

**Original article:**

## **Pharmaco-epidemiological and pharmaco-economic analysis of antiepileptic drugs at a tertiary level health care centre - a cross-sectional prospective study**

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### **Abstract**

**Background:** The need of prolonged treatment of epilepsy along with high cost of new antiepileptic drugs (AEDs) imposes a heavy economic burden on poor rural population. Thus, this study aims to analyze the current pharmacotherapy practices of epilepsy and its economics in a tertiary care rural teaching hospital by correlating the epidemiology and economics of antiepileptic drug (AED) treatment.

**Methods:** A prospective, cross-sectional, observational study was carried out over 1 year. The epidemiological, disease and treatment data were collected from patients with epilepsy from medicine and paediatric out patient departments (OPDs).

**Results:** The study group comprised 180 men and 125 women. The mean  $\pm$  SD (standard deviation) of the patients' age was  $30.2 \pm 15.6$  years. Primary generalized epilepsy (58.5%) and seizures secondary to head injury and infections were the frequent causes. Monotherapy was seen among 60% with maximum number of patients receiving phenytoin (DPH) (41.3%), followed by Carbamazepine (CBZ) (32%), Valproic acid (VPA) (15.4%), and Phenobarbitone (PB) (10.5%). Polytherapy consisted combination of two AEDs or AED with Benzodiazepine (BZD). The relative cost (% GNP/capita) for standard AEDs were as follows: PB, 4.4%; DPH, 7.1%; CBZ, 16.8%; and VPA, 29.5%. Cost minimization analysis showed a higher absolute annual cost of new vs old AEDs ( $p < 0.05$ ).

**Conclusions:** In this study significant high cost of treatment was observed; use of polytherapy further added to the cost of treatment; suggesting the need to design comprehensive treatment plan to encourage more cost effective use of AEDs in poor rural population.

**Key words:** Pharmaco-Epidemiology, Pharmaco-Economics, Antiepileptic Drugs

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### **Introduction**

Epilepsy is a common neurological disorder specially in paediatric age group and has always been a challenge to treat.<sup>1</sup> The desired outcome of AED therapy is for patients to be seizure-free throughout the rest of their lives.

In the last 15 years the treatment of epilepsy has advanced with the development of newer antiepileptic drugs (AEDs) and various other treatment modalities like neurosurgery etc.<sup>2, 3, 4</sup> Though the newer agents have proven efficacy over classical old AEDs, their utilization in the rural population is a query because of the cost factor.

These new agents are generally used as monotherapy, add-on treatments in patients with refractory epilepsy or to improve efficacy of old drugs and are quite expensive when compared with traditional AEDs. Therefore, the use of newer agents is not standardised in developing nations like India.<sup>5</sup>

The economic study outcomes cannot be generalized across different-geographical regions, as seen in trial conducted in Europe.<sup>6</sup> Such differences are attributed to variations in the charges paid to health services in different regions thus emphasizing the need to conduct separate economic studies for each region. More than 90% of the financial burden of epilepsy is carried by developing countries.<sup>7</sup> However, very little information is currently available regarding the pharmacotherapeutic profile of epilepsy from the developing world. The need of prolonged treatment of epilepsy along with high cost of new AEDs imposes a heavy economic burden on poor rural population. The different distribution of costs in children and adults with epilepsy suggest the need for intervention at an early age to try to reduce the long term economic and personal repercussions. The pharmaco-economic evaluation of the new antiepileptic drugs will make it clear whether their considerable cost is worth paying for their greater effectivity. Although, socioeconomic impacts of treatment options have been studied in South India, data from Central India is lacking.<sup>7, 8</sup> Assuming substantial difference in the epidemiological and economic factors of central india from other regions, we formulated this study to evaluate these factors in our tertiary care centre.

#### **Aim**

Prescription profile and cost analysis of use of antiepileptic drugs.

#### **Objectives**

- Epidemiological characteristics of the epileptic patient population.
- Prescription analysis for common drugs, polypharmacy, fixed dose combinations (FDCs)
- Cost analysis of the old and new antiepileptic drugs

#### **Materials & methods**

The study was carried out at the Acharya Vinoba Bhave Rural Hospital, attached to the Jawaharlal Nehru Medical College, Sawangi, Wardha after obtaining approval of the Institutional Ethics committee. 305 patients of proven Epilepsy attending medicine and paediatric OPDs were recruited and studied over a period of 1 year. We also obtained permission from the treating physicians to approach their patients. After explaining about the study procedure, their written informed consent was obtained.

