*ejpmr, 2022, 9(7), 523-528*

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

# PRESCRIPTION PATTERN OF ANTI-EPILEPTIC DRUGS IN IN-PATIENTS WITH EPILEPSY AT A TERTIARY CARE CENTRE.

**[*1]Dr. Divya Amaravadi and [2]Dr. S. Jaypal Reddy**

[1]Assistant Professor, Department of Pharm.D, CMR College of Pharmacy, Hyderabad Telangana.
[2]Spine and Neuro-surgeon, Sai Krishna Neuro Hospital, Kachiguda Hyderabad, Telangana.

***Corresponding Author: Dr. Divya Amaravadi**

Assistant Professor, Department of Pharm.D, CMR College of Pharmacy, Hyderabad Telangana.

**Article Received on 22/05/2022** **Article Revised on 11/06/2022** **Article Accepted on 01/07/2022**

## ABSTRACT

**Background:** Epilepsy is a clinical condition of recurrent spontaneous seizures arising from aberrant electrical activity within the brain. The ideal goal in the management of epilepsy is complete control with minimal side effects. **Objectives:** To study and analyze the pattern and usage of AEDs at a tertiary care hospital. To observe side effects of AEDs and to identify and document common and least common AED in Neuro care unit. **Methodology:** It is a single centre prospective observational study done for a period of six months at Sai Krishna super speciality neuro care and poly trauma hospital located at Hyderabad. Study enrolled 70 patients having epilepsy. Patient data collected from the cases as demographical data, type of epilepsy, comorbid conditions and AEDs used in patients. **Results:** 68.5% were male and 31.4% were female. Maximum patients were of the age group 34-43 years. Generalized tonic-clonic seizures (GTCS) observed to be the most commonly occurring seizure in 55.7% patients. Intravenous administration was the common route of administration in 48.5% patients. Mono-therapy treatment pattern was the preferred choice of therapy in most patients. Significantly, Levetiracetam (newer AED) were found to be the commonly prescribed AED at the study site. Ischaemic stroke was the commonly occurring comorbidity with epilepsy. **Conclusion:** GTCS was most common type of seizure. Levetiracetam was more prescribed. Care should be taken while prescribing poly-therapy which may lead to drug related problems. Therefore patient education and observation were necessary for proper utilization of drugs.

**KEYWORDS:** Epilepsy, AEDs, mono-therapy and GTCS.

## INTRODUCTION

Epilepsy is a group of neurological disorders characterized by epileptic seizures. Epileptic seizures are episodes that can vary from brief and nearly undetectable periods to long periods of vigorous shaking. Epileptic seizures occur due to excessive and abnormal neuronal activity in the cortex of the brain.

The diagnosis involves ruling out conditions such as alcohol withdrawal or electrolyte problems that might cause symptoms of fainting which can be partly done by imaging of brain and performing blood tests.

Epilepsy can often be confirmed by 'Electroencephalogram' (EEG) but normal test does not rule out the condition. In those whose seizures do not respond to medication, surgery, neurotransmission or dietary changes may then be considered.[1]

**Types of Seizures:** Significantly seizures are classified into partial seizures and generalized seizures. Generalized seizures are divided into the following types.

1. **Tonic Seizures:** Tonic seizures most often develop in childhood, although they can occur at any age. Tonic seizures are characterized by facial and muscle spasms, flexion or extension of the upper and lower extremities, and impaired consciousness.[3]
2. **Clonic Seizures:** During this a person may lose control of bodily functions and begin jerking in various parts of the body. He or She may temporarily lose consciousness, followed by confusion. They begin in early childhood.[3]
3. **Tonic-Clonic Seizures:** A tonic-clonic seizure usually lasts one to three minutes, but may last up to five minutes. If seizures last more than five minutes, or occur one after another without recovery between seizures, the individual may be experiencing a life-threatening medical emergency and requires immediate medical help. The person will usually emit a short, loud cry as the muscles in the chest contract and the air rushes between the vocal cords, making a sound. The muscles will stiffen (tonic phase) causing him/her to fall to the floor. [3] The extremities will then jerk and twitch rhythmically (clonic phase). Saliva that has not been

swallowed may froth at the mouth because breathing is irregular as the respiratory muscles may be affected.[3]

