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Original Research Article

Evaluating the prescription pattern of newly diagnosed epilepsy patients in India - a real-world observational study

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ABSTRACT

Background: To determine the demographic details and management choices of anti-epileptic drugs (AEDs) for the newly diagnosed epilepsy patients in India.
Methods: This was a retrospective, observational study conducted among newly diagnosed epilepsy patients in India between Apr 2021 and Mar 2022. The demographic parameters, treatment given, adherence to treatment, and clinician's global assessment for effectiveness and safety of management options were evaluated.
Results: Out of 20,343 patients, majority of the patients were aged between 31-50 years (54.5%), and 62.7% of them were males. Majority of the patients were diagnosed with focal epilepsy (72.2%). Migraine was the most common (28.3%) neuropsychiatric comorbidity among these patients followed by anxiety (19.7%), stroke (18.5%) and depression (11.2%); other commonly reported comorbidities were hypertension (38.27%), gastrointestinal disorders (25.39%), and diabetes (22.06%). Levetiracetam (49.6%) was the most commonly prescribed AED, followed by valproate (29.1%), oxcarbazepine (15.5%), clobazam (13.3%) and lacosamide (8%). With the prescribed AEDs, majority (91%) of the patients had decrease in seizure frequency, most (99.2%) patients had 'good to excellent' adherence to the therapy, and clinicians rated the efficacy and safety of prescribed drugs as 'good to excellent' in most (99.9%) patients.
Conclusions: Epilepsy was common in patients aged 30-50 years with male preponderance. Focal epilepsy was more prevalent. Overall levetiracetam was the most prescribed AED. Levetiracetam and valproate were the most prescribed AEDs among focal and generalized epilepsy respectively. AEDs were well tolerated by most of the patients.

Keywords: Epilepsy, AED, Comorbidities, Seizures

INTRODUCTION

Epilepsy is a central nervous system (CNS) disorder characterized by an enduring predisposition to seizures and is associated with neurological, cognitive, psychological, and social consequences.[1,2] As defined by the international league against epilepsy (ILAE), epilepsy is defined by ≥2 unprovoked seizures within 24 h or a single unprovoked seizure with a recurrence risk of ≥60% within the next 10 years or an identifiable epileptic syndrome.[3] An estimated >10 million (1%) persons with epilepsy are present in India with a higher prevalence in the rural (1.9%) as compared to urban population (0.6%).[4] Only few Indian epidemiology studies are available on epilepsy, and an age-standardized incidence rate of 27.3/100,000 has been reported.[5]

Untreated epilepsy has long been highlighted as a public health concern in lower-income countries, where up to 90% of the patients do not receive regular medications.[6] In India, the magnitude of epilepsy treatment gap ranges

from 22% among urban to 90% in rural population.[7] Circumstantial evidence, mostly from resource poor countries, suggests that about two-thirds of the newly diagnosed cases of epilepsy achieve remission with or without antiepileptic drug (AED) treatment and about one-third persist to have seizures.[8] Non-adherence to medication is generally common in chronic diseases such as epilepsy, which may hamper the quality of life of these patients.[9] This non adherence or discontinuation of AED therapy is generally attributed to socio-economic factors, including lack of access to trained clinicians, cost of AED therapy, superstitious and cultural beliefs, and the predominance of traditional treatments.[6]

Several AEDs are now available worldwide for the treatment of epilepsy. With the availability of second- and third-generation AEDs, many factors may need to be considered in choosing the most appropriate treatment for individual based on tolerability and expected efficacy.[10] Differences do exist between selection of AEDs among developed and developing countries.[11] Although guidelines by neurological associations exist, treatment choices vary among various patient groups, especially in extremes of ages, among women of childbearing age, presence of various of comorbidities etc.[12,13] There is inadequate Indian data in context of choice of AEDs for treatment of newly diagnosed epilepsy. Hence, present observational study was conducted to determine the demographic details of newly diagnosed epilepsy patients and management choices of AEDs by clinicians in India.

METHODS

Study design

This real-world, retrospective, cross sectional, observational EPONE-2 (Evaluating the prescription pattern of newly diagnosed epilepsy 2) study was conducted at various centres across India. These centers included hospitals, clinics, and health care institutes. The study inclusion criteria was patients with epilepsy, who were newly diagnosed and treated by the respective study center physicians or neurologists. The data of these newly diagnosed epilepsy patients was collected by physicians or neurologists in this retrospective study between Apr 2021 and Mar 2022.