**Socio-demographic Data:** Age, sex, the place of residence, marital status of the patient, level of education and occupational status, monthly income were recorded.

**Epilepsy Data:** Patients of all age groups, receiving AEDs, were included. The standard classification of epilepsy was followed to classify the types of patients. This consisted of the primary and secondary types.

**Antiepileptic Drug (AED) treatment data:** The drug treatment data included the number of AEDs (monotherapy/polytherapy), generic/brand name, dose and duration of treatment for each patient.

#### **Data on costs:**

**1. Direct costs:** This included cost of AEDs, hospital resources used and cost of travel. The hospital resources used comprised of out patient consultation

charges and the cost of the investigations. Only investigations done in the last 12 months for purpose of diagnosis or follow up of epileptic seizures were recorded in addition to the distance travelled for visiting the hospital by every patient.<sup>9</sup>

AED acquisition costs were collected from the hospital pharmacy. The local price, in Indian Rupee (INR) was assigned for each AED. The cost of hospital consultation was assigned as INR 20.00 and the cost of investigations was assigned its local price prevailing at the time of study. The cost of hospital resources was obtained from hospital's account department. Travel cost was arbitrarily fixed as INR 5.00 for every kilometre of distance, travelled by the patient.

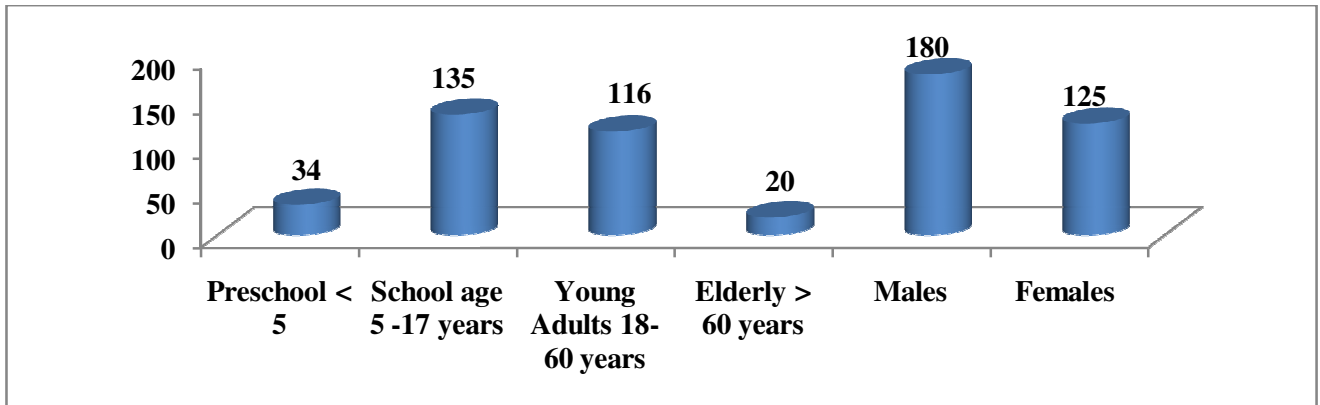
**2. Indirect costs:** This included the cost of travel for accompanying attendees and lost wages. On an average, two attendees accompanied every patient.

The daily wages for the patient were fixed arbitrarily at INR 150.00 per day. This was assumed for all patients, irrespective of the age or their employment status<sup>9,10</sup>.

**Statistical analysis:** Where appropriate, data is presented as means / percentages / p value. Descriptive statistical analysis was carried out using SPSS.

**Results**

Figure 1 shows the demographic characteristics of 305 epilepsy patients from the hospital over a period of 12 months. The study group comprised 180 men (59.01%) and 125 women (40.9%). The mean  $\pm$  SD (standard deviation) of the patients' age was 30.2  $\pm$  15.6 years ranging from 0.5 to 75 years. 60% of the population was from farming background and remaining were students or in service with average monthly per capita income of Rs. 1579 only.



