

Conclusions: This large-scale analysis offers valuable insights into the Indian epilepsy population, highlighting early-onset disease, the predominance of generalized seizures, and a substantial burden of psychiatric comorbidities—particularly depression. These findings emphasize the urgent need for improved diagnostic pathways, equitable treatment access, and integrated neuropsychiatric care to address the multifaceted needs of epilepsy patients in India.

Keywords: Epilepsy; Comorbidity; India; Levetiracetam; Treatment Patterns; Demographics

1. Introduction

Epilepsy is a common chronic neurological disorder that affects nearly 50 million people worldwide and is characterized by recurrent unprovoked seizures resulting from abnormal electrical discharges in the brain. This disorder encompasses a broad spectrum of seizure types and etiologies, often accompanied by significant neurocognitive, psychological, and social consequences. Despite being highly treatable in most cases, epilepsy remains underdiagnosed and undertreated, particularly in low- and middle-income countries (LMICs), where more than 80% of the affected population resides (*WHO; 2019*). These regions face critical barriers such as limited access to neurologists, diagnostic facilities, and antiepileptic drugs (AEDs), as well as persistent stigma (*Ngugi et al., 2010*).

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The global prevalence of epilepsy is approximately 6.38 per 1,000 individuals, though incidence rates are higher in LMICs, reaching up to 190 per 100,000 person-years due to factors such as central nervous system infections, traumatic brain injuries, and perinatal complications (*Jacoby et al., 2005; Allers et al., 2015*). The condition contributes significantly to the global burden of disease, with epilepsy-related disability-adjusted life years (DALYs) accounting for nearly 0.5% of the total disease burden worldwide (*Fisher et al., 2017*). The economic implications are substantial, including direct healthcare expenditures and indirect costs such as loss of productivity, caregiver burden, and reduced educational and employment opportunities (*Smith, 2005*). Additionally, epilepsy is associated with an increased risk of psychiatric disorders, including depression and anxiety, which further contribute to its overall burden (*Engel, 2013*).

Seizure types are classified based on the 2017 International League Against Epilepsy (ILAE) guidelines. Seizures may originate focally within one hemisphere or involve both hemispheres from onset (generalized seizures), and can be characterized by motor (e.g., tonic, clinic, myoclonic) or non-motor symptoms (e.g., absence seizures, sensory phenomena) (*Duncan, 1997*). Clinical assessment remains the cornerstone of diagnosis, with detailed history-taking and eyewitness accounts being vital in seizure characterization. Electroencephalography (EEG), particularly video-EEG monitoring, aids in capturing interictal epileptiform discharges and ictal patterns, offering valuable insights into seizure localization and classification (*Kwan et al., 2010*).

Neuroimaging plays a crucial role in evaluating structural causes of epilepsy. Magnetic resonance imaging (MRI) is the modality of choice for detecting lesions such as hippocampal sclerosis, cortical dysplasia, and neoplasms (*Heck et al., 2014*). In patients with drug-resistant epilepsy, advanced techniques like positron emission tomography (PET), single-photon emission computed tomography (SPECT), and functional MRI (fMRI) assist in identifying the epileptogenic zone. Genetic testing is increasingly being incorporated into clinical practice, especially in cases of early-onset epilepsy and those with a suspected syndromic association. Monogenic disorders such as Dravet syndrome, SCN1A-related epilepsies, and tuberous sclerosis complex represent a growing subset of genetically characterized epilepsies (*Neal et al., 2008*).

Pharmacologic therapy remains the primary mode of epilepsy treatment. First-line AEDs include levetiracetam, brivaracetam, lamotrigine, and valproate, selected based on the type of epilepsy, patient-specific factors, and potential side effects (*Perucca and Gilliam, 2012*). While up to 70% of individuals with epilepsy achieve seizure control with appropriately selected AEDs (*Wirrell et al., 2017, Bruno et al., 2018*), the remainder are classified as having drug-resistant epilepsy, defined as the failure of two adequate trials of tolerated and appropriately chosen AED regimens (*Meyer et al., 2010)*. For these patients, epilepsy surgery offers a potentially curative option, especially in temporal lobe epilepsy, which has the highest surgical success rates (*Löscher et al., 2013*). Pre-surgical evaluation involves comprehensive imaging, neuropsychological testing, and long-term video-EEG monitoring.

