

**TREND ANALYSIS OF ANTIEPILEPTIC PRESCRIPTIONS IN TERTIARY CARE  
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**ABSTRACT**

The study was conducted on a prospective mode and was based on the prescription obtained from the records of the pharmacy department of respective health care establishment. The study spanned through a period of 3 months starting from Jan 2022 to March 2022. Formal permission for the study has been obtained from the respective IEC. Prescription of patients turning up for their first visit were only considered for the study. Patients having active comorbidity or on medication for recurrence or relapse of any other comorbidity were excluded. Epilepsy emerges as a prevalent problem in the district of West Bardhaman fostering generation of more prescriptions for male patients in the age group of 19-60 years. Tonic clonic seizure found to be the chief type prevalent in the district, got treated with monotherapy comprising of valproic acid in majority of the cases. Combination therapy has also been chosen in quite a few cases. The study thus paves the way for analysis of the indicated trend further with additional end points being considered.

**INTRODUCTION****2.1 Epilepsy and age Old Manures**

The word "epilepsy" comes from the Greek and means to be taken, seized or attacked.

Epilepsy is a chronic non-communicable disorder of the brain that affects people of all ages often interfering with education and employment. Epilepsy is defined by international League Against Epilepsy (ILAE) as a condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause. According to the WHO, of the 50 million people with epilepsy worldwide, 80% reside in developing countries.<sup>[1,2]</sup>

It is estimated that there are more than 10 million persons with epilepsy in India. Its prevalence is about 1% in Indian population. The prevalence is higher in the rural (1.9%) compared to urban population(0.6%). The estimated burden of epilepsy using the disability adjusted life years (DALYs) accounts for 1 % of the total burden of disease in the world, excluding that due to social stigma and isolation, which further add to the disease burden.

In many developing countries, people with epilepsy do not receive appropriate treatment for their condition, a phenomenon called treatment gap (TG), which is defined as the number of people with active epilepsy not on treatment (diagnostic and therapeutic) or on inadequate

treatment, expressed as a percentage of the total number with active epilepsy. The magnitude of epilepsy treatment gap in India ranges from 22% among urban, middle-income people to 90% in rural India. In order to reduce this gap in the context of limited resources, it would be necessary to specify the important causes of gap for a particular community and the most cost-effective resource for a particular situation. The Indian pharma market size is expected to grow to US\$ 85 billion by 2020. The growth in Indian domestic market will be on back of increasing consumer spending, rapid urbanization, and raising healthcare insurance and so on. The cost of drug plays a crucial role in patient's care especially in developing countries and constitutes an essential part of rational drug prescription. In recent years more emphasis has been given on cost effective practice which should be adopted by clinicians. Cost of drugs is an important factor influencing compliance with treatment. The epileptic seizures are a common disorder for which patients have to take medication for a prolonged period, sometimes even life-long. It is necessary for the clinicians to prescribe most effective, appropriate and economical treatment regimen available. Estimation of the economic burden of epilepsy is of pivotal relevance to enable a rational distribution of healthcare resources. Being one of the common brain disorders with varying etiologies, which can present at any age, requiring prompt therapy and with the aim to promote rational pharmacotherapy we decided to study the cost of different brands of antiepileptic drugs available in Indian market.

The rationale of this study showed that, how many patients enrolled themselves, which type of epilepsy mainly occurred, which type of drug mainly prescribed, observing the cost variation and identifying less costlier antiepileptic formulation, if they affordable or not, price variation between generic and branded medicine, how much time spend to their recovery by the followed up prescription.

**Significance** – A prospective study was carried out between Jan 2022 to March 2022, to analyze prescription pattern and utilization behaviour of antiepileptic drugs as well as analysis of quality of life data and types of seizures in prescribing antiepileptic drugs and is the cause of concern.

A large number of PPMS have been done all over the world to determine the quality of prescribing practices of physicians and promote RUM. However, it has been observed in the majority of such studies that physicians do not adhere to the guidelines made by regulatory agencies leading to irrational use of medicines. This in turn leads to increase the incidence of treatment failure, antimicrobial resistance and economic burden on the patient and the community as a whole. The treatment of diseases by the use of essential drugs, prescribed by their generic names, has been emphasized by the WHO and the National Health Policy of India. Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The National List of Essential Medicines of India (NLEMI 2011) was revised recently by the Ministry of Health and Family Welfare, Government of India, in June 2011, nearly 8 years after the previous list, on the directions of the Supreme Court of India. The list was accessed from the official website of the drug regulatory authority of India, the Central Drugs Standard Control Organization, downloaded and reviewed by comparing it with the 17th Model WHO EML, March 2011, the 3rd WHO Model EML for children, March 2011 and the National EML 2003.

In United States, drug utilization studies are primarily developed in the form of prescription drug monitoring program (PDMP) at institutional, state and national level. A PDMP is a tool that can be used to address prescription drug diversion and abuse. PDMPs serve multiple functions, including: Patient care tool; drug epidemic early warning system; and drug diversion and insurance fraud investigative tool. They help prescribers avoid drug interactions and identify drug-seeking behaviors or “doctor shopping.” In European countries, drug utilization research also describe and compare the patterns of specific groups of drugs. In developing the

country such as India, PPMS are done at individual level and not as a national program in contrast to developed countries. Hence, the data generated is not analyzed and used in promoting RUM.

A large number of socioeconomic factors affect drugutilization in India. Like; illiteracy, poverty, multiple health care systems, drug advertisement and promotions, sales without prescription, over the counter drugs etc. Cost factors like prices of drug, entry of new drug in market, volume of drug use; Population factors like changes in total population, demographics, change in health status of a population; system factors like changes in health program and health system reforms and restructuring, shift of drug provision from hospital to community, changes in policies and program; research and technology related factors include new treatment approaches, drugs replacing surgery, availability of more diagnostic technologies, evidence-based curative approaches, use of newer pharmaceutical technology; practice and people related factors like changes in prescribing and dispensing, number and mix of prescribers, multiple doctoring, consumer expectations and behavior and wastage; pharmaceutical industry related factors like new drug products, promotion of drugs to physicians, drug sampling and consumer advertising. These factors present important challenges in developing the country such as India for development of indicators to monitor trends and results that affect the performance of health care system and health of the population.

It is very important that the PPMS should be consultative and transparent, selection criteria be explicit, selection of the medicines be linked to evidence-based standard clinical guidelines, clinical guidelines and the list be divided into levels of care, and are regularly reviewed and updated. The effectiveness of PPMSs can be conceptualized in terms of their impact in ensuring the appropriate use of prescription controlled substances, reducing their diversion and abuse, and improving health outcomes, both at the patient and community levels. This impact is maximized when prescription history data are, to the extent technologically feasible, complete and accurate; analyzed appropriately and expeditiously; made available in a proactive and timely manner; disseminated in ways and formats that best serve the purposes of end users; and applied in all relevant domains by all appropriate users. This suggests that PPMSs can be thought of as information systems with inputs, internal operations, outputs, and customers who make use of their products.

The WHO core drug use indicators which include three groups

## 2.2 Prescribing indicators

- Average number of drugs per prescription.
- Percentage of drugs prescribed by generic name.

- Percentage of prescriptions containing antimicrobial agents (antibiotics).
- Percentage of injections per prescription.

**2.3 Percentage Patient-care indicators**

- Average consultation time.
- Average dispensing time.
- Percentage of drugs actually dispensed.
- Percentage of drugs adequately labelled.
- Patients’ knowledge of correct dosage.

**2.4 Health facility indicators**

- Availability of copy of EDL in all OPDs.
- Availability of key drugs.

As important as is the intellectual process of rational drug selection, the processes of prescription and order writing to convert the choice of drug into medication received by the patient is of almost equal importance. A prescription (Rx) is a health-care program that governs the plan of care for an individual patient and is implemented by a qualified practitioner. A prescription

may be taken as a reflection of the physicians attitude to the disease and the role of the drug in its treatment. It also provides an insight into the nature of the health care delivery system. The standard means of giving permission for a medication to be provided (or dispensed) to a patient remains the prescription (for outpatients) or the medication order (for inpatients). Prescriptions and medication orders contain the information necessary to provide a patient with a supply of medication. Certain information is required by law and other sets of information are helpful in avoiding errors. Historically, prescriptions were handwritten and given to the patient, who then takes the prescriptions to a pharmacy to be filled. The prescriber should write out both drug names and instructions, avoiding all abbreviations, and write as legibly as possible. The importance of legible handwriting in the prescription- and order-writing process cannot be overemphasized. At worst, poor handwriting can result in deadly or life-threatening medical errors. At best, it may result in delays in the dispensing of the prescribed medicine.

**2.5 Importance Parts of Prescription**

Prescriber information	To authenticate the prescription before dispensing The prescription is a legal document It can be used in the court of law.
Patient information	For proper identification of a patient and to determine its age group. It is also essential for follow-up of patient or to get in touch with the patient in case of prescribing or dispensing errors.
Data	To know the validity of prescription and to avoid unnecessary refilling of the prescription.
Superscription	It is a sign of practice.
Inscription	Illegible handwriting and too many confusing similar generic & brand names cause difficulties to the Pharmacists to dispensed the drugs.
Subscription	For dispensing of correct and proper medication to the patient.
Signature	Patient needs to know the quantity of tablets/cap/ liquid & number of times the medicine needs to be taken. Oral instructions to patients are most of the times forgotten The pharmacist can also counsel the patient.
Prescriber signature	To confirm authenticity of prescription and to avoid misuse of blank prescription pads.