**Figure 1: age and gender wise distribution of patients**

60.1% patients were suffering from primary generalized epilepsy while remaining (39.9%) were cases of secondary epilepsy; the most common precipitating factors of which were head injury and

infections. Alcoholism, cardio-vascular accidents and neurocysticercosis were the other less frequent causes. Generalized tonic – clonic epilepsy was the commonest presentation. (58%) (Figure 2)

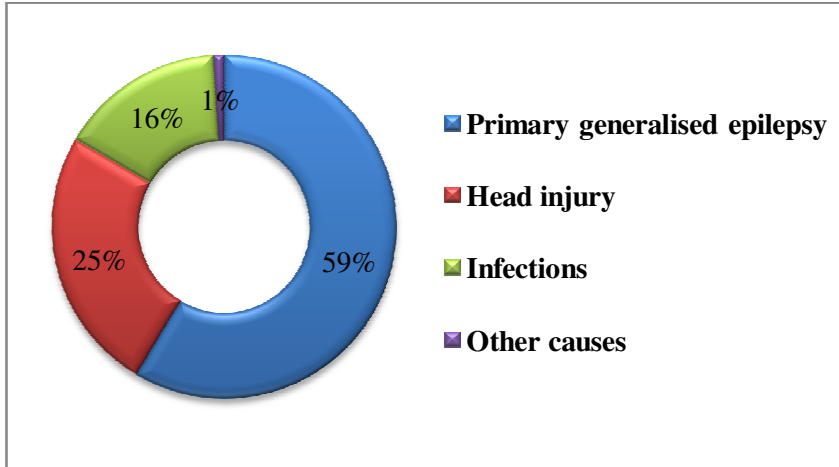


Figure 2: Etiological distribution of Epilepsy

Monotherapy was prescribed to 182 (59.67%) patients. Remaining patients received 2-3 drugs in combinations amounting to an average of 1.44 drugs per prescription. Figure 3 shows the pattern of AED choice among patients of epilepsy receiving monotherapy. Maximum number of patients received

Phenytoin (DPH) (41.3%), followed by Carbamazepine (CBZ) (32%), Valproic acid (VPA) (15.4%), and Phenobarbitone (PB) (10.5%). (Figure 3) Topiramate is an antiepileptic agent indicated as add-on therapy in adults and children with partial seizures, generalised tonic-clonic seizures.

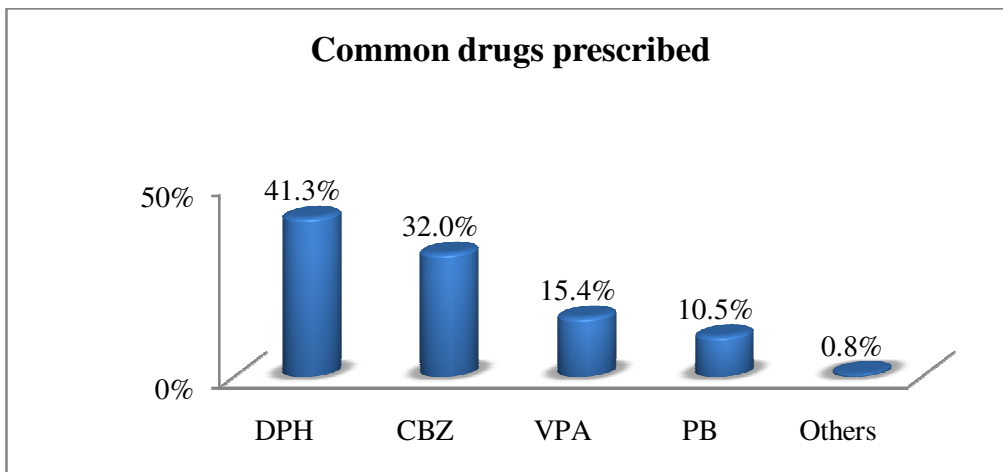


Figure 3: profile of antiepileptic drug use

**Pharmacoeconomic evaluation of drug treatment:**

**The cost of treatment:** In this study it was observed that total annual direct cost per patient was INR 5934.27 while indirect cost was 2163.85. The annual direct medical expenses included costs of outpatient consultation (INR 80), cost of AEDs (INR 3207.64)

and costs of investigations (INR 1973.79). The annual direct non-medical expenses included cost of travel (INR 479) for an average distance of 30 km, per patient. The annual indirect expenses included the lost wages due hospital visits (INR 918.80) and the cost of travel for the attendants (INR 700.80).