In patients who are not surgical candidates, neuromodulator therapies such as vague nerve stimulation (VNS), responsive neurostimulation (RNS), and deep brain stimulation (DBS) of the anterior nucleus of the thalamus provide alternative treatment avenues. These modalities modulate epileptic networks and have demonstrated efficacy in reducing seizure frequency in drug-resistant cases (*Fisher et al., 2010*). Non-pharmacological treatments, including dietary therapies like the ketogenic diet, are especially effective in pediatric patients with intractable epilepsy and specific metabolic or genetic syndromes (*Kossoff and Wang, 2013*).

The field of epilepsy management is undergoing a transformation with the advent of precision medicine. Innovations such as targeted gene therapies and antisense oligonucleotides are being explored for syndromes like Lennox-Gastaut and Dravet (*Miller and Menezes, 2019)*. Digital health technologies, including wearable seizure detectors, mobile applications for seizure tracking, and machine learning algorithms for seizure prediction, are increasingly integrated into patient care and research (*Osorio, 2011*). These tools not only empower patients but also enable real-time data collection and personalized interventions.

Despite these advances, challenges remain in addressing the treatment gap, which exceeds 75% in some LMICs (*Mbuba et al., 2012*). Contributing factors include social stigma, cultural misconceptions, financial constraints, and inadequate healthcare infrastructure. Strategic approaches involving community health worker training, public education campaigns, policy advocacy, and integration of epilepsy services into primary healthcare are critical for closing the gap (*Newton and Garcia, 2012*).

This retrospective study aimed to assess patients' demographics, their clinical profile, and patterns of AED use (monotherapy and add-on therapy)., treatment response-particularly seizure freedom rates with Levetiracetam and Brivaracetam-and the presence of comorbidities in Indian patients with epilepsy.

2. Methods

2.1. Study Design and Population

The study was a retrospective, multicentric, cross-sectional, observational investigation. Data collection occurred across multiple centers in India, encompassing hospitals, clinics, and healthcare institutes. Physicians and neurologists at participating sites collected retrospective data using a REMAP study case record form. Patient selection was solely at the discretion of treating physicians or neurologists, and no additional evaluations or investigations were conducted specifically for data capture in this form.

2.2. Data Collection

The REMAP study collected retrospective data on patient diagnosis, age, gender, smoking history, traumatic injury history, presenting complaints, family history of epilepsy, comorbid conditions, and management/AED prescriptions. Data from across India were compiled and statistically analyzed. Preliminary outcomes analyzed included demographic trends, proportions of newly diagnosed and comorbid patients, complications before diagnosis, correlation of family history with severity, common presenting complaints, monotherapy and combination therapy initiation rates, and AED retention and seizure freedom rates. Treatment responses were also assessed across patient subgroups.

2.3. Ethical Considerations

In accordance with Indian Council of Medical Research (ICMR's) "Ethical guidelines for Biomedical Research on Human participants," the protocol was deemed to present less than minimal risk. Appropriate Ethics Committee (EC) approval was obtained. Given the retrospective nature of the study, where participants were de-identified and could not be contacted, permission for a waiver of consent was secured from the ethics committee. Data identifying each study patient by name remained confidential and was accessible solely to the personnel associated with the investigator and, if necessary, to the Independent Ethics Committee (IEC) and relevant regulatory authorities. The sponsor, during monitoring or auditing of the trial, also had access to the data without violating patient confidentiality, to the extent permitted by applicable laws and regulations. All project-related data were under the custody of the designated investigators. The IEC, sponsor, quality assurance, and regulatory agencies had access to the respective case record forms during inspections and audits.

2.4. Statistical Analysis

Statistical analyses were performed using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY), with significance set at $p < 0.05$. Descriptive statistics summarize continuous variables (e.g., age, height, weight, age of onset) as means and standard deviations, and categorical variables (e.g., gender, smoking status, seizure type, comorbidities, treatment) as frequencies and percentages. BMI was calculated where available and classified per WHO Asian cut-offs. Group comparisons used chi-square tests for categorical variables and t-tests or ANOVA for continuous variables. Missing data were addressed via listwise deletion. Age trends across comorbidities and gender were analyzed using bar graphs and stratified comparisons.

