

Prescription Pattern of Antiepileptic Drugs in Different Types of Seizure Disorder in Children

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Abstract

Original Research Article

Epilepsy is a neurological disorder marked by sudden recurrent episodes of sensory disturbance, loss of consciousness, or convulsions, associated with abnormal electrical activity in the brain. The incidence of epilepsy is highest during childhood, especially for children aged 0 - 14 years. The goal of the study is find out the prescribing pattern of antiepileptic drugs in different types of seizure disorder in children. An educational observational study was carried out among 55 samples in the In-patient Department of Pediatrics, in a tertiary care teaching hospital, Bangalore. The data was collected by using self-designed data collection form. All information's were processed and analyzed by using Microsoft excel. In the present study, breakthrough seizures was the most commonly observed type of seizure followed by simple febrile seizure. The most commonly prescribed antiepileptic drug was levetiracetam, followed by clobazam in monotherapy. Majority of the patients were prescribed with monotherapy followed by dual therapy. Levetiracetam + Clobazam, Levetiracetam + Sodium valproate and Levetiracetam + Phenytoin was the most preferred combination. Drug use pattern of Antiepileptic Drugs was described based on WHO prescription indicators, which shows out of 55 sample size, average number of drugs per encounter was 0.5, 44% of injections were encountered, antibiotics prescribed were 0%, drug prescribed based on generic name were 54% and 93% of drug was encountered based on essential drug list. Antiepileptic prescribing in this study population was only 56% in accordance to the ILAE treatment guidelines for epilepsy.

Keywords: Antiepileptic drugs, Prescription pattern monitoring studies, Essential Drug List, International league against epilepsy.

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INTRODUCTION

Epilepsy, according to the World Health Organization, is a chronic non communicable brain disease that affects approximately 50 million people worldwide [1]. The prevalence of active epilepsy ranges from 4 to 5 per 1000 population and in India, the prevalence rate of epilepsy ranges between 4.15 and 7.03 per 1000 population [2]. The incidence of epilepsy is highest during childhood, especially for children aged 0 - 14 years [2]. The findings in the morbidity and mortality report indicate that seizures affect 0.7% of children and adolescents aged 6–17 years, and, relative to the general population, children and adolescents with seizures are socially and economically disadvantaged, more likely to have co-occurring conditions, and more likely to face barriers to care [3]. Seizures are caused by a variety of factors, including prenatal or perinatal brain

damage (e.g., a lack of oxygen or trauma during birth, low birth weight), congenital abnormalities, a severe head injury, a stroke, a brain infection (meningitis) [4]. An accurate diagnosis of seizures and epilepsy is required for efficient therapy. It depends on taking careful medical history and using brain imaging and other tests to assess abnormal patterns of electrical activity in the brain [5].

Seizures can be controlled. Upto 70% of people living with epilepsy could become seizure free with appropriate use of antiseizure medicines. A documented etiology of the seizure and an abnormal electroencephalography (EEG) pattern are the two most consistent predictors of seizure recurrence [1]. Monotherapy is normally the first line treatment as it has less drug interaction, side effects, lower cost, better

tolerability, and medication adherence [6].

The outcome of AED therapy in children depends on many factors, including selection, dosing and monitoring of AEDs, the identification of underlying cause, the type of seizures and the pharmacokinetic parameters of AEDs [7].

Prescription Patterns describe the extent and profile of drug use, trends, drug quality, and compliance with regional, state, or national guidelines such as standard treatment guidelines, drug use from the essential medicine list, and generic drug use [8]. More than half of all patients do not take their medications as directed. Such inappropriate medication use results in serious adverse events and a lack of satisfactory outcomes [9]. The World Health Organization (WHO) developed and validated core drug use indicators for prescribing, patient care, and facility-specific studies to address these issues [10].

The prescribing indicators assess five key areas: percentage of drugs prescribed by generic name, average number of drugs per prescription, percentage of prescriptions containing antibiotics, percentage of prescriptions containing injectable drugs, and percentage of drugs prescribed from the most recent edition of national Essential Drug Lists (EDL) [11].

MATERIAL AND METHODS

Study Site: The study was conducted in the Inpatient Department of Pediatrics, ESIC MC PGIMSR, Rajajinagar, Bengaluru.

Study Design: This was an Prospective observational study.

Study Duration: 6 months.

Sample Size: A total of 60 subjects enrolled for the study out of which 55 subjects were selected for the study.

Inclusion Criteria

- Pediatric patients willing to participate were approached by the investigator.
- Pediatric patients diagnosed with any type of seizure disorder attending the In -Patient of the Pediatric Department.
- Patient's less than 18 years of age were included in the study.
- Patient's of any gender were included in the study.