Ethics statement

The study was conducted after due approval from ACEAS Independent Ethics Committee, Ahmedabad, India. This was a retrospective study without patient identifiers; hence, informed consent of patients was not taken. There was no confidentiality breach of the data during its analysis and interpretation.

Study variables

Patients were selected based on treating physician's discretion, and no additional evaluation or investigations were performed during data capture. The demographic parameters including age, gender, socioeconomic status, family history of epilepsy, comorbidities and details related to prescribed treatment were recorded. Details related to type and duration of epilepsy, the treatment and management variables including the choice of AEDs, change in seizure frequency after therapy initiation, the presence and severity of side effects with ongoing AEDs, adherence to the drugs and clinician's global assessment for effectiveness and safety of prescribed treatment were recorded.

Sample size and statistical analysis

In this real-world study, patients' data was collected retrospectively without any predetermined sample size. The study did not test any hypothesis and only the observations from patient's records were analyzed. The data was collected from all centers across India and appropriate statistical analysis was performed at Lambda Therapeutics Ltd., Ahmedabad, India. Demographic and baseline characteristics were summarized using descriptive statistics. Categorical variables were summarized with frequency and percentage. Continuous variables were summarized with count, mean, standard deviation, etc. Graphical presentation of data was done using pie chart/bar chart as appropriate. Statistical analyses were performed using SAS® Version 9.4 (SAS Institute Inc., USA).

RESULTS

A total of 20,343 newly diagnosed patients with epilepsy from various centres across India between Apr 2021 and Mar 2022 were evaluated. Table 1 provides the demographic details of patients in this study. The patients had a mean (SD) age of 40.1 (13.61) years. Majority (54.5%) of the patients were between the age of 31-50 years in the study. When gender distribution was assessed, majority of the patients were males (62.7%) while females constituted 37.3% of the population. Focal type of epilepsy was the most common type of epilepsy (72.2%) whereas the remaining 27.8% patients had generalized type of epilepsy. Most of the patients (62.4%) were noted to be from upper middle class when socioeconomic status was evaluated. A family history of epilepsy was reported in 17.7% patients. Majority (68.5%) of the patients were diagnosed within 1-3 year of the disease duration.

Comorbid conditions

Comorbidities were reported in a total of 92.17% patients. Neuropsychiatric comorbidities were quite common among the newly diagnosed epilepsy patients. Migraine was the most common (28.3%) neuropsychiatric comorbid condition followed by anxiety (19.7%), stroke (18.5%), depression (11.2%) and neuropathic pain (10.7%) (Figure 1). Few patients were also reported to

have dementia, attention-deficit/hyperactivity disorder (ADHD) and Parkinson's disease.

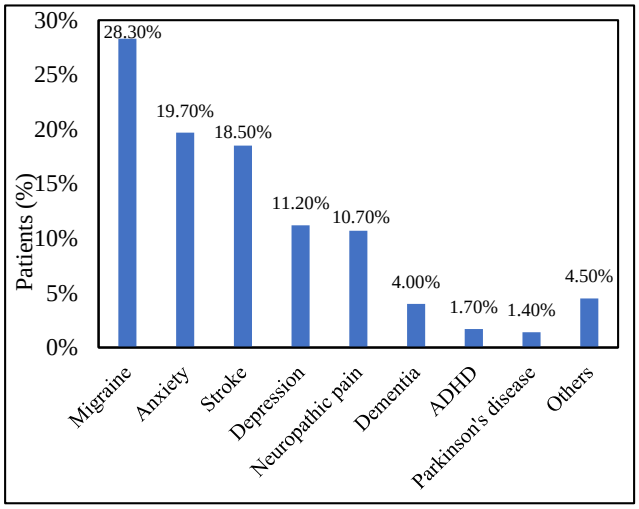

Figure 1: Distribution of patients with neuropsychiatric comorbid conditions.

ADHD, attention-deficit hyperactivity disorder.

The other commonly reported comorbidities included hypertension (38.27%), gastrointestinal disorders (25.39%), and diabetes mellitus (22.06%).

Table 1: Patient characteristics, (n=20343).