3. Results

A total of 9,201 patients were included in the analysis following data cleaning to exclude outliers and abnormal values for age, height, and weight. The patients ranged in age from 18 to 80 years, with a mean age of 43.3 ± 13.4 years. The mean height was 162.5 ± 10.3 cm (range: 76–195 cm), and the mean weight was 66.2 ± 10.6 kg (range: 45–120 kg).

- Males comprised 64.3% of the study population, while females accounted for 35.7%. The mean age at epilepsy onset was 11.0 ± 13.1 years, with additional data recorded in months, weeks, and days for detailed analysis.
- A positive family history of epilepsy was reported in 20.0% of patients. Generalized tonic-clinic seizures were the most common subtype, observed in 61.9% of cases, while 38.1% had focal epilepsy.
- Among the smokers, 5.6% reported a smoking history of 1–5 years, 2.7% had been smoking for 6–10 years, another 2.7% reported a duration exceeding 10 years, and 1.2% had a smoking history of less than one year.
- In terms of treatment, 78.9% of patients were on monotherapy, whereas 21.1% received additional add-on therapy.

Table 1 Summary of Demographic Characteristics

Parameter	**Summary Statistics**	**Overall Total (N=9201) n (%)**
Age (Years)	Mean ± SD	43.3 ± 13.4
Height (cm)	Mean ± SD	162.5 ± 10.3
Weight (kg)	Mean ± SD	66.2 ± 10.6
Age of Onset (Years)	Mean ± SD	11.0 ± 13.1
Gender, n (%)	Male	5919 (64.3)
	Female	3282 (35.7)
Active Smoker, n (%)	No	8080 (87.8)
	Yes-1-5	515 (5.6)
	Yes-6-10	251 (2.7)
	Yes->10	244 (2.7)
	Yes-<1	111 (1.2)
Patients with Family History of Epilepsy, n (%)	Negative	7363 (80.0)
	Positive	1838 (20.0)
Patients Diagnosed with Epilepsy, n (%)	Generalized tonic Colonic	5697 (61.9)
	Focal	3504 (38.1)
Risk/ Trigger factors, n (%)	No	4956 (53.9)
	Not Available	4112 (44.7)
	Yes	133 (1.4)
Details of Epilepsy Treatment, n (%)	Monotherapy	7255 (78.9)
	Monotherapy + add-on therapy	1946 (21.1)

Table No.02 summarizes that depression was the most common comorbidity, followed by sleep issues and psychotic disorders. Many patients had no comorbidities. Other reported conditions included migraine, diabetes, and autoimmune disorders. Physical health comorbidities like cardiovascular issues, allergies, and asthma were relatively rare compared to psychiatric comorbidities.

Table 2 Summary of Presence of Comorbidities

Symptoms	**Overall Total (N=9201) n (%)**
Depression	3132 (34.0)
None	2972 (32.3)
Sleep	1059 (11.5)
Psychotic	783 (8.5)
Migraine	540 (5.9)
Diabetes	291 (3.2)
Autoimmune	233 (2.5)

Figure No. 01 indicates that patients with cardiovascular conditions had the highest average age, followed by those with diabetes and bone-related issues. Psychotic and depression-related comorbidities were also associated with higher average ages. On the lower end, patients with autoimmune conditions, no comorbidities, and allergies tended to be younger on average.

