JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

PREDICTION OF MONOTHERAPY ANTI-EPILEPTIC DRUG

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Abstract— Anti-seizure medication (ASM) that works well and has few side effects are difficult to find. The choice of treatment is guided by the characteristics of the patient; however, approximately 50 percent of epileptic patients do not experience seizure freedom after taking an ASM for the first time. The gold standard for determining treatment efficacy is a randomized controlled trial, but these studies aren't always clinically relevant—especially when it comes to uncommon conditions. Because they are accessible, updated frequently, and have the capacity to hold many patients, registers are important sources of data. The current study aims to assess registers and create machine learning algorithms for epilepsy-specific personalized medicine. The findings suggest that it is possible to estimate ASM retention using register data, and that selecting ASMs based on their individual needs may enhance patient outcomes. Register retention rates are comparable to those of RCTs and RCT meta-analyses. The 5-year retention rate for the initial ASM could potentially be improved by 14–21 percentage, according to a study of patients with epilepsy and comorbidities. Similar to recommendations based on professional advice, ASMs for patient cases are ranked according to retention rates from register data. We also looked at children, a population for which there is little data. Physicians may find specialized machine learning algorithms to be a helpful source of information when choosing ASMs.

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I. INTRODUCTION

A common brain condition, epilepsy has a lifetime prevalence of 0.76% worldwide. Typically, epilepsy is diagnosed following two unprovoked seizures or following one unprovoked seizure along with a high probability of further seizures. Anti-seizure drugs are the most widely used treatment for epilepsy (ASMs). There are about thirty distinct ASMs, each with a unique mode of action and possible adverse effects. Although epilepsy can strike at any age, the incidence is U-shaped, with younger and older people experiencing more onsets. While certain acquired epilepsies following brain damage, such as a stroke, become more common with age, genetic causes are more common in younger ages. Seizures can begin in two ways: focally or through counselling, and sometimes they start for unknown reasons. A seizure that originates in a specific area of the brain is referred to as focal onset, and it suggests a focal disruption of brain activity that may be inherited or acquired. Even in cases where the person experiencing the seizure is immobile, awareness can still be retained or compromised. Seizures with a "generalized onset begin concurrently in both hemispheres. Focal onset seizures have the potential to spread to other brain areas. It is possible to classify a tonic-clonic seizure as either focal or bilateral if it starts in one hemisphere of the brain and moves to the other. The type of epilepsy is determined by the seizure onset; focal epilepsies result in focal seizures. The choice of ASM is influenced by the type of epilepsy; certain ASMs can be selectively effective in treating focal epilepsies, and they can even make counselling ones worse. While counselling epilepsy rarely develops after the ages of 25 to 30, focal epilepsy can begin at any age. Early identification of an appropriate ASM is crucial in order to prevent seizures and the associated risks of head trauma, fractures, and drowning. Some patients never

locate a suitable ASM. The failure of two suitably selected and sufficiently tried ASMs, either as monotherapy or in combination, is referred to as drug-resistant epilepsy. Individuals with drug-resistant epilepsy have a mortality rate 4–7 times higher and an injury rate ranging from 1 in 20 to 1 in 3 person-years. Numerous factors may need to be taken into account when choosing an appropriate ASM. Among other things, ILAE advises considering comorbidities, age, gender, genetics, and epilepsy syndrome. It's crucial to take the patient's preferences into account. Long-term adverse effects of ASMs include cardiac problems, valproic acid, and pregnancy. Even though treating seizures is crucial, misdiagnosing epilepsy—for instance, as cardiac arrest—and initiating epilepsy treatment can have disastrous consequences. Specific gene-related side effects have been linked to certain medications. In Southeast Asian nations, carbamazepine is the primary cause of Stevens-Johnsons syndrome (SJS). High fever, malaise, exanthema, and mucosal involvement are the symptoms of SJS-TEN. ASM side effects have been classified using a modified version of the WHO adverse effect classification. In brief clinical trials, types A and C are more likely to be identified than the other types; in contrast, types B, D, and E occasionally need more time to be identified and comprehended.