Rx is a symbol meaning prescription. It is sometimes transliterated as Rx or just Rx. This symbol originated in medieval manuscripts as an abbreviation of the Late Latin verb recipe, the imperative form of recipe, to take or take thus. Literally, the Latin word recipe means simply Take and medieval prescriptions invariably began with the command to take certain materials and compound them in specified ways. Folk theories about the origin of the symbol Rx note its similarity to the Eye of Horus gods whose protection may have been sought in medical contexts. The word prescription, from pre-(before) and script (writing, written), refers to the fact that the prescription is an order that must be written down before a compound drug can be prepared. Those within the industry will often call prescriptions simply scripts.

The fact that a prescription instructs someone to take rather than give is not a trivial distinction, but makes clear it is directed at the patient, and is not directly an instruction to anyone else. Prescriptions, when

handwritten, are notorious for being often illegible. In the India, medical practitioners sloppy handwriting kills more than 7,000 people annually, according to a July 2006 report from the National Academies of Science's Institute of Medicine (IOM). Predating modern legal definitions of a prescription, a prescription traditionally is composed of four parts: a superscription, inscription, subscription and signature. So long as there were medications and a writing system to capture directions for preparation and usage, there were prescriptions. The concept of prescriptions dates back to the beginning of history. Modern prescriptions are actually extemporaneous prescriptions from the Latin (ex tempore) for at/from time. Extemporaneous means the prescription is written on the spot for a specific patient with a specific ailment. This is distinguished from a non-extemporaneous prescription that is a generic recipe for a general ailment.

The prescriptions were analyzed on the basis of following parameters

- **Demographic data**

Demographic analysis is the study of a population-based on factors such as age, race, and sex. Demographic data refers to socioeconomic information expressed statistically, including employment, education, income, marriage rates, birth and death rates, and more.

The most commonly used demographic segmentation factors are

1. Age.
2. Gender.
3. Ethnicity.
4. Income.
5. Level of education.
6. Religion.
7. Occupation.
8. Family structure.

- **Diagnosis**

The addition of the patient's diagnosis to the prescription enhanced the review of duplicate prescriptions. It permitted the evaluation of not only the prescription-writing process but also the decision-making process that led to writing the prescription. It also permitted a more thorough evaluation of appropriate drug use.

- Number of drugs per patient
- Duration of therapy

The duration of treatment refers to how long (e.g., days, weeks, months, years) a patient should be treated with manual methods for any given problem.

Any specific instructions given to the patients

- **Prescription share in market**

Prescription medicine sharing has been defined as the lending of medicines (giving prescription medicines to someone else) or borrowing of medicines (being given and using a medicine prescribed for another person).

- **Outcomes analysis**

Patient outcomes research provides an opportunity to improve the quality of patient care by modifying the structures and processes of care delivery. Optimal application of outcomes analysis involves collaboration between the health care disciplines. The result of such an endeavor would be the identification of health care practices that lead to desired patient outcomes in the most cost-effective manner.

- **Prescription adherence rate**

Introduction: Patient adherence to a medication regimen is usually expressed as an adherence rate, defined as the proportion of prescribed doses actually taken. An adherence rate threshold, above which the therapeutic effect is maintained, is typically assigned an arbitrary value, commonly 0.8.

Information present on the prescription was analyzed for the different elements of prescriptions and rationality.

## 2.6 Benefits

- a) It is statistical tool that helps to determine future movements of a variable on the basis of its historical trends. There is no specific amount of time for a movement to become a trend.
- b) Types –
  - a) Uptrend – here financial markets and assets move in upward direction.
  - b) Downtrend – here financial markets and assets prices move downwards.
  - c) Sideways – asset price does not move in any direction.

## 2.7 Disease

A disorder in which nerve cell activity in the brain is disturbed, causing seizures.

Epilepsy may occur as a result of a genetic disorder or an acquired brain injury, such as a trauma or stroke.

During a seizure, a person experiences abnormal behaviour, symptoms and sensations, sometimes including loss of consciousness. There are few symptoms between seizures.

Epilepsy is usually treated by medication and in some cases by surgery, devices or dietary changes.

## 2.8 Symptoms

Because epilepsy is caused by abnormal activity in the brain, seizures can affect any process your brain coordinates. Seizure signs and symptoms may include

- Temporary confusion
- A staring spell
- Stiff muscles
- Uncontrollable jerking movements of the arms and legs
- Loss of consciousness or awareness
- Psychological symptoms such as fear, anxiety or déjà vu.

Symptoms vary depending on the type of seizure. In most cases, a person with epilepsy will tend to have the same type of seizure each time, so the symptoms will be similar from episode to episode.

Doctors generally classify seizures as either focal or generalized, based on how and where the abnormal brain activity begins.

## 2.9 Types

### Focal seizures

When seizures appear to result from abnormal activity in just one area of your brain, they're called focal seizures. These seizures fall into two categories

- **Focal seizures without loss of consciousness-** Once called simple partial seizures, these seizures don't cause a

loss of consciousness. They may alter emotions or change the way things look, smell, feel, taste or sound. Some people experience déjà vu. This type of seizure may also result in involuntary jerking of one body part, such as an arm or leg, and spontaneous sensory symptoms such as tingling, dizziness and flashing lights.

**Focal seizures with impaired awareness-** Once called complex partial seizures, these seizures involve a change or loss of consciousness or awareness. This type of seizure may seem like being in a dream. During a focal seizure with impaired awareness, you may stare into space and not respond normally to your environment or perform repetitive movements, such as hand rubbing, chewing, swallowing or walking in circles.

Symptoms of focal seizures may be confused with other neurological disorders, such as migraine, narcolepsy or mental illness. A thorough examination and testing are needed to distinguish epilepsy from other disorders.

### Generalized seizures

Seizures that appear to involve all areas of the brain are called generalized seizures. Six types of generalized seizures exist.

- **Absence seizures-** Absence seizures, previously known as petit mal seizures, typically occur in children. They're characterized by staring into space with or without subtle body movements such as eye blinking or lip smacking and only last between 5-10 seconds. These seizures may occur in clusters, happening as often as 100 times per day, and cause a brief loss of awareness.
- **Tonic seizures-** Tonic seizures cause stiff muscles and may affect consciousness. These seizures usually affect muscles in your back, arms and legs and may cause you to fall to the ground.
- **Atonic seizures-** Atonic seizures, also known as drop seizures, cause a loss of muscle control. Since this most often affects the legs, it often causes you to suddenly collapse or fall down.
- **Clonic seizures-** Clonic seizures are associated with repeated or rhythmic, jerking muscle movements. These seizures usually affect the neck, face and arms.
- **Myoclonic seizures-** Myoclonic seizures usually appear as sudden brief jerks or twitches and usually affect the upper body, arms and legs.
- **Tonic-clonic seizures-** Tonic-clonic seizures, previously known as grand mal seizures, are the most dramatic type of epileptic seizure. They can cause an abrupt loss of consciousness and body stiffening, twitching and shaking. They sometimes cause loss of bladder control or biting your tongue.<sup>[3]</sup>

### 2.10 Causes

Epilepsy has no identifiable cause in about half the people with the condition. In the other half, the condition may be traced to various factors, including:

- **Genetic influence-** Some types of epilepsy, which are categorized by the type of seizure you experience or the part of the brain that is affected, run in families. In these cases, it's likely that there's a genetic influence.
- Researchers have linked some types of epilepsy to specific genes, but for most people, genes are only part of the cause of epilepsy. Certain genes may make a person more sensitive to environmental conditions that trigger seizures.
- **Head trauma-** Head trauma as a result of a car accident or other traumatic injury can cause epilepsy.
- **Brain abnormalities-** Abnormalities in the brain, including brain tumors or vascular malformations such as arteriovenous malformations (AVMs) and cavernous malformations, can cause epilepsy. Stroke is a leading cause of epilepsy in adults older than age 35.
- **Infections-** Meningitis, HIV, viral encephalitis and some parasitic infections can cause epilepsy.
- **Prenatal injury-** Before birth, babies are sensitive to brain damage that could be caused by several factors, such as an infection in the mother, poor nutrition or oxygen deficiencies. This brain damage can result in epilepsy or cerebral palsy.
- **Developmental disorders-** Epilepsy can sometimes be associated with developmental disorders, such as autism.

### 2.11 Risk factors

Certain factors may increase your risk of epilepsy:

- **Age-** The onset of epilepsy is most common in children and older adults, but the condition can occur at any age.
- **Family history-** If you have a family history of epilepsy, you may be at an increased risk of developing a seizure disorder.
- **Head injuries-** Head injuries are responsible for some cases of epilepsy. You can reduce your risk by wearing a seat belt while riding in a car and by wearing a helmet while bicycling, skiing, riding a motorcycle or engaging in other activities with a high risk of head injury.
- **Stroke and other vascular diseases-** Stroke and other blood vessel (vascular) diseases can lead to brain damage that may trigger epilepsy. You can take a number of steps to reduce your risk of these diseases, including limiting your intake of alcohol and avoiding cigarettes, eating a healthy diet, and exercising regularly.
- **Dementia-** Dementia can increase the risk of epilepsy in older adults.
- **Brain infections-** Infections such as meningitis, which causes inflammation in your brain or spinal cord, can increase your risk.
- **Seizures in childhood-** High fevers in childhood can sometimes be associated with seizures. Children who have seizures due to high fevers generally won't

develop epilepsy. The risk of epilepsy increases if a child has a long fever-associated seizure, another nervous system condition or a family history of epilepsy.

## 2.12 Complications

Having a seizure at certain times can lead to circumstances that are dangerous to yourself or others.