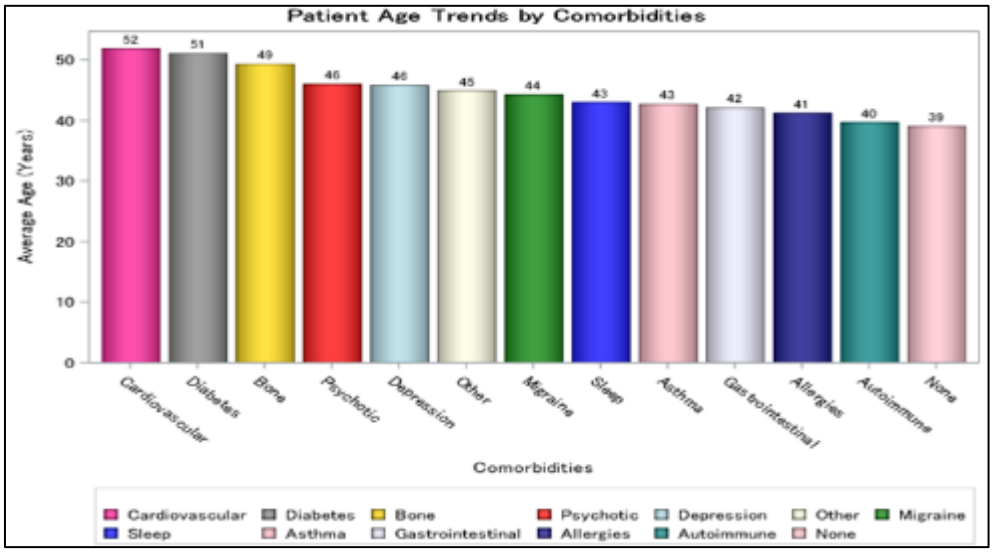

Figure 1 Patient Age Trends by Comorbidities

Figure no. 02 shows that across most comorbidities, females generally showed higher average ages than males. The largest age gap was seen in cardiovascular conditions, where females had a noticeably higher mean age. Conditions like asthma, allergies, and gastrointestinal issues also showed notable gender differences in age. For many other comorbidities, age differences between genders were relatively small.