Clinical Trials of ASMS

The literature currently in publication demonstrates the challenges in ascertaining the comparative effectiveness of ASMs in a way that is clinically significant. RCTs, uncontrolled trials, and observational studies are examples of traditional methods. Below is a discussion of the advantages and drawbacks of these tactics as well as the gaps in research questions that are pertinent to personalized medicine. The following is one recommendation from the hierarchy of evidence for choosing a patient's initial ASM:

1. Individual patient data meta-analysis
2. Systematic review and meta-analysis of large RCTs
3. Large RCTs
4. Systematic reviews of small RCTs
5. Small RCTs
6. The consensus of expert opinion
7. Individual expert opinion
8. Case series
9. Individual case repo

The gold standard for assessing epilepsy treatments is randomized controlled trials (RCT). These studies, however, are frequently carried out for regulatory purposes using a single comparator or a placebo as the reference. It can be difficult to extrapolate treatment efficacy to all patients due to the stringent eligibility requirements in clinical trials, which are often implemented to protect vulnerable populations like the elderly or pregnant patients from potential adverse effects. Moreover, the regulatory study protocols provide minimal to no leeway in dosing schemes, which could impact the study's applicability to clinical practice and the interpretation of drug efficacy.It's also possible that trials are too brief to identify the best dosage for patients. Pregabalin, for instance, was found to be less effective than lamotrigine; this could be due to the fact that pregabalin was ineffective at the initial maintenance dose and the trial's duration precluded comparison of efficacy at higher doses. Limited generalizability of clinical trials with 3–6-month follow-up occurs from the challenge of determining drug effectiveness in such a short period of time. Because of the high costs and ethical challenges associated with conducting controlled trials, uncontrolled studies frequently yield inaccurate estimates of both efficacy and side effects because of confounders. By selecting the eligibility requirements, formulation, target doses, titration rates, or interpretation of the data, non-regulatory trials may be biassed in favour of the sponsor's product. When patients have uncontrollable seizures, ASMs are frequently tested as an adjunctive treatment in clinical trials. When a new ASM hits the market, these are frequently the only efficacy data that clinicians have access to. Then, especially if the medication is used as monotherapy, clinicians need to exercise caution when determining how best to use it.

ASM	Effectiveness, evidence level 2006	Effectiveness, evidence level 2013
Carbamazepine	A	A
Gabapentin	C	C
Lamotrigine	C	C
Oxcarbazepine	C	C
Phenobarbital	C	C
Phenytoin	A	A
Topiramate	C	C
Valproic acid	B	B
Vigabatrin	C	C
Clonazepam		D
Levetiracetam		A

Primidone		D
Zonisamide		A

Table 1 Effectiveness Comparison

II. LITERATURE REVIEW

Arvind Kumar; Chintalapati Janaki et al. [1] indicated that the process of finding potential drug targets for anti-epileptic medications is difficult and frequently combines computational and experimental methods. In this context, machine learning has been applied more and more to speed up the drug discovery process. The following list of popular machine learning methods and strategies can be used to determine potential drug targets for anti-epileptic medications. Targets and chemical and structural information of recognized anti-epileptic medications can be used to train machine learning models. This can involve techniques like virtual screening to find possible drug candidates and QSAR (Quantitative Structure-Activity Relationship) counselling to estimate the bioactivity of compounds.

Naymee J. Velez-Ruiz; Page B. Pennell et al. [2] Research revealed that women with epilepsy might experience difficulties and problems because of their condition. Here is a list of some of the most important problems that women who have epilepsy frequently face. The frequency and severity of seizures can be influenced by hormonal changes that occur during the menstrual cycle, pregnancy, and menopause. In order to manage these hormonal fluctuations and modify their treatment, women with epilepsy may need to collaborate closely with their healthcare providers. Hormonal contraceptives and certain antiepileptic medications (AEDs) can interact negatively and lessen the effectiveness of both. To reduce risks during pregnancy, women with epilepsy must carefully consider their family planning options and choose their methods of contraception. It can be difficult for women with epilepsy to become pregnant. They might be more susceptible to problems, and some AEDs might be harmful to the growing fetus. A safe pregnancy requires careful management, which includes prenatal care and medication adjustments.