**Table 1: ATC Codes Defined Daily Dose (DDD) of Antiepileptic Drugs (AEDs) with Absolute Acquisition costs**

Antiepileptic Drug	ATC Code	DDD in mg	Absolute Cost (INR)
Phenytoin	N 03 AB 02	300	3.60
Phenobarbitone	N 03 AA 02	100	2.40
Carbamazepine	N 03 AF 01	1000	8.15
Sodium Valproate	N 03 AG 01	1500	19.89
Oxcarbazepine	N 03 AF 02	1000	16.50
Topiramate	N 03 AX 11	300	52.50
Gabapentin	N 03 AX 12	1800	29.40
Lamotrigine	N 03 AX 09	300	34.50
Clobazam	N 05 BA 09	20	14.74
Clonazepam	N 03 AE 01	8	17.08

*\*WHO "Anatomical Therapeutic Chemical (ATC) classification index - 2015".*

**Cost Minimisation Analysis:**

The average, absolute annual cost, according to Defined daily dose standards of old AEDs was INR 1039.8 and the new AEDs was INR2584.13 The difference between these absolute cost was found to be statistically significant (p <0.05).

**Discussion**

Epilepsy is usually a chronic disease of all age groups with variable outcomes. Thus, its successful treatment with minimal expenses is a responsibility of the treating physicians. The epidemiological and economical analysis of the AED therapy would provide a good framework to develop ideal prescribing practices for the doctors. Cost minimization analysis of the therapies is considered

as an ideal tool to reduce the expenses on drug therapy. Thus, the main aim of our study was to consider the socio-economic impact of the therapy on poor rural population. The epidemiological profile of our patient population was found to be similar to studies done in south India by Sigamani A.<sup>9</sup> and Radhakrishnan K.<sup>7</sup> and other countries<sup>11</sup> with higher number of male patients than females. On the contrary a study done in Oman contained higher no of female patients.<sup>12</sup>

The average age of our patient population was 30 years; which was identical to studies in India<sup>7,9</sup> and Oman<sup>12</sup> but lower than the studies done in western countries.<sup>11, 13</sup> In our study primary generalised seizures accounted for more than 50% of the cases of

epilepsy. Similar findings were observed by Sigamani<sup>9</sup>, Hanssens<sup>12</sup> and Mattson<sup>14</sup>. In contrast, the studies from developed countries show that partial seizures account for more than 50% of the cases.<sup>7,15</sup>

Higher percent of patients received monotherapy in our study; which is an ideal practice in terms of improving compliance, success rate and reducing the cost of therapy. But this also indicates higher incidence of simple uncomplicated seizures; as complicated epilepsy warrants polytherapy. Studies done in south India have comparable findings.<sup>7,16</sup> It may also be noted that, dual or polytherapy leads to the increased chances of side effects and drug-drug interactions, which ultimately increases the cost of therapy.

The commonest AED used in our study was phenytoin followed by carbamazepine and valproate. In the last few years there has been considerable change noted in the choice of AEDs. Though the side effect profile of phenytoin is higher than other AED, it is still first choice AED as monotherapy until contraindicated. The profile is similar to the studies done in south India.<sup>17, 18</sup> The availability of new drugs like lamotrigine, gabapentin, vigabatrin, oxcarbazepine and topiramate is altering the prescriptions of epileptic therapy. Though, lamotrigine and oxcarbazepine have been licensed for monotherapy in partial seizures;<sup>19,20</sup> our study and many other studies observed their use as 'Add On Therapy' only.

The pharmacoeconomic analysis of the AEDs is the need of time because of the increased use of newer

AEDs, which are comparatively costlier than old AEDs. There are considerable number of factors which influence the cost of epilepsy therapy. The studies from Netherlands<sup>21</sup>, UK<sup>22</sup> and Oman<sup>23</sup> showed the influence of prognosis of seizures, the cost of hospitalization, the cost of new AED and radio imaging tests on the costs of treatment of epilepsy. The total cost per patient with epilepsy was found to be approximately INR 8098.12 and 73.2% of this cost was related to the direct medical expenses. The direct costs included the consultation costs, cost of new AEDs and the cost of investigations like EEG and MRI as seen in our study and in the studies conducted in south India.<sup>9,16,23</sup>

The cost-minimization analysis shows a higher absolute cost of newer antiepileptic drugs over the old once. However, we also have to consider the improved rates of permanent control of epilepsies achieved by newer AEDs over older drugs. As it may affect the functional days of the patient and reduce the losses of daily wages incurred due to epilepsy and prolonged treatments with hospitalizations. Thus, the better tool to compare the efficacy of AEDs will be cost-effectiveness analysis of the older and newer antiepileptic drugs.

### **Conclusion**

In the present study, significant high cost of treatment was observed. Use of polytherapy further added to the cost of treatment; suggesting the need to design comprehensive treatment plan to encourage more cost effective use of AEDs, to reduce economic burden of epilepsy on poor rural population.

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