4. **Myoclonic Seizures:** Myoclonic seizures occur in several different types of childhood epilepsy. They involve abrupt muscle jerks in parts or all of the body. Myoclonic seizures should not be confused with tics or "startle" responses.[3]
5. **Absence Seizures:** In an absence seizure, epileptic activity occurs throughout the entire brain. It is a milder type of activity that causes unconsciousness without convulsions. After the seizure, the person has no memory of it. It usually lasts only two to ten seconds.[3]
6. **Status Epilepticus:** Status epilepticus (SE) is a single epileptic seizure lasting more than five minutes or two or more seizures within a five-minute period without the person returning to normal between them. It can be life-threatening if medical emergency particularly is delayed.[7]

## PATHOPHYSIOLOGY

Seizures result from excessive excitation or in the case of absence seizures from disordered inhibition of a large population of cortical neurons. There are multiple mechanisms that might contribute to synchronous hyper excitability including: Biochemical modifications of receptors, modulation of second messaging systems and gene expression, alterations in the distribution, number, type and biophysical properties of ion channels in the neuronal membranes, changes in extracellular ion concentrations, alterations in neurotransmitter uptake and metabolism in glial cells, modifications in the ratio and function of inhibitory circuits.[4]

## CLINICAL PRESENTATION

Partial (focal) seizures effects one of the hemisphere of the brain. It shows alterations in motor functions, sensory or somatosensory symptoms and automatisms. Partial seizures with no loss of consciousness are classified as simple partial (SP). Partial seizures with an alteration of consciousness are described as complex partial (CP). The patient can have automatisms, periods of memory loss, or aberrations of behaviour. Generalised seizures have clinical manifestations that indicate involvement of both hemispheres. Generalised absence seizures are manifested by a sudden onset, interruption of ongoing activities, a blank stare and possibly a brief upward rotation of the eyes. They generally occur in young children through adolescence. It is important to differentiate absence seizures from complex partial seizures.[5] Frequent symptoms are: fainting / fatigue, rhythmic muscle contractions or muscle spasms, Aura, anxiety and depression.[4]

**Classification of Anti-Epileptic Drugs:** There are various classes of epilepsy drugs such as: Barbiturates – Phenobarbitone. Deoxybarbiturate – Primidone. Hydantoin – Phenytoin, Fosphenytoin. Iminostilbene – Carbamazepine, Oxcarbazepine. Succinimide – Ethosuximide. Aliphatic carboxylic acid – Valproic acid (sodium valproate), Divalproex. Benzodiazepines – Clonazepam, Diazepam, Lorazepam, Clobazam. Phenyltriazine – Lamotrigine. Cyclic GABA analogue – Gabapentine. Newer drugs as Vigabatrin, Topiramate, Tiagabine, Zonisamide, Levetiracetam are some of the drugs being used in recent time.[6]

## METHODOLOGY

It is a single centre prospective observational study conducted in in-patients of tertiary care centre for a period of six months (October `2018 – March `2019). The study was conducted at Sai Krishna Super speciality Neuro and poly trauma Hospital, located at Kachiguda, Hyderabad, Telangana. Sample size taken was 70 patients admitted in the in-patient department.

**Inclusion criteria**- All Female and male patients admitted to the acute neuro-care unit in Intermediate care unit (IMCU) and also admitted in IP-general ward department of neuro unit were included in study. Patients of the age group (4 to 70) years were included.

**Exclusion criteria**- Patients with mental and physical disabilities, pregnant and lactating women shall be excluded and out patients were excluded from the study.

A data collection form was designed to collect patient demographics including name, age, sex, height, weight, family history, past medical history, complication and lifestyle modifications, diagnosis and medications prescribed, side effects, co-morbid conditions and other relevant information. The collected data was analysed using descriptive statistics for finding out average, mean, median, mode; frequency was calculated by using the demographic data collected. Ethical clearance was obtained from 'Institutional Ethics committee' (IEC) at School of Pharmacy, Anurag group of institutions, Hyderabad.

## RESULTS

In our study a total of 70 cases were collected of In-patients suffering from Epilepsy. The findings observed were that maximum number of patients were between the age group of 34-43 years (22.8%) followed by age group of 44-53 years (20%), 24-33 years (20%), 54-63 years (12.8%), >64 years (11.4%), 14-23 years (7.1%) and 4-13 years (5.7%).

**Table 1**: shows the gender wise distribution of study population where maximum were male patients of 68.5% and female patients were 31.4%.