Anahita Aghaei-Lasboo; Robert S. Fisher et., al [3] In-depth seizure frequency and severity measurement is essential to managing epilepsy and assessing treatment efficacy. Seizures can be observed using a variety of techniques and instruments. These are a few widely used techniques to gauge the frequency and intensity of seizures. Every seizure episode can be documented in-depth seizure diaries, which patients or their carers can keep. This includes details about the type of seizure, its date, duration, and potential triggers, as well as any noteworthy observations. Seizures must be recorded in order to monitor the frequency of seizures and spot trends. During clinical visits, neurologists and medical professionals evaluate the frequency and intensity of seizures. To assess the effects of seizures on a person's life, they consult the descriptions and records provided by patients in addition to their own observations. An EEG is frequently used to diagnose epilepsy. It captures the brain's electrical activity. Long-term video EEG monitoring or ambulatory

Laura M Borgelt; Felecia M Hart; Jacquelyn L Bainbridge et al. [4] found that women with epilepsy face difficulties, especially with regard to hormonal effects, pregnancy, and contraception. For women with epilepsy, effective management techniques are crucial to enhancing their quality of life. This is a synopsis of women-focused management strategies. Achieving optimal seizure control means weighing the advantages of seizure reduction against the possible negative effects of antiepileptic medications (AEDs). Medical professionals will customize the AED selection based on the kind of seizures, possible side effects, and patient-specific variables. Women need to be made aware of the possible influence of hormone changes on the frequency of seizures. Certain women undergo alterations in their seizure patterns because of menstruation, pregnancy, and menopause. Medication adjustments and careful observation may be required. Women who have epilepsy should talk to their medical professionals about their options for contraception.

III. SYSTEM ARCHITECTURE

The system architecture begins its journey by obtaining input data, which forms an essential base layer for later phases. This data, which includes a variety of patient details pertinent to the management of epilepsy, acts as the raw material. Next, the architecture determines the patient's seizure status, which is a critical first step in understanding the patient's immediate health state. This early evaluation helps with timely medical intervention decision-making and provides information for later analyses. After determining the seizure status, the architecture smoothly incorporates a clustering algorithm intended to group patients according to age groups. This stratification is a sophisticated method that acknowledges the impact of age on the features of epilepsy and the reactions to treatment. The clustered data paves the way for more specialized analyses, guaranteeing that later architectural stages can modify their techniques to suit the distinct features of various age groups. The accuracy and efficiency of the system are improved by this dynamic adaptation. The architecture advances to the dosage analysis stage, which is a crucial stage in the prescription of anti-epileptic medications. The patient's age group, medical history, and other relevant variables are carefully taken into account when determining the dosage.

By determining the ideal dosage amounts for given durations, this step seeks to maximize treatment outcomes. By incorporating this dosage analysis step, the system complies with the principles of personalized medicine, which recognize

the variation in patient responses to medication. Towards the end, the architecture makes use of the abundance of data that has been analyzed to produce predictions about which anti-epileptic medication would be best for each individual. The previous phases come together to form this predictive capability, which gives medical professionals important information to make medication decisions based on the individual profiles of each patient. This system architecture's comprehensiveness highlights its potential to transform epilepsy management by providing a tailored and nuanced approach to treatment.

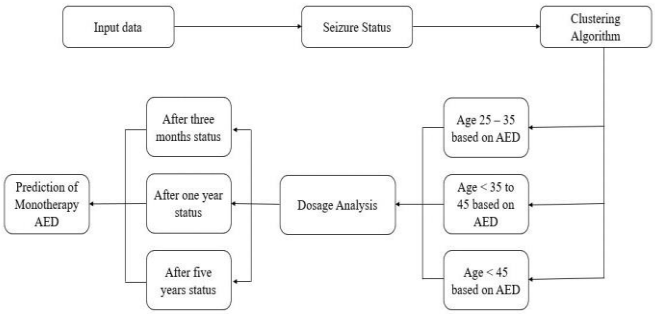

Fig 1 System Architecture

IV. PROPOSED SYSTEM

Module Description:

Module 1: Data input

The algorithm's data input comes from this module. The data set contains the values that were entered. The data set comprises 19 attributes and approximately 210 data.

Module 2: Anti-Epileptic Drug (AED)

The two major steps involved for AED are:

a) Fit free rate

b) Relapse of fit rate

a) Fit free rate

Several drugs are recorded for the women, and based on the outcome status, a percentage is computed. This data can be analyzed to determine a drug's fit free rate, which is then recommended.

a) Relapse of fits rate

Several drugs are recorded for the women, and based on the outcome status, a percentage is computed. These findings can be used to identify a drug's higher risk rate, which makes it less desirable.

Methodology

Using machine learning (ML) to detect monotherapy epilepsy drugs entails creating a model that can precisely detect the presence of particular drugs in a patient's system. The ML model can be trained on a dataset containing details about patients' drug use and related test results in order to accomplish this.