Exclusion Criteria

- Patients with other genetic or medical disorder.

Ethical Approval

The study was approved by Institutional Ethics Committee of the tertiary care teaching hospital, Bengaluru in accordance with the guidelines issued by ICMR. (No.532/L/11/12/Ethics/ESICMC&PGIMSR/Estt.Vol.-IV)

Source of Data

Patient profile and treatment details collected from inpatient case sheets while going forward rounds in the inpatient department of pediatrics.

Study Tools

- Self-designed and validated data collection form:** A data collection from designed to collect sample demographics, medication administered, and the disease diagnosed.

Study Procedure

Subjects for the study were identified by the investigators during hospital visits based on the inclusion and exclusion criteria. The patients were explained the purpose of the study and the informed consent was obtained. Relevant data (demographic details, prescription details) was recorded, and the subjects were given the study tools to obtain relevant information. The data thus obtained was entered in a Microsoft Excel sheet and appropriate analysis was performed.

Statistical Analysis

All the recorded data were entered using MS Excel software and analyzed using SPSS 22 version software for determining for the statistically significant. Descriptive statistics such as percentages were calculated for categorical variables. Histogram and pie charts were applied to find the nature of data distribution.

RESULTS

The study was conducted in the In -Patient Department of Paediatrics, Bangalore. The study was carried out for a period of 3 months from July 2022 to September 2022, and a total of 60 of samples were collected and out of these 5 samples were dropped out due to insufficient data and the overall sample size was 55.

Distribution of Subjects According to Gender

Subjects were categorized based on gender as shown in Figure 1. Among the study population male patients (67%) were found to be higher than that of females (33%).



Figure 1: Distribution of subjects based on Gender

Distribution of Subjects According to Age

Subjects were categorized based on different age groups as shown in Figure 2. The age distribution of study shows that the maximum number of patients were in between 3-6 years and 6-12 years that is 29 % of

patients belonged to pre-school and school age child, followed by toddlers that is 20 %, then by Adolescent that is 18 %. The minimum number of patients belonged to the age group (1 month – 1year) that is infant which is 4 %.

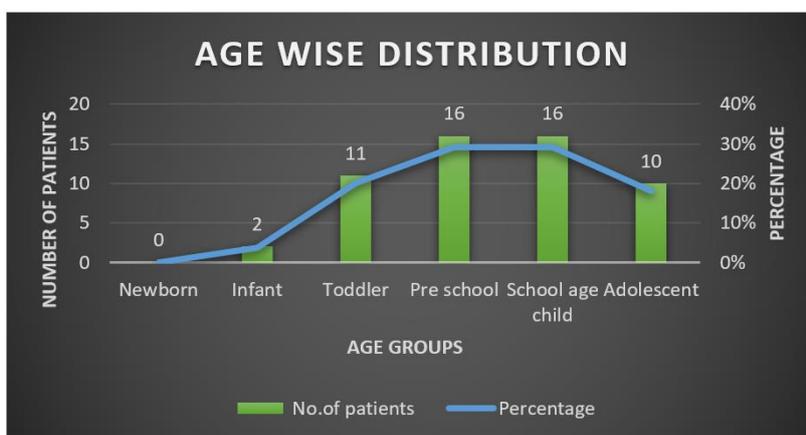


Figure 2: Distribution of subjects based on Age

Distribution of Subjects According to Etiology

Out of 55 subjects, Figure 3 reveals the seizure aetiology in the present study was found to be the most with family history 19(35%), followed by fever

15(27%), traumatic brain injury 7(13%), global developmental delay 4(7%), Idiopathic seizures 4(7%), and least was found to have Hypoxic ischemic brain injury 3(5%), Infection 3(5%).