**Table 1: Gender wise distribution.**

| Gender | Number of patients | Percentage | Total patients |
|---|---|---|---|
| Male | 48 | 68.5% | 70 |
| Female | 22 | 31.4% | |

**Table 2:** shows that 55.70% patients were suffering from GTCS followed by 18.5% patients were suffering from simple partial seizures, 10% suffering from focal seizures, 2.8% patients suffering from status epilepticus and 12.8% suffering from acute focal seizures.

**Table 2: Types of epilepsy.**

| Types of Epilepsy | Number of patients | Percentage |
|---|---|---|
| Generalised tonic-clonic seizures (GTCS) | 39 | 55.7% |
| Simple partial seizures | 13 | 18.5% |
| Focal seizures | 7 | 10% |
| Status epilepticus | 2 | 2.8% |
| Acute focal seizures | 9 | 12.8% |
| | Total = 70 | |

**Table 3:** shows the commonly prescribed drug for GTCS was Levetiracetam, for simple partial seizures was Sodium valproate, for Focal seizures it was Levetiracetam, for status epilepticus it was Phenytoin & Fosphenytoin and for acute focal seizures was Lorazepam.

**Table 3: Commonly prescribed AEDs according to type of seizure.**

| Type of seizure | Preferred drug |
|---|---|
| GTCS | Levetiracetam |
| Simple partial seizures | Sodium valproate |
| Focal seizures | Levetiracetam |
| Status epilepticus | Phenytoin, fosphenytoin |
| Acute focal seizures | Lorazepam |

**Figure 1**: shows that the most common route of administration was intravenous route (IV) (48.5%) followed by IV to oral route (41.4%) and oral route (10%). IV to Oral route was changed when the patient was in a conscious state and in a position to self-take the medication.

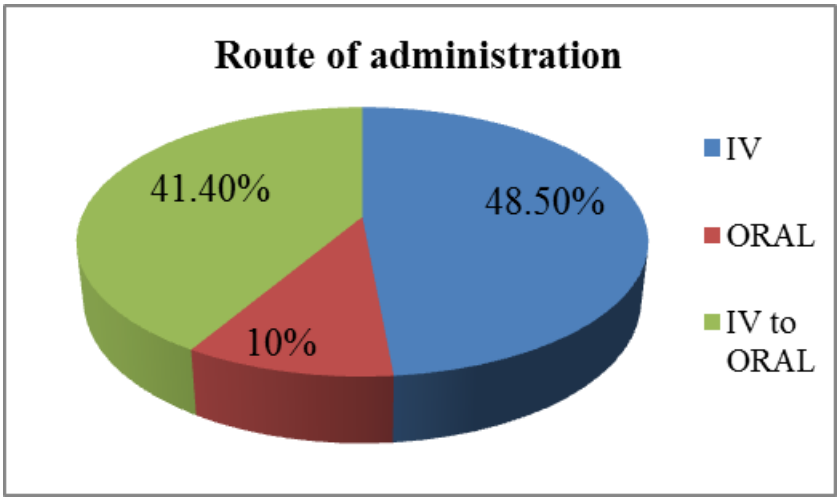


**Figure 1: Route of administration.**

**Figure 2:** describes the therapy choice for antiepileptic drugs depending on type of epilepsy. Most commonly used AED was Levetiracetam. The pattern of AED therapy varies in accordance to the type of seizure. Monotherapy treatment pattern was the preferred choice to the types of epilepsy, rather than dual, triple and quadruple therapy.