Data Collection

DETAILS	EEG	MRI	CALCIUM VALUE	ANY CO-MORBIDITIES			TREATMENT			OUTCOME
DELIVERY STATUS				DM	HT	OTHERS	DRUG NAME	DOSE	DURATION	
	0	0	0	9	NIL	NIL	Phenytoin	100 mg	1	0
							Carbamazepine	200 mg	1	
							Sodium Valproate	200 mg	1	
	0	0	0	8.2	104 MG	140/80	NIL	phenobarbitone	30 mg	1	0
							Sodium Valproate	200 mg	1	
							Phenytoin	100 mg	1	
	0	0	0	9.2	NIL	110/70	NIL	Phenytoin	100 mg	1	0
							Carbamazepine	100 mg	1	
							Sodium Valproate	200 mg	1	
							Clobazam	5 mg	1	
							Levetiracetam	250 mg	1	
	0	0	0	8.8	NIL	110/70	NIL	Phenobarbitone	60 mg	1	0
							Phenytoin	200 mg	1	
							Clobazam	5 mg	1	
							Sodium Valproate	200 mg	1	
	0	0	0	9.2	NIL	110/80	NIL	Phenytoin	200 mg	1	0
							Sodium Valproate	200 mg	1	
							Phenytoin	100 mg	1	
	1	0	0	7.8	NIL	150/100	NIL	Carbamazepine	100 mg	1	0
							Clobazam	10 mg	1	
							Sodium Valproate	200 mg	1	
	1	0	0	9	NIL	120/70		Phenytoin	200 mg	1	0
							Clobazam	5 mg	1	
							Carbamazepine	400 mg	1	
							Sodium Valproate	200 mg	1	
	0	0	1	10	NIL	120/70	NIL	Phenytoin	200 mg	1	1
	0	1	0	10.3	NIL	110/70	NIL	Carbamazepine	150 mg	1	1
								folvite	5 mg	1	
	0	1	1	5.8	NIL	160/90	NIL	Phenytoin	100 mg	1	1

To develop an ML model for monotherapy drug detection in epilepsy, you would need a dataset that includes the following information:

- Patient Records: Collect patient records that include details such as age, gender, medical history, and epilepsy diagnosis.
- Drug Information: Gather information about the drugs commonly used in monotherapy for epilepsy, such as phenytoin, valproate, carbamazepine, and lamotrigine.
- Drug Test Results: Collect data on drug test results for patients who are on monotherapy. This could include blood tests, urine tests, or other relevant diagnostic tests.

Data Preprocessing and Feature Engineering

Once you have collected the necessary data, you would need to preprocess and engineer features to make the data suitable for ML model training. This might include:

- Data Cleaning: Remove any missing or erroneous data points.
- Data Integration: Combine relevant data from different sources to create a comprehensive dataset.

- Feature Extraction: Extract relevant features from the data, such as drug dosage, drug administration frequency, and duration of drug usage.

- Labelling: Label the data to indicate whether a patient is on monotherapy for epilepsy or not.

Model Training

After preprocessing the data, you can train an ML model to detect monotherapy epilepsy drugs. You could use various ML algorithms, such as logistic regression support vector machine (SVM), random forests, or neural networks. Considerations when training the model include:

- Feature Selection: Select the most informative features that are likely to contribute to accurate drug detection.

- Model Evaluation: Split the dataset into training and testing sets to evaluate the model's performance. Metrics like accuracy, precision, recall, and F1 score can be used to assess the model's effectiveness.

V. EXPERIMENTAL RESULTS

READ DATA

Reading the relevant data from the data provided and process the drug information for processing to provide suitable drug for the patient and proceeds to evaluation of drugs. The given screenshot shows data's being imported to the program for reading.

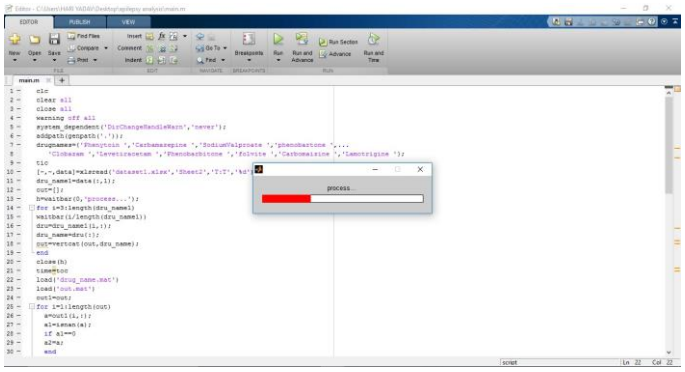

Figure 2 Reading Data

EVALUATING THE DRUGS

After reading the data the data are processed using the formula and the fit free percentage is displayed for further analysis.