- **Falling-** If you fall during a seizure, you can injure your head or break a bone.
- **Drowning-** If you have epilepsy, you're 13-19 times more likely to drown while swimming or bathing than the rest of the population because of the possibility of having a seizure while in the water.
- **Car accidents-** A seizure that causes either loss of awareness or control can be dangerous if you're driving a car or operating other equipment.

Many states have driver's license restrictions related to a driver's ability to control seizures and impose a minimum amount of time that a driver be seizure-free, ranging from months to years, before being allowed to drive.

- **Pregnancy complications-** Seizures during pregnancy pose dangers to both mother and baby, and certain anti-epileptic medications increase the risk of birth defects. If you have epilepsy and you're considering becoming pregnant, talk to your doctor as you plan your pregnancy.

Most women with epilepsy can become pregnant and have healthy babies. You'll need to be carefully monitored throughout pregnancy, and medications may need to be adjusted. It's very important that you work with your doctor to plan your pregnancy.

- **Emotional health issues-** People with epilepsy are more likely to have psychological problems, especially depression, anxiety, and suicidal thoughts and behaviors. Problems may be a result of difficulties dealing with the condition itself as well as medication side effects, but even people with well-controlled epilepsy are at increased risk.

## 2.13 Pinpointing seizure location

To diagnose your condition, your doctor will review your symptoms and medical history. Your doctor may order several tests to diagnose epilepsy and determine the cause of seizures. Your evaluation may include

- **A neurological exam-** Your doctor may test your behavior, motor abilities, mental function and other areas to diagnose your condition and determine the type of epilepsy you may have.
- **Blood tests-** Your doctor may take a blood sample to check for signs of infections, genetic conditions or other conditions that may be associated with seizures.

Your doctor may also suggest tests to detect brain abnormalities, such as

- **Electroencephalogram (EEG)-** This is the most common test used to diagnose epilepsy. In this test, electrodes are attached to your scalp with a paste-like substance or cap. The electrodes record the electrical activity of your brain.

If you have epilepsy, it's common to have changes in your normal pattern of brain waves, even when you're not having a seizure. Your doctor may monitor you on video when conducting an EEG while you're awake or asleep, to record any seizures you experience. Recording the seizures may help the doctor determine what kind of seizures you're having or rule out other conditions.

The test may be done in a doctor's office or the hospital. If appropriate, you may also have an ambulatory EEG, which you wear at home while the EEG records seizure activity over the course of a few days.

Your doctor may give you instructions to do something that will cause seizures, such as getting little sleep prior to the test.

- **High-density EEG-** In a variation of an EEG test, your doctor may recommend high-density EEG, which spaces electrodes more closely than conventional EEG — about a half a centimeter apart. High-density EEG may help your doctor more precisely determine which areas of your brain are affected by seizures.
- **Computerized tomography (CT) scan-** A CT scan uses X-rays to obtain cross-sectional images of your brain. CT scans can reveal abnormalities in the structure of your brain that might be causing your seizures, such as tumors, bleeding and cysts.
- **Magnetic resonance imaging (MRI)-** An MRI uses powerful magnets and radio waves to create a detailed view of your brain. Your doctor may be able to detect lesions or abnormalities in your brain that could be causing your seizures.
- **Functional MRI (fMRI)-** A functional MRI measures the changes in blood flow that occur when specific parts of your brain are working. Doctors may use an fMRI before surgery to identify the exact locations of critical functions, such as speech and movement, so that surgeons can avoid injuring those places while operating.
- **Positron emission tomography (PET)-** PET scans use a small amount of low-dose radioactive material that's injected into a vein to help visualize metabolic activity of the brain and detect abnormalities. Areas of the brain with low metabolism may indicate where seizures occur.
- **Single-photon emission computerized tomography (SPECT)-** This type of test is used primarily if you've had an MRI and EEG that didn't pinpoint the location in your brain where the seizures are originating.

A SPECT test uses a small amount of low-dose radioactive material that's injected into a vein to create a detailed, 3D map of the blood flow activity in your brain during seizures. Areas of higher than normal blood flow during a seizure may indicate where seizures occur.

Doctors may also conduct a form of a SPECT test called subtraction ictal SPECT coregistered to MRI (SISCOM), which may provide even more-detailed results by overlapping the SPECT results with a patient's brain MRI.

- **Neuropsychological tests-** In these tests, doctors assess your thinking, memory and speech skills. The test results help doctors determine which areas of your brain are affected.

Along with your test results, your doctor may use a combination of analysis techniques to help pinpoint where in the brain seizures start

- **Statistical parametric mapping (SPM)-** SPM is a method of comparing areas of the brain that have increased blood flow during seizures to normal brains, which can give doctors an idea of where seizures begin.
- **Electrical source imaging (ESI)-** ESI is a technique that takes EEG data and projects it onto an MRI of the brain to show doctors where seizures are occurring.
- **Magnetoencephalography (MEG)-** MEG measures the magnetic fields produced by brain activity to identify potential areas of seizure onset.

Accurate diagnosis of your seizure type and where seizures begin gives you the best chance for finding an effective treatment.

## 2.14 Treatments

Doctors generally begin by treating epilepsy with medication. If medications don't treat the condition, doctors may propose surgery or another type of treatment.

- **Medication**

Most people with epilepsy can become seizure-free by taking one anti-seizure medication, which is also called anti-epileptic medication. Others may be able to decrease the frequency and intensity of their seizures by taking a combination of medications.

Many children with epilepsy who aren't experiencing epilepsy symptoms can eventually discontinue medications and live a seizure-free life. Many adults can discontinue medications after two or more years without seizures. Your doctor will advise you about the appropriate time to stop taking medications.

Finding the right medication and dosage can be complex. Your doctor will consider your condition, frequency of seizures, your age and other factors when choosing

which medication to prescribe. Your doctor will also review any other medications you may be taking, to ensure the anti-epileptic medications won't interact with them.

Your doctor likely will first prescribe a single medication at a relatively low dosage and may increase the dosage gradually until your seizures are well controlled.

There are more than 20 different types of anti-seizure medications available. The medication that your doctor chooses to treat your epilepsy depends on the type of seizures you have, as well as other factors such as your age and other health conditions.

These medications may have some side effects. Mild side effects include:

- Fatigue
- Dizziness
- Weight gain
- Loss of bone density
- Skin rashes
- Loss of coordination
- Speech problems
- Memory and thinking problems

More-severe but rare side effects include

- Depression
- Suicidal thoughts and behaviors
- Severe rash
- Inflammation of certain organs, such as your liver

To achieve the best seizure control possible with medication, follow these steps

- Take medications exactly as prescribed.
- Always call your doctor before switching to a generic version of your medication or taking other prescription medications, over-the-counter drugs or herbal remedies.
- Never stop taking your medication without talking to your doctor.
- Notify your doctor immediately if you notice new or increased feelings of depression, suicidal thoughts, or unusual changes in your mood or behaviors.
- Tell your doctor if you have migraines. Doctors may prescribe one of the anti-epileptic medications that can prevent your migraines and treat epilepsy.

At least half the people newly diagnosed with epilepsy will become seizure-free with their first medication. If anti-epileptic medications don't provide satisfactory results, your doctor may suggest surgery or other therapies. You'll have regular follow-up appointments with your doctor to evaluate your condition and medications.

- **Surgery**
- **Epilepsy surgery**

When medications fail to provide adequate control over seizures, surgery may be an option. With epilepsy surgery, a surgeon removes the area of your brain that's causing seizures.

Doctors usually perform surgery when tests show that:

- Your seizures originate in a small, well-defined area of your brain
- The area in your brain to be operated on doesn't interfere with vital functions such as speech, language, motor function, vision or hearing

For some types of epilepsy, minimally invasive approaches such as MRI-guided stereotactic laser ablation may provide effective treatment when an open procedure may be too risky. In these procedures, doctors direct a thermal laser probe at the specific area in the brain causing seizures to destroy that tissue in an effort to better control the seizures.

Although many people continue to need some medication to help prevent seizures after successful surgery, you may be able to take fewer drugs and reduce your dosages.

In a small number of cases, surgery for epilepsy can cause complications such as permanently altering your thinking (cognitive) abilities. Talk to your surgeon about his or her experience, success rates, and complication rates with the procedure you're considering.

## 2.15 Therapies

### **MRI of deep brain stimulation**

Apart from medications and surgery, these potential therapies offer an alternative for treating epilepsy

**Vagus nerve stimulation-** In vagus nerve stimulation, doctors implant a device called a vagus nerve stimulator underneath the skin of your chest, similar to a heart pacemaker. Wires from the stimulator are connected to the vagus nerve in your neck.

The battery-powered device sends bursts of electrical energy through the vagus nerve and to your brain. It's not clear how this inhibits seizures, but the device can usually reduce seizures by 20-40%.

Most people still need to take anti-epileptic medication, although some people may be able to lower their medication dose. You may experience side effects from vagus nerve stimulation, such as throat pain, hoarse voice, shortness of breath or coughing.

**Ketogenic diet-** Some children with epilepsy have been able to reduce their seizures by following a strict diet that's high in fats and low in carbohydrates.

In this diet, called a ketogenic diet, the body breaks down fats instead of carbohydrates for energy. After a few years, some children may be able to stop the ketogenic diet — under close supervision of their doctors — and remain seizure-free.

Consult a doctor if you or your child is considering a ketogenic diet. It's important to make sure that your child doesn't become malnourished when following the diet.