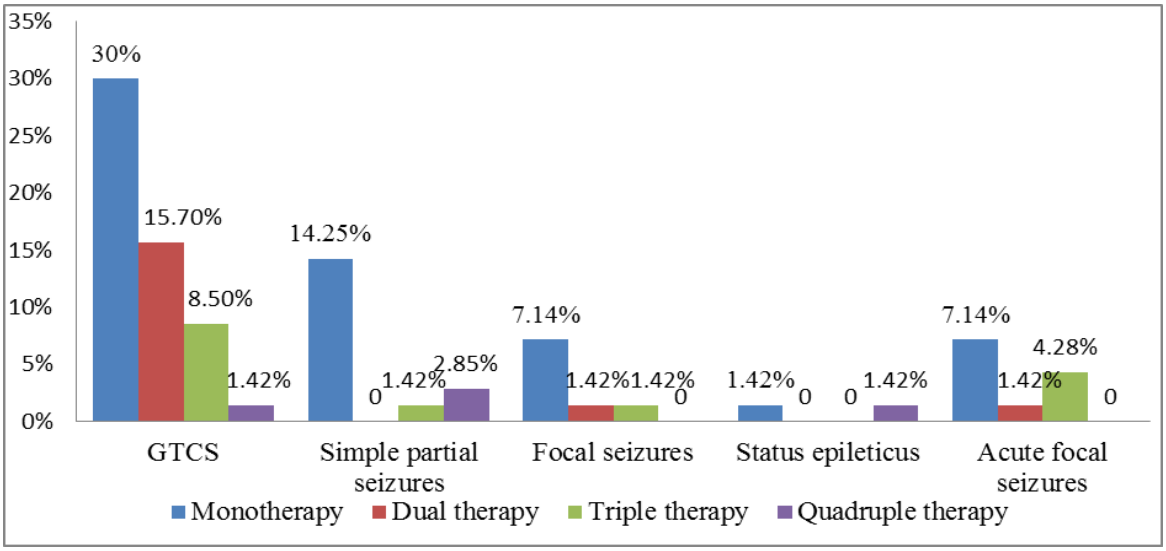


**Figure 2: Therapy type with AEDs in various epilepsy cases.**

**Table 4**: shows that commonly prescribed AEDs at the study site was Levetiracetam (47.4%), Sodium valproate (25.8%), Phenytoin (7.75%), Lacosamide (5.10%), Fosphenytoin (4.31%), Carbamazepine (2.58%), Clobazam (0.86%), Topiramate (0.86%) and Gabapentine (0.86%).

**Table 4: Utilisation of AEDs**

| Antiepileptic drugs | No. of cases AEDs prescribed | Percentage |
|---|---|---|
| Levetiracetam | 55 | 47.4% |
| Sodium valproate | 30 | 25.8% |
| Phenytoin | 9 | 7.75% |
| Lacosamide | 6 | 5.17% |
| Fosphenytoin | 5 | 4.31% |
| Carbamazepine | 3 | 2.58% |
| Clobazam | 3 | 0.86% |
| Topiramate | 3 | 0.86% |
| Gabapentine | 2 | 0.86% |

**Figure 3**: shows the co-morbid condition presented in the epilepsy patients at the study site and the most commonly occurring co-morbid condition in the patients was ischemic stroke (30.30%), Hypertension (21.2%), Cerebral palsy (18.1%), Diabetes mellitus (9.09%), Metabolic encephalopathy (9.09%), Acute headaches (6.06%), Meningitis (3.03%) and Hypothyroidism (3.03%).

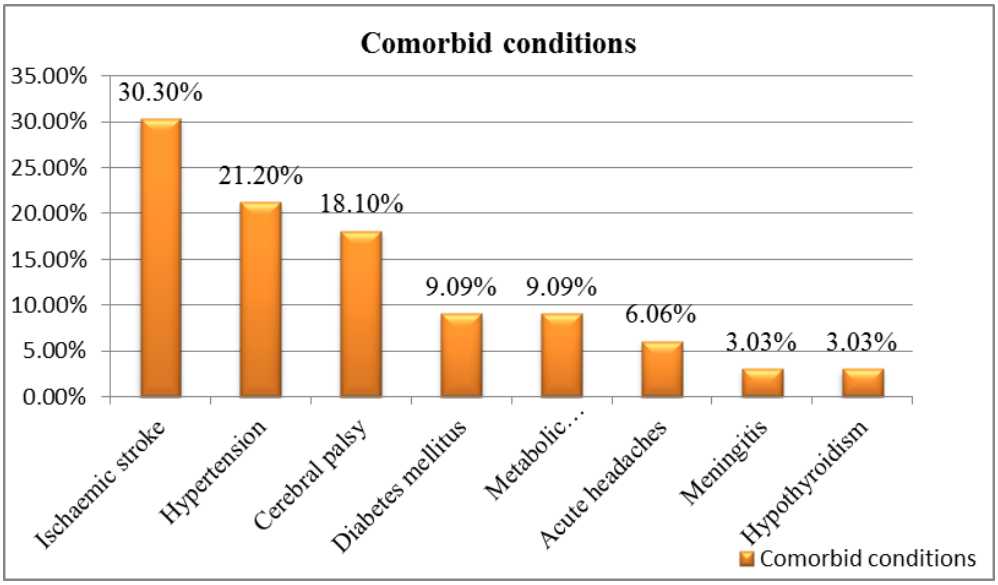


**Figure 3: Co-morbid conditions observed.**

Out of all 70 cases, the average number of AEDs prescribed was calculated as shown in **Table 5.**

**Average number of AEDs prescribed to each patient =**
**Total no. of AEDs prescribed to all patients included in the study**
**Total no. of patients**

The values are entered by calculation from table 4 as 116 and the total no. Of patients/cases collected were 70. Hence on applying the above formula: 116/70 was 1.65.