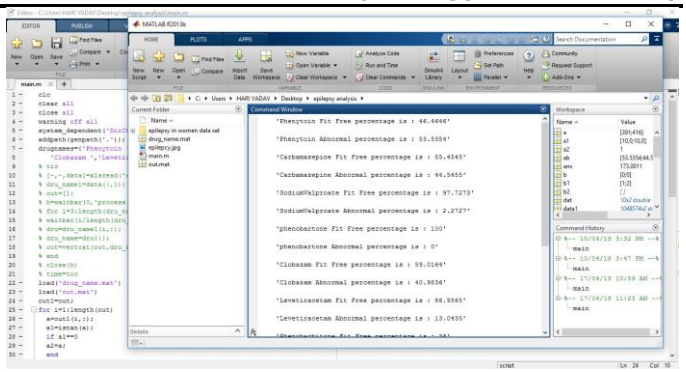

Figure 3 Evaluating the Drugs

COMPARISON TABLE

The Comparison Table is displayed after evaluating the data's where it contains the details it contains the comparison percentage of the drugs which are fit free and abnormal according to the collected data.

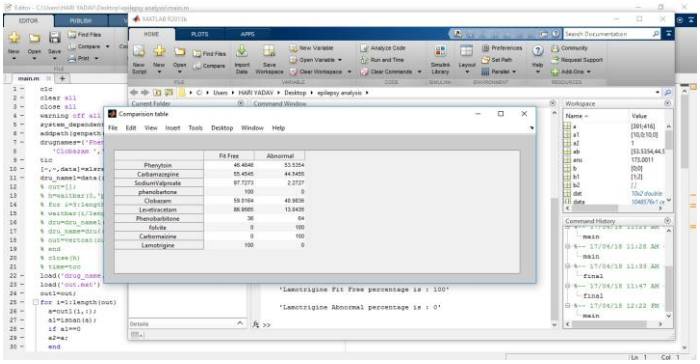

Figure 4 Comparison Table

RESULTANT GRAPH FOR FIT FREE

The Graph is shown to give the visual representation of the better fit free drug as the result of the analysis. They describe the efficient ASM rate gap.

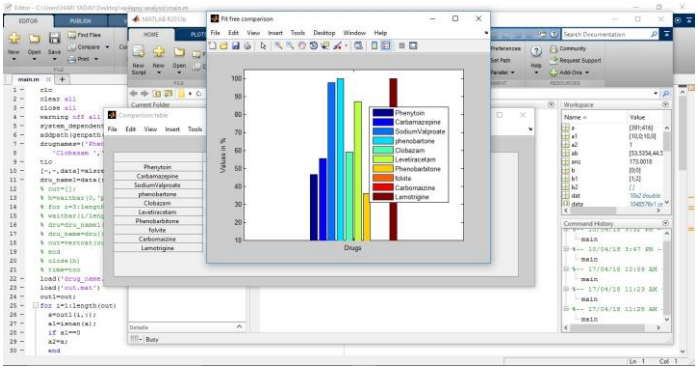

Figure 5 Graph for Fit Free

RESULTANT GRAPH FOR RELAPSE OF FITS

The Graph is shown to give the visual representation of the relapse fit free drug as the result of the analysis. They describe the efficient ASM rate gap without any side effects to the patients who have taken those medications.