Side effects of a ketogenic diet may include dehydration, constipation, slowed growth because of nutritional deficiencies and a buildup of uric acid in the blood, which can cause kidney stones. These side effects are uncommon if the diet is properly and medically supervised.

Following a ketogenic diet can be a challenge. Low-glycemic index and modified Atkins diets offer less restrictive alternatives that may still provide some benefit for seizure control.

**Deep brain stimulation-** In deep brain stimulation, surgeons implant electrodes into a specific part of your brain, typically your thalamus. The electrodes are connected to a generator implanted in your chest. The generator regularly sends electrical pulses to your brain at timed intervals, and may reduce your seizures. Deep brain stimulation is often used for people whose seizures don't get better with medication.

**Responsive neurostimulation-** These implantable, pacemaker-like devices can help significantly reduce how often seizures occur. These responsive stimulation devices analyze brain activity patterns to detect seizures as they start and deliver an electrical charge or drug to stop the seizure before it causes impairment. Research shows that this therapy has few side effects and can provide long-term seizure relief.

### **Potential future treatments**

Researchers are studying many potential new treatments for epilepsy, including

- **Continuous stimulation of the seizure onset zone (subthreshold stimulation)-** Subthreshold stimulation — continuous stimulation to an area of your brain below a level that's physically noticeable — appears to improve seizure outcomes and quality of life for some people with seizures. Subthreshold stimulation helps stop a seizure before it happens. This treatment approach may work in people who have seizures that start in an area of the brain that can't be removed because it would affect speech and motor functions (eloquent area). Or it might benefit people whose seizure characteristics mean their chances of successful treatment with responsive neurostimulation are low.
- **Minimally invasive surgery-** New minimally invasive surgical techniques, such as MRI-guided focused ultrasound, show promise at treating

seizures with fewer risks than traditional open-brain surgery for epilepsy.

- **Transcranial magnetic stimulation (TMS)-** TMS applies focused magnetic fields on areas of the brain where seizures occur to treat seizures without the need for surgery. It may be used for patients whose seizures occur close to the surface of the brain and are not candidates for surgery.
- **External trigeminal nerve stimulation-** Similar to vagus nerve stimulation, this device would stimulate specific nerves to reduce frequency of seizures. But unlike vagus nerve stimulation, this device would be worn externally so that no surgery to implant the device is needed. In studies, external trigeminal nerve stimulation provided improvements in both seizure control and mood.<sup>[2]</sup>

### Treatment problem

Epidemiology relevance of Epilepsy in Global and Indian context-Epilepsy is one of the most common serious neurological disorders, responsible for substantial morbidity and mortality due to the seizures and the available medications. Around 50 million people in the world have epilepsy and approximately 5% of the general population experience at least one seizure, excluding febrile seizures, at some time in their lives. The prevalence of epilepsy is around 0.5-1%, and its overall annual incidence ranges from 50-70 cases per 100,000 in industrialized countries and up to 190 per 100,000 in developing countries. Around 80% of people with epilepsy reside in developing countries. The high incidence in developing countries is attributed to poor obstetric services and the greater risk of intracranial infections and head injuries. Furthermore in these countries 80-90% of epileptic patients have difficulties in accessing treatment. This treatment gap has been mainly ascribed to inefficient and unevenly distributed health-care systems, cost of treatment, cultural beliefs, and unavailability of antiepileptic drugs. The diagnosis of epilepsy in developing countries is a difficult task. Video-electroencephalogram (EEG) and ambulatory long-term EEG monitoring provide a great help for the differential diagnosis of epilepsy and other paroxysmal events, but in many areas of developing countries, especially rural areas, these diagnostic techniques are not available. Due to lack of these facilities, high rates of misdiagnosis are likely in these countries. Most studies suggest there is a slightly higher incidence of epilepsy in males than females.

Mortality in epileptic patients is two- to three-times that of the general population, and sudden unexpected death in epilepsy (SUDEP) is the most important direct epilepsy-related cause of death. SUDEP is defined as a non-traumatic and non-drowning death in patients with epilepsy that is sudden, unexpected, witnessed or unwitnessed, and with or without evidence of a seizure. It occurs in 1-3 per 1,100 epileptic patients per year. Risks for SUDEP are higher if patients are male, 20-40

years of age, have generalized seizures, and are pharmacoresistant.

### Age group

The incidence of epilepsy is higher in childhood and in the elderly than in young people. In about 50% of cases the onset of epilepsy occurs in childhood and in the elderly, with half of those being under one year of age. It has been well established that early in life the brain is more seizure susceptible, and seizures in the immature brain are likely to be dependent on different mechanisms than those in the adult. Epilepsies in early childhood frequently are difficult to treat. This may depend on physiological immaturities in ion homeostasis and other developmental characteristics, but also on the severity of early onset epilepsy. Neonatal brain dysfunction and its behavioral expression may originate in the antepartum period. It seems that short gestational age, low birth weight, and intrauterine growth restriction are associated with an increased risk of afebrile seizures in the first year of life. Children of a low birth weight or born preterm also have an increased risk of febrile seizure. Early-life seizures do induce much less chronic morphologic changes in the hippocampus than seizures in adult temporal lobe epilepsy. Recurrent early life seizures may nevertheless result in permanent behavioural abnormalities and enhance epileptogenicity.

Epileptic seizures are considered as the third most frequent neurological problem encountered in the elderly. Treatment of epilepsy in the elderly is complicated since these patients are very often prescribed other long term medication for disorders other than epilepsy that may result in deleterious drug interactions.

### 2.16 Pathology

A seizure is the clinical manifestation of epilepsy. This occurs basically due to excessive firing of the neurons and fast spread of these impulses over the brain. Thus there are two phenomenons in the pathophysiology of a seizure:-

- hyper-excitability of a neuron
- hyper synchronization

Hyper synchronization means that a hyper-excitabile neuron leads to excessive excitability of a large group of surrounding neurons. This means that when a large electrical impulse is generated in one part of the brain from a focus of tissues millions of neurons in the brain fire excessively in addition bringing on a seizure.

Seizure is defined as an “involuntary alteration of behavior with or without loss of consciousness accompanied by an abnormal electrical discharge in the brain.”

### Types of causation and epileptogenesis

Seizures may be due to a reason or reactive seizures or may be without cause (idiopathic). Reactive seizures

occur in normal nonepileptic tissue. This may be seen in cases like those with hypoglycaemia who develop seizures due to excessive low blood sugar. Seizures may also occur in patients with encephalitis or meningitis due to inflammation of the brain tissues. Other causes include low blood sodium (hyponatremia), severe dehydration, low blood oxygen (hypoxia) etc.

Idiopathic epileptic seizures occur in chronically epileptic tissue. The steps by which a normal brain tissue become epileptic is called epileptogenesis. The normal neuronal networks become hyper-excitability networks. There are various factors which may lead to epileptogenesis. This includes genetic predisposition, infections or induced by medications.

### Types of seizures

There are two types of seizures – partial and generalized. The difference between the two is of loss of consciousness. In partial cases a focal point of the brain is affected. In generalized seizures the impulses comes out from both sides of the brain at the same time.

Partial seizures may generalize; start from one site in the brain and spread to involve the whole brain. This is called secondary generalization.

### Neuronal Excitability

Neuronal messages are transmitted by electrical impulses called the Action Potential. This is actually a net positive inward ion flux that leads to depolarization or voltage change in the neuronal membrane. The ions involved include sodium, potassium, calcium and chloride. Normally brain tissues prevent hyper excitability by several inhibitory mechanisms involving negative ions like chloride ions.

Disturbance in this normal excitability leads to hyper-excitability. In this state there is increases excitatory transmission of impulses and decreases inhibitory transmission. In addition there is alteration in the voltage gated ionic channels. These ion channels normally open when the voltage difference across the neuronal membrane is changed favourably.

Once activated the impulses flow via the neuronal circuits along the axons of the nerves. An action potential travels down the axon to the terminal buttons and then releases neurotransmitters in the synaptic cleft. This carries the action potential from one nerve to another.

### Transmission

There are two types of transmission of impulses - excitatory and inhibitory. Excitatory transmission involves Glutamate that is the principal excitatory neurotransmitter in the brain. GABA or Gamma amino butyric acid is the principal inhibitory neurotransmitter in the brain.

There are two groups of glutamate receptors - Ionotropic (NMDA receptors) that modulate calcium and sodium channels and are responsible for fast synaptic transmission and Metabotropic (non NMDA receptors) that are for slow synaptic transmission. GABA is mediated via Chloride and Potassium channels.

### Mechanism of seizure formation

- Excitation of a group of nerves. This is caused by inward currents of Na, Ca and involvement of excitatory neurotransmitters like Glutamate and Aspartate.
- Too little inhibition.
- Epileptogenesis and hyperexcitability and hypersynchronization of neurons that facilitates spread. There has to be abnormal synchronization – a property of a population of neurons to discharge together independently. Alone, a hyperexcitable neuron cannot generate a seizure.

### Electroencephalography or EEG

An EEG is graphical depiction of cortical electrical activity recorded by probes placed over the scalp. EEG helps in the diagnosis of epilepsy, sleep problems, altered consciousness etc. Typical EEGs show wave forms that help in diagnosis.

### Drugs used for epilepsy

The first-line treatment for epilepsy is antiseizure medication. These drugs are designed to help reduce the frequency and severity of seizures. They cannot stop a seizure that's already in progress, and they are not a cure for epilepsy.

These medications are absorbed by your stomach. They then travel through your bloodstream to your brain. They affect neurotransmitters in a way that reduces the electrical activity that leads to seizures.