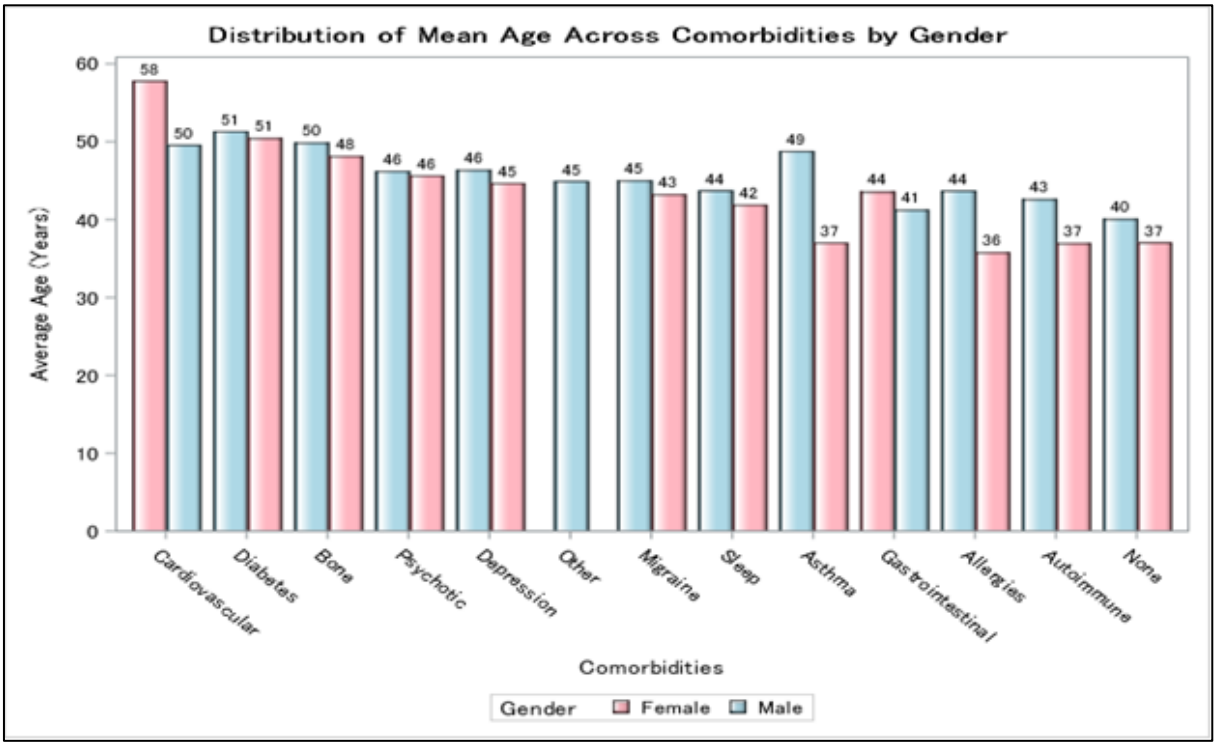

Figure 2 Distribution of Mean Age Across Comorbidities by Gender

The symptoms have been summarized here in Figure No. 03. The most reported symptoms included uncontrollable jerking, stiff muscles, temporary confusion, and loss of consciousness. These often occur in combination. Psychological symptoms such as fear and anxiety were also frequently noted, along with episodes of staring and sudden falls. Overall, the symptom patterns were varied.

The graph shows that, for most comorbidities, males outnumber females. In categories like depression, sleep disorders, psychotic disorders, migraine, autoimmune conditions, and diabetes, males consistently have higher counts than females. This trend is seen across nearly all comorbidity categories displayed.

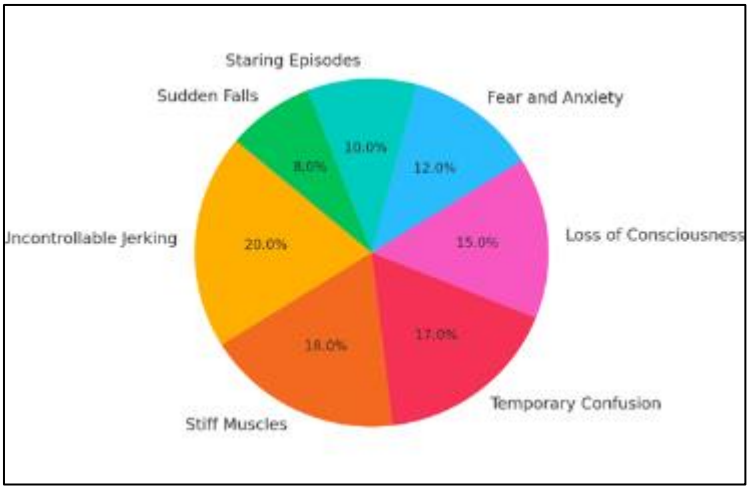

Figure 3 Distribution of Reported Epileptic Symptoms

- ***Summary of Investigations Conducted for Diagnosis:*** The most used diagnostic approaches included EEG, review of medical history, and imaging studies such as CT and MRI scans. Blood tests were also frequently conducted, either alone or as part of broader diagnostic combinations. Many patients underwent multiple investigations in combination, reflecting a thorough, multi-faceted diagnostic process. Overall, EEG, medical history review, imaging, and blood tests formed the core of the diagnostic workup.
- ***Summary of Epilepsy Treatment:*** The most prescribed antiepileptic drug was levetiracetam, the term appeared in multiple forms, suggesting underlying inconsistencies in the recorded data entry. Other frequently used medications included brivaracetam (also listed with multiple name variants), lacosamide, oxcarbazepine, and valproate. A range of other treatments such as lamotrigine, clobazam, and phenytoin were also used but less frequently. Overall, the data indicates a clinical preference for levetiracetam-based therapies, despite variation in recorded drug names, reflecting common clinical practice in epilepsy management.

4. Discussion

This large, multicentric, retrospective study provides valuable real-world insights into the demographic and clinical profiles, treatment patterns, and comorbidities of Indian patients with epilepsy. The study enrolled 9,201 patients, offering one of the more comprehensive overviews of epilepsy management in the country to date.

The mean age of patients was 43.3 years, with a wide age range of 18-80 years. A study by Singh et al. in India also reported similar age trends, emphasizing a broad demographic impact of epilepsy across age groups *(Singh et al., 2020).* Notably, the mean age of epilepsy onset in our cohort was 11 years, reinforcing the early onset nature of the condition- a figure consistent with global literature indicating that approximately 75% of epilepsy cases begin before the age of 20 *(Hauser et al., 1993)* Our data revealed a male predominance (64.3%), which is consistent with other Indian studies reporting higher prevalence among males *(Amudhan et al., 2015).* This may reflect sociocultural factors, such as greater access to healthcare for men or underreporting in women, rather than a true biological difference.