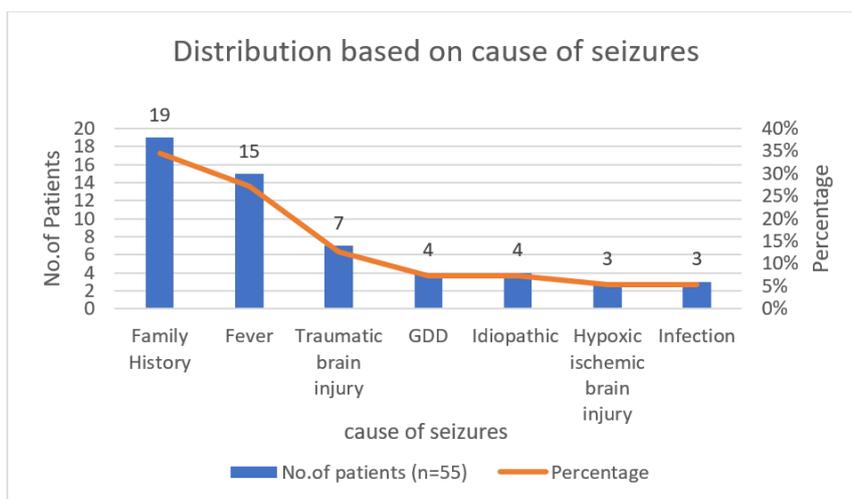


Figure 3: Distribution of subjects based on Etiology

Distribution of Subjects based on the Diagnostic Tests

Subjects were classified based on the diagnostic tests performed as shown in Figure 4, out of 55 subjects,

16(29%) of them had not done any of the diagnostic tests, majority of them has undergone MRI that is 19(35%), followed by EEG 18(33%) and CT 2(4%).

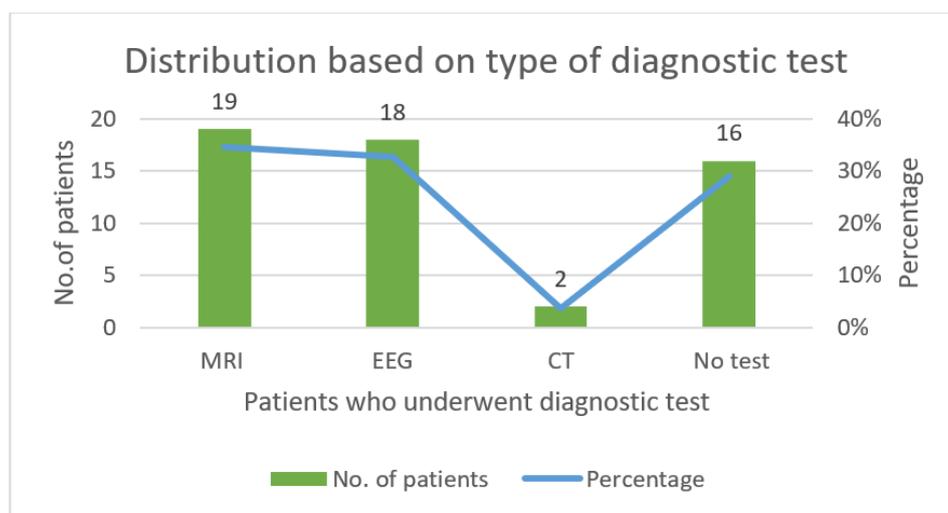


Figure 4: Distribution of subjects based on the type of diagnostic test

Distribution of Subjects based on the Scanning Reports

Out of 39 patients who underwent the diagnostic tests as shown in Table 1, it was found that

majority of the scanning reports were abnormal that is 22(56%) followed by normal reports which was 17(44%).

Table 1: Distribution based on the scanning report

Scanning Report	Number of Patients	Percentage
Abnormal	22	56%
Normal	17	44%
Total	39	100%

Distribution of Subjects based on the Type of Seizure

Subjects were classified based on the type of seizure as shown in Table 2 and it was found that most of the subjects were diagnosed with Breakthrough seizure 19(35%), simple febrile seizure 12(22%),

followed by GTCS 6(11%), unprovoked seizure 6(11%), and the least number of subjects were diagnosed with complex partial seizure 4(7%), febrile status epilepticus 3(5%), myoclonic seizure 2(4%), simple partial seizure 2(4%), complex febrile seizure 1(2%).

Table 2: Distribution based on the type of seizure

TYPES OF SEIZURES	Number of patients	Percentage
Breakthrough seizures	19	35%
Simple febrile seizure	12	22%
Generalized tonic clonic seizures	6	11%
Unprovoked seizure	6	11%
Complex partial seizure	4	7%
Febrile status epilepticus	3	5%
Myoclonic seizure	2	4%
Simple partial seizure	2	4%
Complex febrile seizure	1	2%
Total	55	100%

Distribution of Subjects based on the Type of Episode

Subjects were classified based on the type of the episode as shown in Table 3 and it was found that

majority of them had relapsed episode which was 42(76%) and those with 1st episode was least with 13(24%).

Table 3: Distribution of subjects based on the type of episode

Type of Episode	Number of patients	Percentage
Relapsed Episode	42	76%
1 st Episode	13	24%
Total	55	100%

Distribution based on the most Commonly Prescribed Antiepileptic Drugs

Out of 55 subjects, most commonly prescribed antiepileptic drugs as shown in Table 4 are as follows levetiracetam 24(44%), followed by clobazam 14(25%),

sodium valproate 5(9%), phenytoin 5(9%), carbamazepine 3(5%), and the least commonly prescribed AEDs were oxcarbamazepine 1(2%), clonazepam 2(4%), brivaracetam 1(2%).