There are many antiseizure drugs on the market. Your doctor can prescribe a single drug or a combination of drugs, depending on your type of seizure.

Common epilepsy medications include

- Levetiracetam (Keppra)
- Lamotrigine (Lamictal)
- Topiramate (Topamax)
- Valproic acid (Depakote)
- Carbamazepine (Tegretol)
- Ethosuximide (Zarontin)

These medications are generally available in tablet, liquid, or injectable forms and are taken once or twice a day. Your doctor will initially prescribe the lowest possible dose, which can be adjusted until it starts to work. These medications must be taken consistently and as prescribed.

Some potential side effects may include

- Fatigue

- Dizziness
- Skin rash
- Poor coordination
- Memory problem

Rare, but serious side effects include depression and inflammation of the liver or other organs.

### Limitations of Conventional Antiepileptic Therapy

AED	ADVANTAGES	DISADVANTAGES
Pregabalin	<ul style="list-style-type: none"> <li>• Add on efficacy: partial onset seizures, no drug interactions.</li> <li>• No hypersensitivity skin reactions.</li> <li>• Work also in neuropathic pain and generalized anxiety disorders.</li> </ul>	<ul style="list-style-type: none"> <li>• Weight gain.</li> <li>• Increased side effect risk in patients with low glomerular filtration rate requires a lower dose.</li> <li>• Seizure aggravation in idiopathic generalized epilepsy (absence or myoclonic seizures).</li> </ul>
Phenobarbital/ primidone	<ul style="list-style-type: none"> <li>• Efficacy: partial-onset seizures and generalized myoclonic seizures.</li> <li>• Rash is uncommon.</li> <li>• Phenobarbital is widely available and inexpensive parenteral formulation.</li> </ul>	<ul style="list-style-type: none"> <li>• Drug interactions(may lower the efficacy of concomitant medications metabolized by the P450 hepatic enzyme system).</li> <li>• Sedation, cognitive slowing, arthralgia</li> </ul>
Phenyton	<ul style="list-style-type: none"> <li>• Efficacy: partial-onset seizures.</li> <li>• Long accumulated experience.</li> <li>• Can be loaded orally or intravenously (intravenous phenytoin or the prodrug fosphenytoin).</li> </ul>	<ul style="list-style-type: none"> <li>• Drug interaction (through P450 enzyme induction and extensive protein binding).</li> <li>• Nonlinear pharmacokinetics (small changes in dose or bioavailability may produce large fluctuations in level).</li> <li>• Ataxia, rash.</li> <li>• Seizures aggravation in idiopathic generalized epilepsy (absence or myoclonic seizures).</li> </ul>
Rufinamide	<ul style="list-style-type: none"> <li>• Efficacy: Lennox-Gastaut syndrome.</li> </ul>	<ul style="list-style-type: none"> <li>• Drug interactions ( clearance decreased by valproate and increased by enzyme inducers, may reduce efficacy of oral contraceptives ).</li> </ul>
Tiagabine	<ul style="list-style-type: none"> <li>• Efficacy: partial-onset seizures.</li> <li>• Does not affect other AEDs.</li> <li>• Relatively favorable cognitive profile</li> </ul>	<ul style="list-style-type: none"> <li>• Only indicated as adjunctive therapy.</li> <li>• Requires a slow titration, given three or four times daily.</li> <li>• Can cause nonconvulsive status epilepticus or encephalopathy that resembles nonconvulsive status epilepticus, even in the absence of prior epilepsy.</li> </ul>
Topiramate	<ul style="list-style-type: none"> <li>• Efficacy: partial-onset seizures and generalized seizures.</li> <li>• Rash is uncommon.</li> <li>• Efficacy against migraine.</li> <li>• Weight loss.</li> </ul>	<ul style="list-style-type: none"> <li>• Weight loss; aphasia and cognitive impairment, nephrolithiasis, metabolic acidosis, hypohidrosis.</li> <li>• Requires slow titration rate because of adverse cognitive effects</li> </ul>
Valproate	<ul style="list-style-type: none"> <li>• Wide spectrum of efficacy against partial-onset seizures and generalized seizures.</li> <li>• No hypersensitivity skin reactions.</li> <li>• Work for bipolar disorder and migraine.</li> <li>• Intravenous preparation.</li> </ul>	<ul style="list-style-type: none"> <li>• Weight gain; encephalopathy, tremor, Parkinsonian syndrome.</li> <li>• Teratogenicity and permanent adverse cognitive outcomes in fetus.</li> <li>• Drug interaction (due to inhibition of P450 enzymes and extensive protein binding).</li> </ul>
Vigabatrin	<ul style="list-style-type: none"> <li>• Add-on efficacy for partial-onset seizures and West syndrome.</li> <li>• No interactions.</li> </ul>	<ul style="list-style-type: none"> <li>• Concentric visual field defects, irreversible.</li> </ul>
Zonisamide	<ul style="list-style-type: none"> <li>• Efficacy: partial-onset seizures; generalized- onset seizures (evidence not rigorous).</li> <li>• Long half-life (allows once daily dosing).</li> <li>• Weight loss</li> </ul>	<ul style="list-style-type: none"> <li>• Weight loss, aphasia and cognitive impairment, nephrolithiasis, metabolic acidosis; anhidrosis in children (fever).</li> </ul>

## LITERATURE REVIEW

### I) Literature Review on Ethiopathogenesis of Epilepsy

**a. Devender Bhalla et al. in June 2011** published that, epilepsy is a complex and heterogeneous disorder with long list of risk factors. They reviewed epilepsy etiologies and highlighted the main risk-defining parameters as far as possible (injury severity, low grade tumors especially of temporal or rolandic localization, early onset, genetic origin of AD and so on), which might promote timely identification of a suitable target Population (people at risk of developing epilepsy). Variable significance of individual etiologies (stroke, perinatal trauma, infections in low-middle income countries) and presence of cofactors may lead to region-specific epilepsy frequencies.

A direct role of alcohol in epilepsy onset is less convincing. Many Gene mutations representing rarer epilepsy forms have been discovered but are of limited day-to-day clinical value.

Most drugs of today are seizure-controllers. This should go hand-in-hand with the need to develop specific epilepsy prevention methods that may constitute newer research avenues. Finally, there is a need to develop LMIC – specific ‘ideal epilepsy epidemiology monitoring criteria’ since the guidelines that currently exist do not fit the challenges that an epidemiological investigation on epilepsy in these countries may have. Problems in these countries are different and may need different solutions.

**b. Katrine Heger et al. in March 2022** published that, similar prescription patterns of the most common ASMs in children/adolescents as compared to adults. In contrast, there were major differences among the selected ASMs, where the extent and increased use of e.g., ethosuximide, sulthiame and clobazam was more prominent in the younger age groups than in adults, and the most recently approved ASM was limited in children. Clobazam was predominantly used in epilepsy. The use of valproate in adolescent girls was restrictive with moderate changes over the last decade. The use of ASMs in non-epilepsy indications is limited in children and adolescents, in contrast to the wide non-epilepsy use in adults. The NorPD enables surveillance of special patient groups, as children and adolescents, as well as new and special ASMs, as part of pharmacovigilance and patient safety evaluations.<sup>[4]</sup>

**c. Wong IC et al. in 2001** published that, the best results from LTG treatment in terms of freedom from seizures and long-term retention of treatment were obtained in patients with generalized epilepsy. Retention of treatment was enhanced by VPA not only in generalized but also in focal epilepsy. The importance of a low starting dose of LTG was again confirmed. The apparent negative effect of CBZ in patients taking LTG merits further investigation.<sup>[5]</sup>

**d. Giovanna Vitaliti et al. in May 2019** published that, epileptic encephalopathy represents a treatment challenge for neurologists, pediatricians and neonatologists. Identification of biological markers as an expression of the involvement of the immune system in the disease etiology is fundamental to both, determination of the prognosis following the first seizure as well as the likelihood of drug-resistance.<sup>[6]</sup>

### ii) literature review on anti epileptic therapy and its limitations

**a. Liang-Po Hsieh et al. in November 2008** published that, analyze and evaluate antiepileptic drug (AED) utilization among adults in Taiwan. A random sample of 167,377 patients from the National Health Insurance (NHI) reference database was used. Prescription records were retrieved for all patients prescribed AEDs during 2004. The prescribed daily dose/defined daily dose (PDD/DDD) ratio was used to assess the adequacy of AED dosing.

Seventy-one percent (n=518) of patients used only one AED, while 29% (n=212) used more than two AEDs in 2004. For monotherapy, the most frequent regimens included carbamazepine (41.9%), followed by phenytoin (27.3%) and valproic acid (17.8%). For polytherapy, the most commonly used combination was valproic acid and carbamazepine. For adults, the mean PDD/DDD ratio for each AED used for either monotherapy or polytherapy was less than 1.00. Additionally, adult patients treated with more than one AED during 2004 in Taiwan took each drug in higher dose than patients using the same AED in monotherapy. In Taiwan antiepileptic drug therapies appear to be still dominated by the first generation drugs. The mean dosages of most antiepileptic drugs were lower than that of WHO suggested.<sup>[7]</sup>

**b. S. Shanmugapriya et al. in 2018** published that, prescribing indicators has clearly delineated that the prescribing practices for antibiotics and injections are appropriate and rational; conformity to essential drugs list is considerably good, though scope for improvising is certainly evident. However, the degree of polypharmacy is higher than the standard. Generic prescribing is also an element that needs to be vastly improved on. Therefore, appropriate measures to reduce polypharmacy and increase generic prescribing by clinicians have to be implemented by the administrative team and policymakers to ensure rational and safe prescribing.<sup>[8]</sup>

**C. Jincy George et al. in 2016** published to evaluate the drug utilization of anti epileptic drugs in in-patient admission of medicine and pediatric departments at tertiary care teaching hospital. conventional AEDs are used as monotherapy was more effective in terms of reduction of seizures, as they are available at low costs and are more affordable than the newer drugs and polytherapy. The study concludes the effective use of benzodiazepines along with AED. Due to the lack of

specific guidelines for the usage of AED in India, the rationality in the prescription is variable and poor.