In terms of seizure type, generalized tonic-clonic seizures (GTCS) were the most reported (61.9%), followed by focal seizures (38.1%). This is in line with prior Indian community studies where CTCS were predominantly diagnosed, especially in rural areas *(Mani et al., 2012).* However, it should be noted that focal seizures may be underreported or misclassified due to lack of access to advanced diagnostics like video EEG and MRI in many centers, as observed in studies from similar LMIC settings *(Kariuki et al., 2015).*

Approximately 20% of patients reported a positive family history of epilepsy. This is notably higher than the 4.7% prevalence reported in a community-based study from Jaipur, Rajasthan, which surveyed both urban and rural populations using WHO-adapted screening tools. Discrepancy may reflect differences in study populations, methodologies, or increased awareness *(Panagariya et al., 2018).*

BMI data was unavailable for nearly 45% of patients, likely due to gaps in recordkeeping—a common challenge in retrospective datasets. Among patients with available data, most fell within the normal BMI range, though 7.5% were overweight and 2.7% obese per WHO Asian cutoffs. While underweight status (4.1%) may reflect socioeconomic disparities, the relatively low obesity rate could be attributed to the younger average age and increased metabolic demands in epilepsy patients on long-term AEDs, especially enzyme inducers such as carbamazepine or phenytoin *(Verrotti et al., 2014).*

Only 1.4% of patients reported known risk or triggering factors, and nearly 54% reported none. This suggests that for many patients, epilepsy may be idiopathic or due to undetected perinatal or infectious etiologies, both of which are prevalent in LMICs. The high rate of missing data (44.7%) underscores the need for improved clinical documentation in epilepsy care.

The comorbidity profile revealed depression as the most common coexisting condition (34%), followed by sleep disturbances (11.5%) and psychotic disorders (8.5%). This is comparable to global data, which report mood disorders in 30–50% of epilepsy patients *(Tellez-Zenteno et al., 2007).* Psychiatric comorbidities in epilepsy are often underdiagnosed and undertreated, despite their significant impact on quality of life and treatment adherence, underscoring the need for integrated care approaches. *(Kanner AM, 2003).*

The lower frequency of physical comorbidities like cardiovascular disease (0.6%) and diabetes (3.2%) may reflect the younger age profile of the cohort, though underreporting is possible. Regarding treatment, 78.9% of patients were on monotherapy, and 21.1% received additional therapy—closely mirroring global estimates that about 65-70% of patients achieve seizure control with a single AED *(Kwan and Brodie, 2000).*

The most prescribed drug was levetiracetam, followed by brivaracetam, lacosamide, and valproate. This aligns with current trends favoring newer AEDs due to better tolerability and lower drug interaction profiles *(Perucca and Gilliam, 2012).* However, inconsistency in recorded drug names across sites highlights a real-world limitation in data integrity and suggests a need for standardization in digital records.

Finally, gender-stratified analysis showed that females with cardiovascular comorbidities had a significantly higher mean age than males, a trend seen across several comorbid conditions.

This study is not without limitations. Being retrospective can lead to potential selection bias; it was dependent on the quality of existing records and may be subject to data incompleteness or misclassification. BMI and risk factor data were frequently missing, and AED name variations indicate inconsistencies in documentation. Additionally, causality between epilepsy and comorbidities cannot be inferred due to the cross-sectional design.

5. Conclusion

The high prevalence of psychiatric comorbidities highlights the need for integrated neuropsychiatric care, and the preference for newer AEDs like levetiracetam reflects a shift in clinical practice towards better-tolerated therapies. Despite the above limitations, this large-scale study provides valuable insight into the demographic trends, treatment patterns, and comorbidities among Indian patients with epilepsy. Improved standardization in data recording and broader access to diagnostics will be crucial for optimizing epilepsy care in India.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors report no conflicts of interest relevant to this research.

Statement of ethical approval

Our original manuscript titled for your consideration. The work is original, not under review elsewhere, and approved by all authors.

Statement of informed consent

Given the retrospective design and the use of de-identified data, a waiver of informed consent was granted by the EC.

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