Parameters	All patients, N (%)
Age, years, mean (SD)	40.1 (13.61)
Age group, (Years), n (%)	
<10	364 (1.8)
11 to 20	1057 (5.2)
21 to 30	3451 (17)
31 to 40	5574 (27.4)
41 to 50	5510 (27.1)
51 to 60	3087 (15.2)
> 60	1300 (6.4)
Gender, n (%)	
Men	12752 (62.7)
Women	7591 (37.3)
Socioeconomic status, n (%)*	
Affluent	898 (6.8)
Upper middle class	8278 (62.4)
Middle class	1404 (10.6)
Lower middle class	2058 (15.5)
Labourer class	625 (4.7)
Family history of epilepsy, n (%)	
Yes	3606 (17.7)
No	16737 (82.3)

*n=13263; SD, standard deviation.

Anti-epileptic drugs

Overall, levetiracetam (49.6%) was the most prescribed AED; valproate (29.1%), oxcarbazepine (15.5%), clobazam (13.3%) and lacosamide (8%) were the other commonly utilized AEDs in the present study.

For the treatment of focal epilepsy, the most prescribed AEDs were levetiracetam (51.1%) followed by valproate (24.4%), oxcarbazepine (19.8%), clobazam (13.7%) and lacosamide (8.8%) (Figure 2 A). For the treatment of generalized epilepsy, valproate (36.1%) followed by levetiracetam (29.10%), clobazam (12.3%), oxcarbazepine (6.6%) and lacosamide (6.4%) were the most commonly utilized AEDs (Figure 2 B).

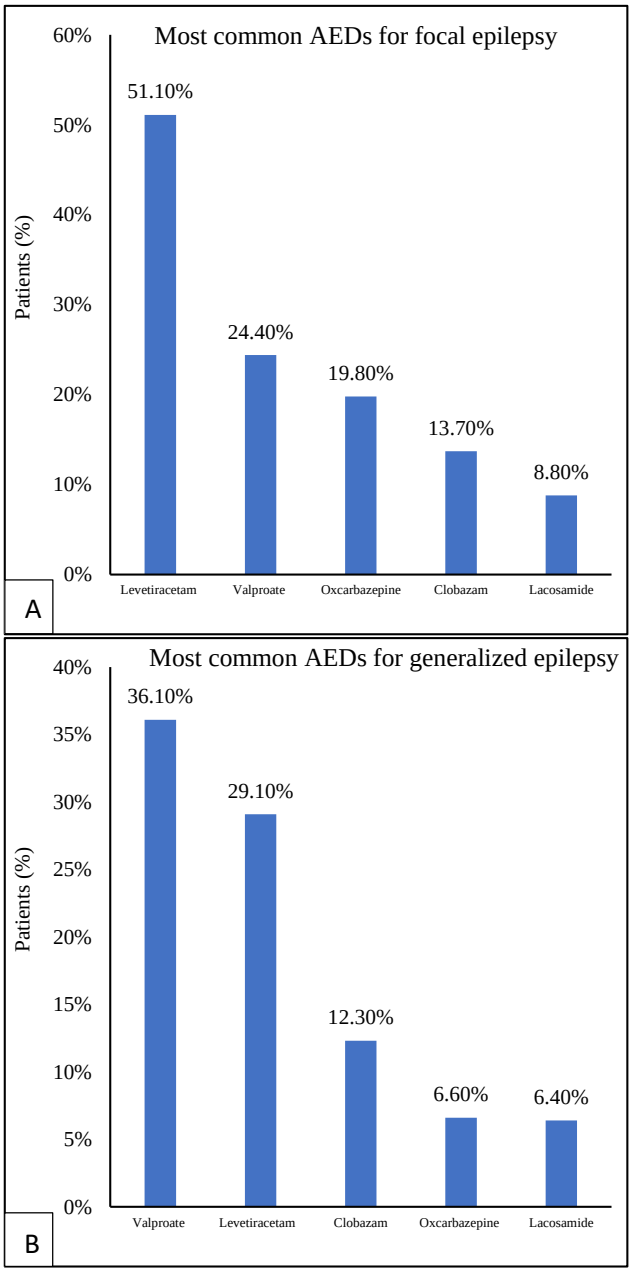

Figure 2 (A and B): Most commonly used AEDs for focal epilepsy and generalized epilepsy.