**d. Victor Patterson et al. in May 2020** published that, a proven epilepsy diagnosis smartphone application has led to an epilepsy management app. The summary generated by this app can be emailed or messaged to more-experienced doctors for advice. The app was both easy to use, and accurate for the diagnosis of episodes, seizures, and epilepsy types. This epilepsy management app has the potential to improve epilepsy care in resource-limited settings.<sup>[9]</sup>

### iii) Literature Review On Importance Of Trend Analysis In Rationalising Prescription

**a. Chun-Yu Liang et al. in January 2022** published that, Valproic acid was the most prescribed AED for prevalent patients with epilepsy. The mean PDDs of most AEDs were lower than the DDDs developed by the World Health Organization to evaluate the prescription patterns and prescribed daily dose (PDD)/defined daily dose (DDD) ratios of antiepileptic drugs (AEDs) in prevalent patients with epilepsy in Taiwan. A nationwide retrospective cross-sectional study was conducted for prevalent patients with epilepsy in 2016 using the Taiwanese National Health Insurance Research Database. A total of 118,937 prevalent patients with epilepsy were enrolled. The prescription records of AEDs of all prevalent patients with epilepsy were retrieved. The mean PDDs and PDD/DDD ratios of AEDs in adult patients were obtained to evaluate dosing adequacy. A chi-square test and two-sample test were used to analyze the differences in AED prescription patterns and dosages, respectively, among patients with different ages, sexes, comorbidities, and therapeutic approaches.<sup>[10]</sup>

**b. Krishnamoorthy Gayathri et al. in June 2020**, to observe the drug pattern of epileptic patients with their seizure type, to analyze the type of therapy received by the patients, to observe if epileptic patients are receiving an appropriate dose, to identify the side effects in epileptic patients associated with drug treatment and to observe the cost of conventional and newer antiepileptic drugs (AED's). This was a cross-sectional observational study conducted in the Neurology department. A total of 150 patients were selected based on the inclusion and exclusion criteria. Symptomatic localization (64%) was the most commonly observed epilepsy syndrome. The commonly observed type of therapy among the patients was dual therapy. AED dose prescribed for most of the adult population was at a sub-optimal level, as explained by the daily defined dose/ prescribed daily dose (DDD/PDD) ratio (<1). Carbamazepine and oxcarbazepine were prescribed at a suboptimal level in the paediatric population. Excessive somnolence, fatigue, weight gain were the most commonly reported side effects. The observed mean cost of newer drugs was more than conventional drugs. Despite the appropriate selection of AED, patients had increased frequency of

seizures with the incidence of side effects. This problem could have been overcome by prescribing optimal doses and avoiding the use of polytherapy wherever possible.

**C. Urszula Religioni et al. in May 2020** published that, the management of medicinal products in hospitals is a multidisciplinary area requiring coordinated staff activities to design, implement, and regularly update drug management policies. Rational drug management plays a crucial role in the management of healthcare entities due to economic consequences and providing patients with adequate care quality. Despite the development of international organizations' recommendations for rational drug management, this area is very neglected in many countries. Therefore, it is necessary to create national guidelines for the rationalization of the use of medicines adapted to the local conditions and existing law. However, the most important is to develop internal drug management standards in each hospital, whose primary goal will be to provide patients with high-quality care.

All activities taken at the state and hospital level will lead to the optimization of the entire patient treatment process. Rationalization of costs in hospital healthcare will contribute to significant savings in the whole healthcare system. Thus, it will be possible to better allocate funds allocated to healthcare, which will optimize patients' health outcomes and ensure access to high-quality care for a more significant part of the population.<sup>[11]</sup>

**d. Mallik Angalakuditi et al. in Sep. 2011** published that, describing many aspects of epilepsy in emerging markets. Overall, the reported incidence of epilepsy is low in the general population and, overall, treating patients with epilepsy is inexpensive and decreases the use of health care resources.<sup>[12]</sup>

However, the identified clinical studies generally lacked standardized diagnosis criteria and used ineffectual methods with which to grade symptoms. Standards of care and baseline medications varied greatly between populations and adjunctive medications were often arbitrarily examined. Studies with longer follow-up periods and larger patient populations are needed to document the long-term effectiveness of several AEDs. Many of the observations discussed in this review need to be further confirmed in larger prospective trials, and, looking for specific characteristics of patients responding to certain drugs may lead to useful guidelines for drug choice in treating epilepsy. Knowledge gained in these areas will enable improvement to the care of people with epilepsy both in emerging markets and elsewhere.

### Rationale

The present study aims to through life on certain aspect of national reviews of anti epileptic treatment. The endover to be relevant the prospect of epilepsy in consideration of the fact that epilepsy are generally

exposed to the drug regimen. For a major fraction of their life owing to the natural of the chronic nature of the disease. The study begins with the assessment of demographical difference of the disease and excentto identification of type of seizure and the drug used commonly to treat such episource. The analysis is belief to provide newer insights into the suitability of drug utilization in eileptics in community setting.

**Aim**

Trend analysis of antiepileptic prescriptions in tertiary care hospital in district of West Bardhaman.

**Objectives**

1. To determine demographic variation of patient making up healthcare suitability.
2. To assess the trend of occurrence of different seizures as evident form prescription.
3. To identify the pattern of the drug regimen as evident from prescription.

**Plan for Work**

1. Collection of prescription through a stipulated period of time.
2. Shorting of prescription on basis of Identification of specific parameters in the collected prescription.

3. Quantitative representation of the parameters of choice.
4. Comprehensive of data and flaming of conclusion.

**Methodology**

The study was conducted on a prospective mode and was based on the prescription obtained from the records of the pharmacy department of respective health care establishment The study spanned through a period of 3 months starting from Jan 2022 to March 2022. Formal permission for the study has been obtained from the respective IEC. Prescription of patients turning up for their first visit were only considered for the study .Patients having active comorbidity or on medication for recurrence or relapse of any other comorbidity were excluded.

**RESULT**

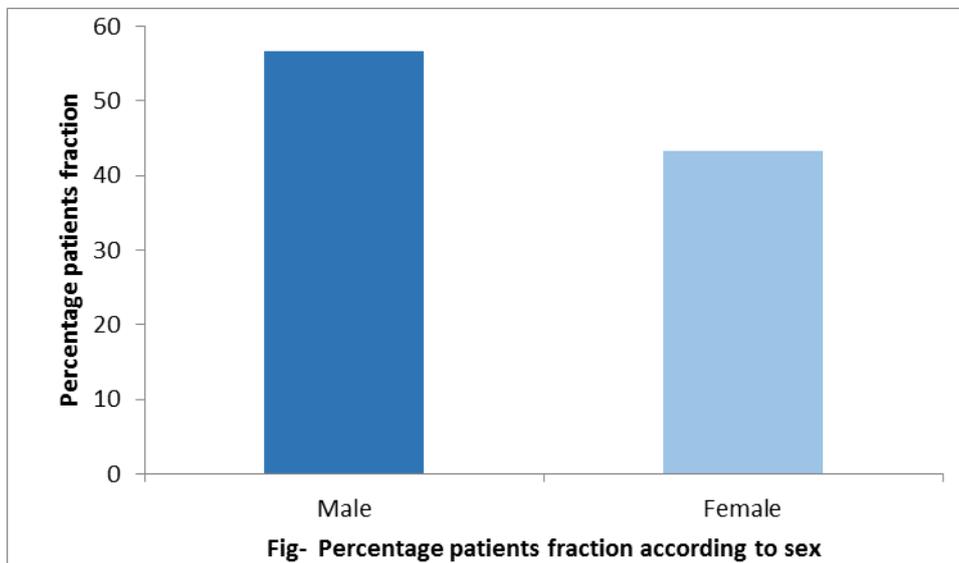
**1. Socio demographic details of subjects**

Through the span of three months, a total of 150 new prescriptions got generated.. Out of 150 prescriptions generated 85 were for male patients and 65 turned out to be for females. As depicted in the graph,Epilepsy was more commonly seen in the patients of age group of 19-60 years. The socio-demographic features considered of are represented below (Table 8.1, Figure 8.1).