This helps to study the number of AEDs prescribed to a patient in order to know the intensity of poly-pharmacy. Here 1.65 was found to be the average number of AEDs prescribed to each patient in our study, which shows that the potential for poly-pharmacy with AEDs was less.

## DISCUSSION

This study was conducted in Sai Krishna super speciality hospital in Kachiguda, Hyderabad, Telangana. Total of 70 patients of both genders suffering from epilepsy were included in the study. Male patients (68.5%) were reportedly more compared to female patients (31.4%) in the study population. In our study average number of AEDs per patient was found to be 1.65 which was near to our value in another study conducted by **Meenakshi B et al.,**[25] in a tertiary care teaching hospital of south Tamil Nadu where the average number of AEDs per patient was 1.37.

For patients hard to control seizures multiple drugs are utilized simultaneously. The age distribution in our study shows that the maximum patients were of age group 34-43 years (22.8%), followed by 44-53 years (20%), 24-33 years (20%), 54-63 years (12.8%), >64 years (11.4%), 14-23 years (7.1%) and less number of patients in the age group 4-13 years (5.7%), where as in a study conducted by **Vishwas A.T.L et al.,**[26] it was found that the peak was observed at the age group of 40-49 years (32.7%), followed by 18-30 years (24.5%), 31-39 years (20%), >60 years (11.8%) and 50-59 years (10.9%).

The drug utilization pattern shows that most of the patients received mono-therapy rather than dual, triple and quadruple therapy. Out of 70 patients 60% were treated with mono-therapy, 18.5% with dual therapy, 15.7% with triple therapy and 5.7% with quadruple therapy where as in a study conducted by **Sami Parajuli et al.,** [27] showed that out of 206 patients mono-therapy was prescribed to 141 patients (68.4%), followed by dual therapy to 45 patients (21.8%), triple therapy to 18 patients (8.5%) and quadruple therapy to 2 patients (1.0%) and was found to be similar to our study.

Our study also reveals that out of 70 patients 39 (55.7%) were suffering from Generalised Tonic-Clonic seizures (GTCS), followed by 13 (18.5%) from Simple partial seizures, 7 (10%) of Focal seizures, 2 (2.8%) from Status epilepticus and 9 (12.8%) from acute focal seizures. This was slightly different on comparison with another study conducted by **Sami Parajuli, et al.,**[27] which showed that the types of seizures observed in total number of patients were GTCS 44 (21.4%), clonic seizures 14 (6.8%), focal seizures 12 (5.8%), complex partial seizures 1 (0.5%), febrile seizures 1 (0.5%), pseudo seizures 1 (0.5%), status epilepticus 1 (0.5%).

At our study site out of 116 antiepileptic drugs the most prescribed was Levetiracetam (47.4%) followed by Sodium valproate (25.8%), Lorazepam (4.31%), Lacosamide (5.1%), Clobazam (0.86%), Phenytoin (7.75%), Fosphenytoin (4.31%), Carbamazepine (2.58%), Topiramate (0.86%) and Gabapentine (0.86%). The above studies justify the use of Levetiracetam (new AED) because it was as equally effective as other AEDs when used in mono-therapy. In another study the findings observed by **Sami Parajuli, et al.,**[27] showed that the most common drug prescribed was Levetiracetam 120(41.6%), followed by phenytoin 67(22.5%), diazepam 22(7.65), carbamazepine 18(6.2%), gabapentine 12(4.1%), lorazepam 12(4.1%), pregabalin 11(3.8%), sodium valproate 9(3.2%), clonazepam 9(2.8%), topiramate 4(1.4%). Clobazam 4 (1.4%) and phenobarbitone 1 (0.3%).