Levetiracetam was the most commonly used AED in patients with neuropsychiatric comorbidities. In patients with comorbid migraine, levetiracetam was the most

commonly prescribed (50.50%) AED while valproate was next most common (30.70%). Other commonly prescribed AEDs were oxcarbazepine, clobazam and lacosamide. Levetiracetam was the choice of AED in 50.70% of epilepsy patients with anxiety followed by valproate in 34.9% of cases. In 48.2% cases of epileptic patients with co-morbid depression, levetiracetam was the choice of drug followed by valproate (34.8%). Levetiracetam was also the most common prescribed (55.8%) AED in epilepsy patients with stroke followed by valproate (21.3%) (Figure 3).

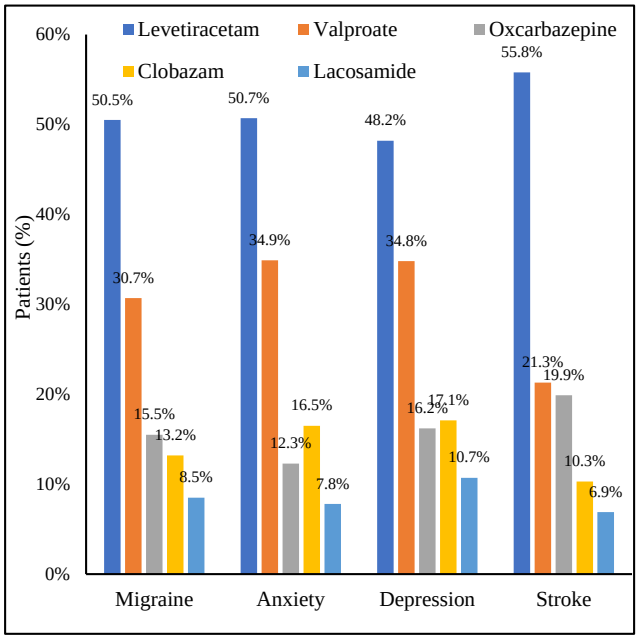

Figure 3: Use of AEDs in epilepsy patient with neuropsychiatric comorbidities.

A decrease in the seizure frequency after starting the AED was reported in 91% patients. In most (99.2%) of the patients, adherence to AEDs was 'good to excellent'. Clinician's perception for the overall efficacy and safety of the prescribed management strategy was 'good to excellent' in most (99.9%) of the patients.

Safety

In patients prescribed with levetiracetam, valproate, oxcarbazepine, clobazam, and lacosamide, at least one adverse event (AE) was reported in 62.2%, 81.1%, 85.2%, 80.4% and 83.4% patients, respectively. Mild AEs were reported by 46.6% patients who were prescribed levetiracetam, 61% with valproate, 56.3% with oxcarbazepine, 57.1% with clobazam and 60.3% with lacosamide.

DISCUSSION

The present real-world observational study was conducted across India in 20,343 newly diagnosed epilepsy patients to determine the demographic patterns and the management of epilepsy. The cases of epilepsy were mostly between 30-50 years of age, with male preponderance. Hypertension, gastrointestinal disorders, migraine, anxiety, and stroke were associated comorbidities. Majority of the patients had focal epilepsy wherein levetiracetam was the clinician's choice of AED, followed by valproate and oxcarbazepine. For generalized epilepsy, valproate was preferred followed by levetiracetam. In this study, the AEDs were found to be effective and well-tolerated.

The study showed that majority (55%) of the patients were between 30-50 years of age. Changing patterns are observed in the age-specific occurrence of epilepsy in India. Nandi et al reported a higher prevalence of epilepsy in the first decade of life.[14] Later, majority of the studies from India reported a higher prevalence during the second decade, while Raina et al reported a higher prevalence in the fourth decade.[5,15,16] The changing patterns might be linked to demographic transition, changing living conditions, improved healthcare services, changing dietary habits, increased awareness, and better help-seeking behaviours.[17] Majority of the newly diagnosed epilepsy patients in this study were males (62.7%). These results are in concordance with earlier published reports from India which have shown a male preponderance in this disease.[17-19]

Globally, low socioeconomic status, low income, and less education are regarded as risk factors for epilepsy.[20] Socioeconomic factors have a strong association with birth trauma, infections, poor nutrition, poor hygiene, and poor health-seeking behaviour, which greatly influence the risk of epilepsy.[17] These factors significantly impact hospitalization, seizure frequency, and drug-related side effects.[21] In a hospital-based study on 196 cases in Karnataka state, more than 80% patients belonged to low socioeconomic status and were unskilled workers.[22] In the current study, 62% of the patients with epilepsy belonged to upper middle class while 15% were from lower middle class. The probable reasons for the high incidence of epilepsy in upper middle class in this study could be due to higher proportion of patients from private clinics which were predominantly located in urban areas.