**Table: Socio-demographic details of the epileptic patients.**

**Table 8.1: Percentage patients fraction according to sex.**

Gender	No. Of patients	Percentage patients fraction
Male	85	56.66 %
Female	65	43.33 %



**Figure 8.1:**

**Table 8.2: Percentage patients fraction according to age.**

Age group	No. Of patients	Percentage patients fraction
0-18	42	28 %
19-60	108	72 %

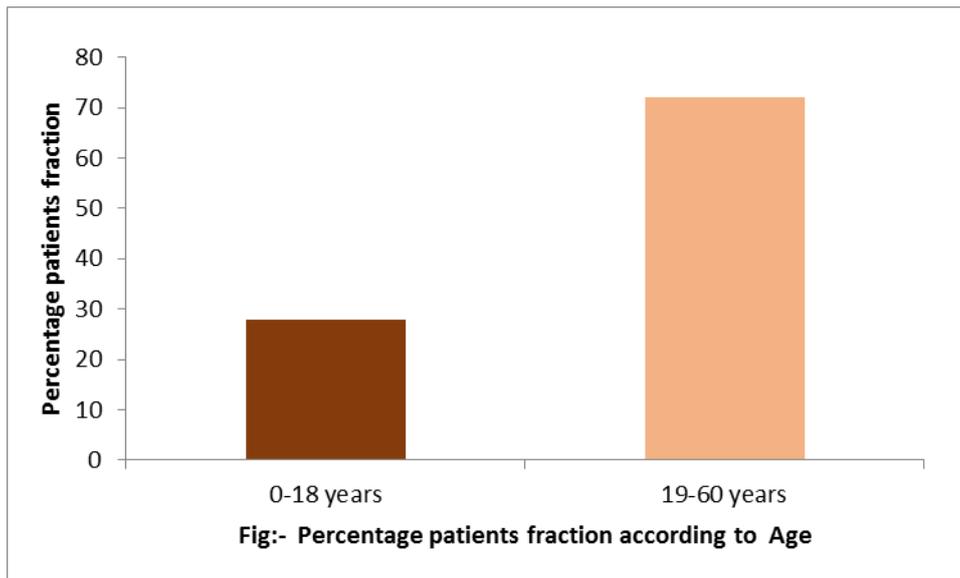


Figure 8.2:

**Types of Seizure**

Data of 150 patients turning up to hospital and diagnosed with epilepsy were collected and analyzed. The commonest type of epilepsy for both group 0 – 18 year and 19 – 60 years age was Generalized tonic clonic

seizure. And the second most common in 0-18 years group was Atonic seizure and for the 19-60 years age group was Simple partial seizure. The type of seizure considered of are represented below (Table 8.3, Figure 8.3. and 8.4)

**Table 8.3: Different type of Seizure prevalent in different age groups (Total – 150 Patients).**

Age Group(0-18)		Age Group(19-60)	
Type	Number	Type	Number
Generalized tonic-clonic seizure	26	Generalized tonic-clonic seizure	82
Myoclonic seizure	3	Myoclonic seizure	9
Complex partial seizure	2	Simple partial Seizure	17
Simple partial seizure	4		
Atonic seizure	7		

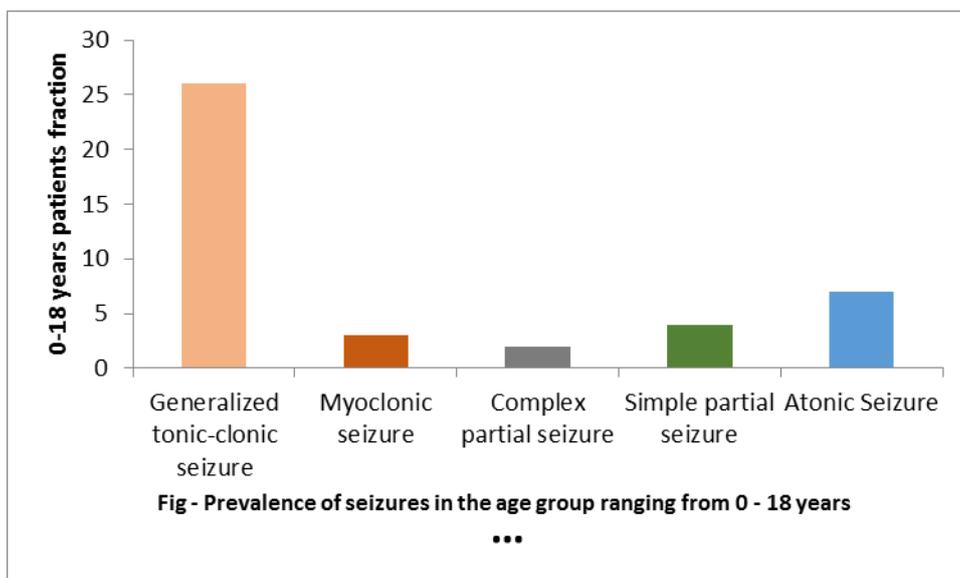


Figure 8.3:

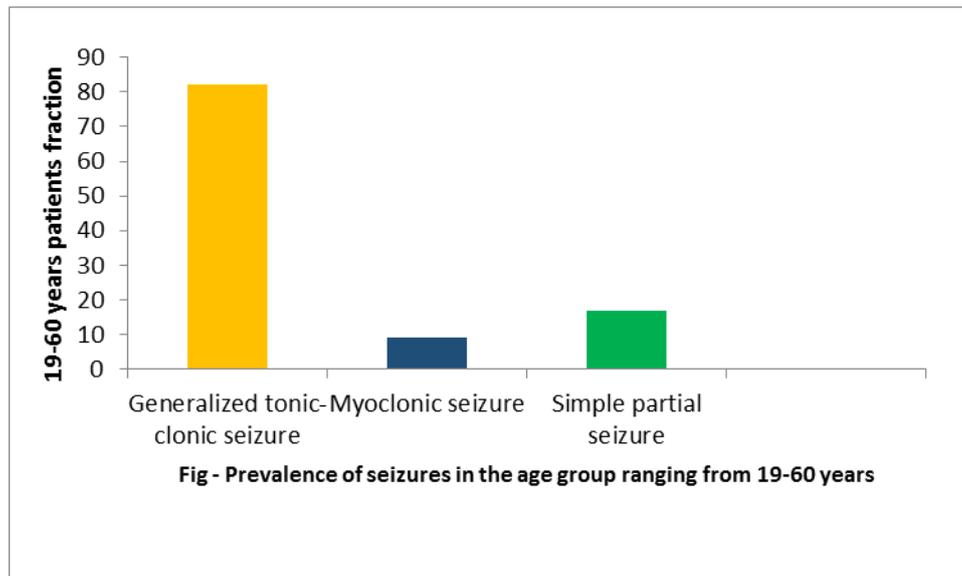


Figure 8.4:

**2) Comparison of monotherapy and polytherapy across group**

Out of 150 patients, majority of them received monotherapy with various drugs(108). About 42 patients

received combination therapy with two or more drugs. This data is reported in (Table 8.5 , Fig.8.6. )

Table 8.4: Comparison of mono and polytherapy according to age.

Types of AED therapy	No of Prescription according to age	
	0 - 18 years	19 – 60 years
Monotherapy	30	80
Polytherapy	12	28
Total	42	108

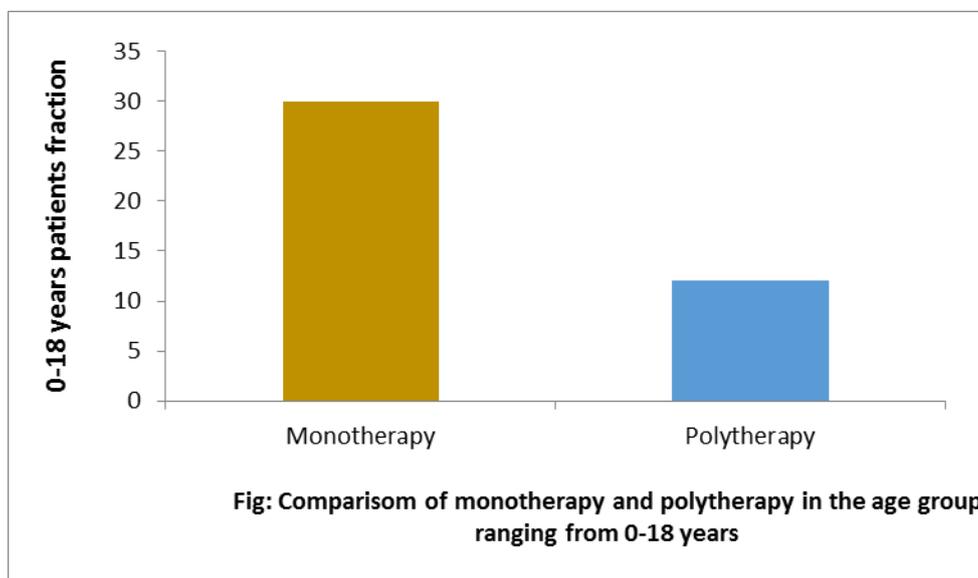


Figure 8.5:

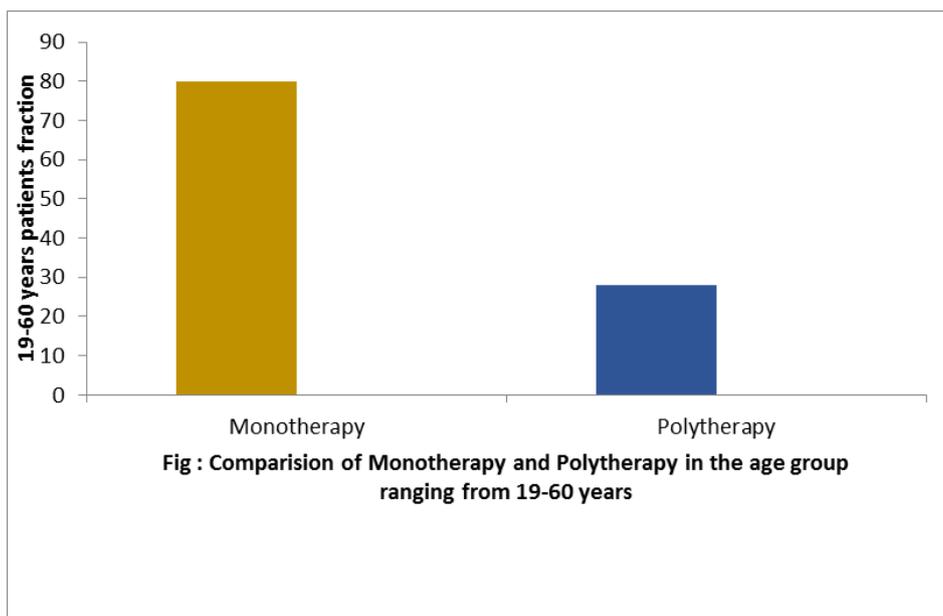


Figure 8.6:

**Prescription pattern**

Out of 110 patients who were on monotherapy, most commonly prescribed AED was Phenobarbital followed by Phenytoin, Carbamazepine, Valproic acid, Oxcarbazepine, Levetriacetam, Lacosamide which is depicted in.