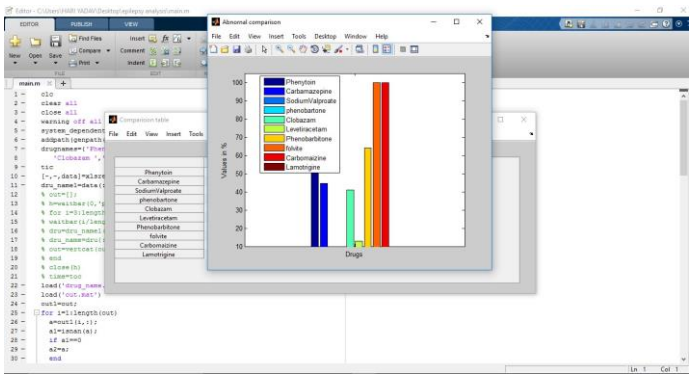

Figure 6 Graph for Relapse of Fits

VI. CONCLUSION

Summary

A patient suspected of having epilepsy usually comes in with a history of one or more brief episodes of neurological dysfunction, the clinical characteristics of which point to the potential for seizures. Most epileptic patients who receive generally well-tolerated anti-seizure medication will experience a long-lasting remission of their seizures. There is an immediate need for new drugs that are more effective and have fewer side effects than existing AEDs. the use of data mining methods to predict the effects of anti-epileptic medications and monotherapy in the context of epilepsy. By outlining the importance of epilepsy as a medical condition and introducing the idea of data mining classes. The goal of our project was to predict which anti-epileptic medications and monotherapy would be best for people with epilepsy. the categorization of seizures and supplied crucial contextual data. Our work was based on a thorough literature review that identified prior studies and approaches in this area. To sum up, the study is a big step forward in using data mining techniques to forecast anti-epileptic medications and monotherapy. With more individualized treatment options available, this work may help people with epilepsy live better lives. Nevertheless, additional investigation and verification are required to enhance and broaden the potential of our predictive algorithm.

Future Works

In the future major analysis can be done as the following:

- Pregnancy Statical Analysis: The SPSS PC+ program was used to examine the data once it was assembled on the Fox plus database. AEDS was momentarily stopped during descriptive statistics, which comprised mean, standard deviations, and range. Whenever feasible, the outcomes were contrasted with those of Keralan women. Significant tests (unpaired test or "chi square test") were only used in the case where both groups' group means were known. The Pearson correlation coefficient was used to determine whether there was any relationship between any malformations and various clinical or pharmacological parameters.

- Pregnancy Results: Six of the 190 women with epilepsy who responded to us extremely slowly were not included in the analysis. The average age of the ladies when they became parents. There were 28.5 8 years of study in all. Just 108 of them (58.7%) were married, and they were divided into three age groups based on their current ages: thirty years or more, forty-nine, twenty- to thirty-nine, and less than twenty. Six of the 190 women with epilepsy who responded to us extremely slowly were not included in the analysis. The average age of the ladies when they became parents. There were 28.5 8 years of study in all. Of them, 108 (58.7%) were married, and as of the present age, they had separated. In the 15–49 age range, 65% of women are married (3). These patients didn't have any divorces. At marriage, the average age was 22.0 5.8 years. In Kerala, women married at an average age of 21.9 in 1981 and 22.3 in 1991 (4).

- Pregnancy Clinical Characteristics: The average age of epilepsy onset was 14.9 ± 9.2 years. There were several different forms of seizures that they experienced: absence (3.5%), tonic-clonic seizures (34.5%), myoclonic seizures and other generalized seizures (13.3%), complex partial seizures (35.3%), and other partial seizure types (14.2%). They might be classified as generalized epilepsies (57%), localization-related epilepsies (41.9%), and others (1.2%) in accordance with the ILAE terminology. In two third of the patients, there was aberrant EEG activity. For 19.7% of the patients, the frequency of seizures was four or more per month, 1-3 per month for 50.8%, and fewer than one per month for 29.5%. In this group, just one patient experienced seizure-free living for longer than two years. Only 84 patients' treatment details were provided. Only 59 patients (82.1%) received

monotherapy, while 15 patients (17.9%) received polytherapy. Phenobarbitone was prescribed to 14 patients (16.7%), phenytoin to 22, (26.2%), carbamazepine to 51 (60.7%), and sodium valproate to 19 (22.6%) individuals. Clonazepam was being given to one patient.

- Reproductive Outcome: 26 women (24.1%) out of the 108 married women had one or more abortions. Compared to women in Kerala (8%) (3), this is three times greater. (table I). In total, there were 36 abortions: one for every 18 women, two for every six women, and three for every two women. Nine ladies out of the 108 married women had kids. For every 93 women, there were 176 live 4// children (55.4% boys and 44.6% girls). These women had the following family sizes: 32 women each had one child, 49 had two, 8 had three, and 2 each had five or six children.

- Birth Defects: Out of the 176 children, seven (4%) had a congenital abnormality or malformation, which was twice the number observed in the general population. Among these birth anomalies were congenital facial or limb malformations and atrial septal defects. There was no statistically significant relationship found between the kind, frequency, duration, or type of epilepsy and the existence of congenital abnormality. But compared to monotherapy, abnormalities were substantially more common with polytherapy (< 0.02). Clonazepam, carbamazepine, sodium valproate, phenobarbitone, and phenytoin have all been linked to congenital abnormalities.

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