Table 4: Distribution based on the commonly prescribed anti-epileptic drug.

Anti epileptic drugs	Number of patients	Percentage (%)
Levetiracetam	24	44%
Clobazam	14	25%
Sodium valproate	5	9%
Phenytoin	5	9%
Carbamazepine	3	5%
Clonazepam	2	4%
Oxcarbamazepine	1	2%
Brivaracetam	1	2%
Total	55	100 %

Distribution based on the Class of Antiepileptic Drugs Prescribed

Subjects were distributed based on the class of antiepileptic drug prescribed as shown in Table 5 among

which out of 55, majority were prescribed with the 1st generation antiepileptic drugs which was 29(53%), followed by the 2nd generation antiepileptic drugs which was 26(47%).

Table 5: Distribution based on the class of Anti- epileptic drug prescribed.

Class of AED prescribed	Number of patients	Percentage
1 st generation AEDs	29	53%
2 nd generation AEDs	26	47%
Total	55	100%

Distribution Based on the Type of the Therapy

Subjects were distributed based on the type of the therapy they received as shown in Table 6, among

which majority of the subjects received monotherapy 35(64%), followed by dual therapy 15(27%), triple therapy 4(7%), polytherapy 1(2%).

Table 6: Distribution based on the therapy received by the subjects.

TYPE OF THERAPY	Number of Patients	PERCENTAGE
Monotherapy	35	64%
Dual therapy	15	27%
Triple therapy	4	7%
Polytherapy	1	2%
Total	55	100%

Distribution based on the Commonly Prescribed Drug in Each Therapy

Subjects were classified based on the therapy and the commonly prescribed AEDs as shown in the Table 7, it was found that in the monotherapy the commonly prescribed antiepileptic drug was levetiracetam 21(38%), clobazam 11(20%), sodium valproate 2(4%), oxcarbamazepine 1(2%). In the dual therapy the most prescribed combination of antiepileptic drugs were levetiracetam + clobazam 3(5%), levetiracetam + sodium valproate 3(5%), followed by

clobazam + sodium valproate 2(4%), levetiracetam + phenytoin 3(5%), and least prescribed combination were, sodium valproate + phenytoin 1(2%), clobazam + clonazepam 1(2%), brivaracetam + carbamazepine 1(2%), levetiracetam + clonazepam 1(2%). Mostly prescribed combination in the triple therapy was levetiracetam + sodium valproate + carbamazepine 2(4%), and the least prescribed combination was levetiracetam + clobazam + sodium valproate 1(2%), levetiracetam + clobazam + phenytoin 1(2%) and finally

in polytherapy the combination was levetiracetam + clobazam + sodium valproate + oxcarbamazepine 1(2%).

Table 7: Distribution based on the commonly prescribed AEDs in each therapy.

Therapy (Drugs)	No. of Patients (%)
Monotherapy	
1.Levetiracetam	21(38%)
2.Clobazam	11(20%)
3.Sodium Valproate	2(4%)
4.Oxcarbamazepine	1(2%)
Dual therapy	
1.Levetiracetam + Clobazam	3(5%)
2.Levetiracetam + Sodium Valproate	3(5%)
3.Levetiracetam + Phenytoin	3(5%)
4.Clobazam + Sodium Valproate	2(4%)
5.Sodium Valproate + PHEN	1(2%)
6.Clobazam + Clonazepam	1(2%)
7.Brevaracetam + Carbamazepine	1(2%)
8.Levetiracetam + Clonazepam	1(2%)
Triple therapy	
1.Levetiracetam + Sodium Valproate + Carbamazepine	2(4%)
2.Levetiracetam+ Clobazam + Sodium Valproate	1(2%)
3.Levetiracetam+ Clobazam + Phenytoin	1(2%)
Polytherapy	
1.Levetiracetam + Clobazam + Sodium Valproate + Oxcarbamazepine	1(2%)
TOTAL	55(100%)

Distribution based on the Commonly Prescribed Dosage form

Out of 55 prescriptions which had 166 drug products as shown in Table 8, the most commonly

prescribed dosage form was injections which was found to be 73(44%), followed by the tablets which was found to be 47(28%), and the least prescribed dosage form was syrup which is 46(28%).

Table 8: Distribution based on the commonly prescribed dosage form.