**Table 8.6**

In Polytherapy, commonly used drug combination was Oxcarbazepine with Phenytoin, Phenobarbital with Levetriacetam, Oxcarbazepine with Valproic acid, Phenobarbital with Lacosamide, and Carbamazepine with Levetriacetam which is depicted in **Table 8.7**

**Table 8.6: Drugs used in Monotherapy.**

Drugs name	No. of patients	Percentage of Prescription (%)
Phenytoin	20	13.3
Oxcarbazepine	25	16.6
Valproic acid	33	22
Phenobarbital	15	10
Levetriacetam	10	6.6
Lacosamide	07	4.6

**Table 8.7: Pattern of prescribing AEDs in single or combination dosage.**

Age (years)	Types of AED		
	Older drugs	Newer drugs	Older + Newer drugs
0 – 18	Phenobarbital	Oxcarbazepine	Oxcarbazepine + Phenytoin
	Phenytoin	Levetriacetam	Phenobarbital + Levetriacetam
	Valproic acid		Oxcarbazepine + Valproic acid
19 - 60	Phenobarbital	Lacosamide	Phenobarbital + Lacosamide
	Carbamazepine	Levetriacetam	Carbamazepine + Levetriacetam

**Table 8.8: Drugs used in Polytherapy.**

Drugs name	No. of Patients	Percentage of prescription
Oxcarbazepine + Phenytoin	12	08
Phenobarbital + Levetriacetam	05	3.3
Oxcarbazepine + Valproic acid	19	12.6
Phenobarbital + Lacosamide	03	02
Carbamazepine + Levetriacetam	01	0.6

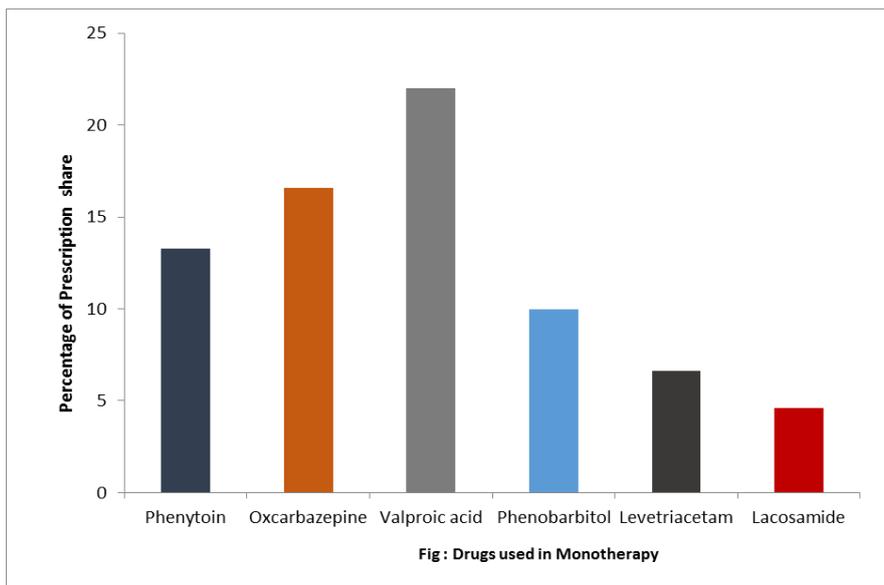


Figure 8.7:

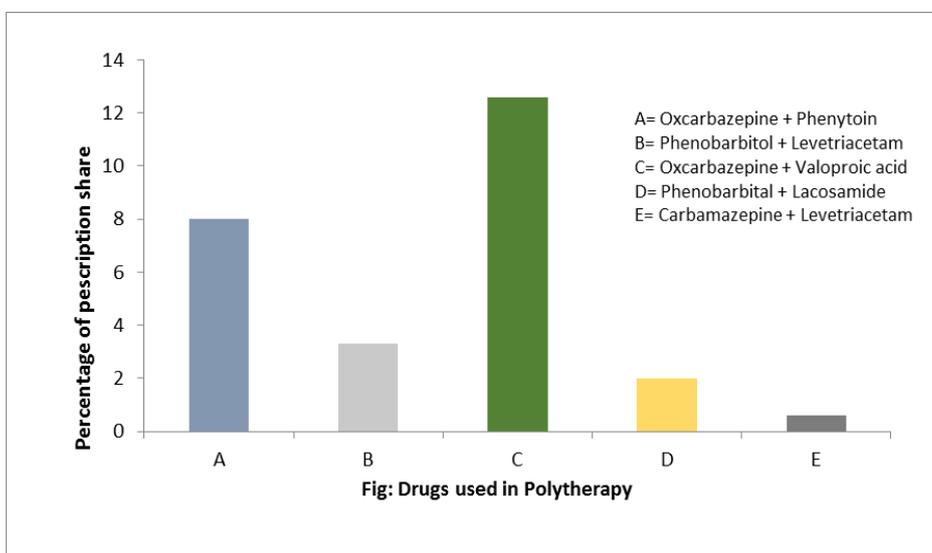


Figure 8.8:

**DISCUSSION**

Trend analysis studies play a key role in helping the healthcare system to understand, interpret and improve the prescription, administration and use of medications, where principal aim is to facilitate rational use of drugs. Patient files and computer registries are widely used as instruments for collecting information on drug.

Analysed of prescription help us in understanding the target patients, the various indications as well as the rationality of drug usage. Study in chronic disease like epilepsy is essential because in such diseases patients are exposed to drugs for a long time and sometimes lifelong. Adverse effects, drug interactions, enhanced economic burden on the patients are the main drawbacks of polytherapy. So the various prescribing indices should be understood in such situations. In the present study, various drug usages and patient characteristics in epilepsy was analysed.

Epilepsy is a chronic condition which impair quality of life due to physical, physiological and socioeconomic consequences. The prime requirements are a complete diagnosis, selection of optimal treatment, and counselling appropriate to individual needs. The aim of treatment is cessation of seizures without side effects. Pharmacological factors influencing the choice of drug include efficacy, toxicity, and ease of use, all of which should be considered with respect to individual patient needs.

In this study, a total of 150 prescriptions of epilepsy were studied. By the analysis of sociodemographic data, it was found that percentage of male patients (56.66 %) was higher than percentage of female patients (43.33 %) (table 8.1). Male preponderance is seen in gender distribution in our study, which is similar to reports from other studies in countries of Asia. In India, less number of females may be due to higher illiteracy, social stigma

and need for the male relatively to concern and accompany the female for hospital visit.

Maximum patients in this study were of age group 19-60 years (72 %) followed by 0-18 years (28 %) Bimodal distribution is seen with the incidence of epilepsy. With a peak incidence in elderly patients and then in first decade.

The most common type of epilepsy seen in this study was Generalized tonic-clonic seizure (72 %) which is followed by Simple partial seizure (13 %). Our studies were similar to the reports from most of the Asian countries.

Monotherapy is mostly preferred to minimize the risk of adverse drug reactions, dose related toxicity, drug interactions, non compliance and economic burden. Monotherapy was practiced in 73 % of our patient, which is similar in many studies with its many advantages.

Nevertheless, multiple drug therapies are unavoidable in some patients, even though polypharmacy adversely affect the quality of life. In 42 patients seizures were managed with dual therapy.

The commonly prescribed Anti-epileptic drug was Phenytoin, Valproic acid, Oxcarbazepine, Levetiracetam, as they are available at low cost and are more affordable. Nevertheless, polytherapy is unavoidable in some patients, though it adversely affects the quality of life and increases the chances of drug related problems. The newer Anti-epileptic drugs like Oxcarbazepine, Levetiracetam, Lacosamide, Levetiracetam were used in few cases with old Anti-epileptic drugs.

Oxcarbazepine with Valproic acid is mostly prescribed. Valproic acid is the most effective drug for Myoclonic seizures. It is useful in atonic seizures, in which control is often incomplete, but valproic acid is the drug of choice. Valproic acid has some prophylactic efficacy in migraine.

The newer Anti-epileptic drugs used in this study are Oxcarbazepine, Levetiracetam, Lacosamide, Levetiracetam. Newer Anti-epileptic drugs were not commonly prescribed due to higher cost and non availability in government supply, as they are still not included in Essential Drug List.

Comparing the study data with international and national guidelines we conclude that the trend analysis of antiepileptic prescription for Antiepileptic drugs is in accordance with the standard guidelines.

## CONCLUSION

Epilepsy emerges as a prevalent problem in the district of West Bardhaman fostering generation of more prescriptions for male patients in the age group of 19-60

years. Tonic clonic seizure found to be the chief type prevalent in the district, got treated with monotherapy comprising of valproic acid in majority of the cases. Combination therapy has also been chosen in quite a few cases. The study thus paves the way for analysis of the indicated trend further with additional end points being considered.

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