Studies have reported that family history of epilepsy is a strong independent predictor of epilepsy.[23,24] In this study, 17% of the patients had a family history of epilepsy. Migraine and epilepsy occur together irrespective of the seizure type, age of onset, and etiology, and possibly have a common genetic susceptibility.[25,26] A review of 13 studies reported that the prevalence of epilepsy in patients with migraine ranges from 1 to 17% with a median of 5.9%.[27] In another study conducted in India, migraine was observed in 26% of epilepsy patients as compared to 15% in the control group.[28] In the present study, migraine was present in 28.3% and other common neuropsychiatric comorbidities included anxiety (19.7%), stroke (18.5%) and depression (11.2%). Although according to Babu et al., hypertension,

diabetes, osteoarthritis, asthma, hypothyroidism, and acid-peptic disease are less common reported comorbidities in epilepsy patients of the current study, the prevalence of hypertension was 38.3%, gastrointestinal distress was 25.45% and diabetes was 22.1%.[29] The etiology of epilepsy is linked to the seizure types. Hospital-based studies have reported a higher frequency (57-80%) of partial epilepsies; while community-based studies recorded a higher frequency for generalized epilepsies (54.5-79%).[30,31] In the present study, focal epilepsy was the most common type (72%).

Epilepsy treatment gap in India ranges from 22% among urban to 90% in rural areas.[32] The most common prescribed AEDs in the present study were levetiracetam (49.6%), valproate (29%), oxcarbazepine (15%), clobazam (13.3%) and lacosamide (8%). Same preference order for AEDs was observed in patients with focal epilepsy. In patients with generalised epilepsy, the prescription pattern was valproate (36.1%), levetiracetam (29.1%), clobazam (12.3%) and lacosamide (6.4%). Overall, levetiracetam was the preferred AED in this study. Studies have reported that levetiracetam is globally established leading AED due to advantages in terms of lack of drug interactions, and excellent efficacy and tolerability profiles.[33] As per the guidelines of management of epilepsy in India laid by the Indian epilepsy society, the choice of AED should be based on seizure type, affordability and the availability of AEDs.[34] Majority of the patients (91.4%) in this study responded to the treatment as evident from the reduced frequency of epileptic attack. Side effects with most of the AEDs were mild and AEDs were tolerated well. Treatment adherence was good with AEDs. The clinician's perception on the overall efficacy and safety of the management strategy was reported as good.

The study strength is inclusion of patients with newly diagnosed epilepsy across the country of different age groups, socioeconomic strata and comorbidities. The recorded treatment patterns considering the efficacy, safety and adherence reflect the real-world scenario of epilepsy patients. A major limitation of the study was that the treatment outcomes at various time intervals were not available. As epilepsy is a chronic disorder requiring longer treatments with frequent follow-ups, a long term prospective, cohort study may make further addition to our insight on the matter.

CONCLUSION

The occurrence of epilepsy was common between the age 30 and 50 years and in males. Focal epilepsy was more prevalent. Levetiracetam was the most prescribed AED. Levetiracetam and valproate were the most prescribed AEDs among focal and generalized epilepsy, respectively. Anti-epileptic treatment reduced the frequency of seizures. The prescribing clinician's perception on the overall efficacy and safety of the management strategies was good. The study outcomes would help to device optimum prevention and management related clinical strategies collectively.

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Conflict of interest: Dr. Meera Kacha, Dr. Amit B. Jain, Dr Nilanj Dave and Dr. Alok Chaturvedi are employees of Intas Pharmaceuticals Limited. Ankita Shah is an employee of Lambda Therapeutic Research Ltd., Ahmedabad, Gujarat, India
Ethical approval: The study was approved by the Institutional Ethics Committee

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