This study reveals the most common comorbid conditions associated with Epilepsy to be Ischaemic stroke (30.3%), Cerebral palsy (18.1%), Meningitis (3.03%), Hypertension (21.2%), Diabetes mellitus (9.09%), Acute headaches (6.06%), Metabolic encephalopathy (9.09%) and Hypothyroidism (3.03%). Another study conducted by Sami Parajuli, et al,[27] showed maximum patients 18(8.8%) had brain tumors, 16 (7.8%) renal tubular acidosis (RTA), 15 (7.2%) suffered from brain injury, 15 (7.2%) patients had cerebral haemorrhage, 11(5.2%) had stroke, 6(2.9%) had migraine and 6(2.9%) had diabetic neuropathy.

Our study also reveals that out of 70 patients, 34 (48.5%) patients received AEDs via only intravenous route (IV), 29 (41.40%) patients received via IV to oral route and 7 (10%) patients received via only oral route. By this we conclude that the most preferred route to administer AEDs is IV route as they are not in a state to self-take the medications as in case of oral route.

## CONCLUSION

Our study gives an insight about prescription pattern to promote rational drug use by optimal antiepileptic drug selection, utilising mono-therapy and poly-therapy when and where required. The study also revealed that parenteral route of administration was mostly prescribed than oral route of administration.

The study shows that the most commonly occurring seizure is (GTCS) Generalised tonic-clonic seizure (55.7%) and the least common is Status epilepticus (2.28%). It was observed that patients can be effectively managed by the use of newer AEDs such as Levetiracetam and conventional therapy such as Sodium valproate & phenytoin.

Our study reveals that unlike the previous studies, newer AED like Levetiracetam (47.4%) was the most commonly prescribed AED. The most preferred treatment pattern for epilepsy was mono-therapy seen in 60% of cases. Hence, it is seen that a physician has a vital role during the selection of AEDs. Clinical pharmacist could help in this area by monitoring and identifying any drug related problems.

Care should be taken while prescribing poly-therapy as it may lead to drug-related problems and drug interactions, which in turn can affect seizure control and toxicity. This concludes that patient education and observation are very necessary for proper utilization of drugs and better patient care.

**ACKNOWLEDGEMENT**

We sincerely thank Sai Krishna Super speciality Neuro care hospital, for their cooperation to permit us for conduct of the study. We extend our sincere gratitude to Dr. S. Jaypal Reddy (Spine & Neurosurgeon) for his valuable guidance. We would also like to thank Dr. Vasudha Bakshi, (Dean-AGI) and management of AGI for their timely support, guidance and encouragement throughout the study.

**CONFLICT OF INTEREST**: Nil

**REFERENCES**

1. Lowenstein DH. Seizures and epilepsy. In: Fauci AS, Kasper DL, Longo DL, editors. Harrison's Principles of Internal Medicine, 17th edition. New York, Mc Graw-Hill, 2008; 363-1-52.
2. Lowenstein DH. Seizures and epilepsy. In: Fauci AS, Kasper DL, Longo DL, editors. Harrison's Principles of Internal Medicine, 17th edition. New York, Mc Graw-Hill, 2008; 250-1-50.
3. Scheuer ML, Pedley TA. The evaluation and treatment of seizures. N Engl J Med, 1990; 323: 1468-74.
4. Dr. Ananya Mandal. April Cashin-Garbutt, MA (Cantab). Epilepsy-pathophysiology, 2006.
5. Cascino GD, Sharbrough FW. Symposium on epilepsy. Foreward Mayo clinic Proc, 1996; 71: 403-4.
6. Patrick M. Malone; Nancy L. Fagan; Mark A. Malesker; Paul J. Nelson; Drug evaluation Monographs CH-13-Drug information: A guide for pharmacists, 5e.
7. Al-Mufti, F; Claassen, J (Oct 2014). "Neurocritical Care: Status Epilepticus Review". Critical Care Clinics. 30.
8. Meenakshi B, Ezhil Ramya.J, Ananthy Shri T.R.R. An analysis of prescription pattern and adverse drug profile in children treated with antiepileptic drugs in a tertiary care teaching hospital-International journal of basic and clinical pharmacology, 2016 April; 5(2): 389-393.
9. Dr. Vishwas A.T.L, Dr. Suresh B.S, Dr. Bhanushree D.M, Chetan B, Vinutha M.D, Prashanthi B. Assesment of prescription pattern of anti-epileptic drugs in epilepsy-European Journal of pharmaceutical and medical research, 2018; 5(10): 299-305.
10. Sami Parajuli, Kejeeya Baskota and Mahadevamma L. A study on trends in prescribing pattern of anti-epileptic drugs in private health sector-World Journal of pharmacy and pharmaceutical sciences, 2018; 7(1).