Dosage form	Number of drug products in overall prescription	Percentage
Injections	73	44%
Tablets	47	28%
Syrups	46	28%
Total	166	100%

Drug use Pattern based on WHO Prescription Indicators

Table 9, describes briefly about the drug use pattern of AEDs, based on WHO prescription indicators which shows out of 55 sample size, average number of

drugs per encounter was 0.5,44% of injections were encountered, antibiotics prescribed were 0%, drug prescribed based on generic name were 54% and 93% of drug was encountered based on essential drug list.

Table 9: Drug use pattern of AEDs based on WHO prescription indicators

Prescribing Indicators	WHO reference value	Average / Percent
Average number of drugs per encounter	< 2	0.5
Percentage of encounters with an injection prescribed	< 20%	50%
Percentage of encounters with an antibiotics prescribed	< 30%	0%
Percentage of drugs prescribed based by generic name	100%	54%
Percentage of drugs prescribed by essential drug list	100%	93%

Drug use Pattern as Per ILAE

Table 10, describes briefly about the drug use pattern as per ILAE recommendation. It shows that out

of 55 prescriptions, 23 (44%) indicates incorrect prescription of AEDs and not as per ILAE recommendation.

Table 10: Drug use pattern as per ILAE

DRUG	REASONS FOR USE	No. of patients prescribed	Percentage
1. Levetiracetam	Breakthrough seizure	11	20%
	Complex febrile seizure *	1	2%
	GTCS	5	9%
	Myoclonic seizure	1	2%
	Simple partial seizure	1	2%
	Complex partial seizure	1	2%
	Unprovoked seizure *	2	4%
	Febrile status epilepticus*	2	4%
2. Clobazam	Breakthrough seizure	2	4%
	Simple febrile seizure *	11	20%
	Myoclonic seizure	1	2%
	Unprovoked seizure *	1	2%
3.Sodium valproate	Breakthrough seizure	2	4%
	Myoclonic seizure *	1	2%
	Unprovoked seizure	1	2%
	Febrile status epilepticus *	1	2%
4.Phenytoin	Breakthrough seizure	2	4%
	Unprovoked seizure *	1	2%
	Febrile status epilepticus *	2	4%
5.Carbamazepine	Breakthrough seizure	2	4%
	GTCS	1	2%
6.Clonazepam	Simple febrile seizure	1	2%
7.Oxcarbamazepine	Breakthrough seizure *	1	2%
8. Brivaracetam	Complex partial seizure	1	2%
	TOTAL	55	100%

* Indicates incorrect use of AED and not in accordance with the ILAE guidelines.

DISCUSSION

In our study, the demographic data indicated that majority of them were male subjects (67%) than females subjects (33%) which was similar to the study conducted by Sebastian *et al.*, [12]. The dominant age group in our study was pre- school (3-6yrs) and school age child (6-12yrs) which was found to be 29% each. This result was slightly contrast to the study conducted by Sonia *et al.*, in which the dominant age group was (5-9yrs) [13]. The major cause of seizures were a positive family history (35%) followed by febrile condition (27%) and other causes. This result was slightly contrast to the study conducted by Antham *et al.*, in which the major cause was febrile condition followed by idiopathic seizure [14]. Majority of the subjects underwent an MRI scan (35%) followed by EEG (33%). Among this maximum number of subjects presented with abnormal reports (56%) and then followed by normal reports (44%). This result was similar to the study conducted by Antham *et al.*, [14]. Majority of the subjects in this study were diagnosed with Breakthrough seizures (35%), followed by Simple febrile seizures (22%) and other seizures. This result was slightly contrast to the study conducted by Sonia *et al.*, in which most of the subjects were diagnosed with simple febrile seizure followed by complex partial seizure [13]. Most of the subjects in the

study had relapsed episode (76%) and some of them had their 1st episode (24%). This result was similar to the study conducted by Antham *et al.*, [14].

Majority of subjects were prescribed with levetiracetam (44%), followed by clobazam (25%), sodium valproate and phenytoin constitute about (9%) each, carbamazepine (5%), clonazepam (4%), oxcarbamazepine and brivaracetam constitute (2%) each. This finding was similar to the study conducted by Lekshmi *et al.*, [15]. Among the 55 subjects, 29 subjects were prescribed with 1st generation antiepileptic drugs – (carbamazepine, clobazam, clonazepam, phenytoin, sodium valproate), 26 subjects were prescribed with 2nd generation antiepileptic drugs – (levetiracetam, oxcarbamazepine, brivaracetam) and none of them were prescribed with 3rd generation antiepileptic drugs. This result was similar to the study conducted by Joshi *et al.*, [16]. The prescription pattern of antiepileptic drugs was categorized into 4 types: monotherapy, dual therapy, triple therapy and polytherapy. It is important to maintain patients on mono-therapy as compliance is better, side effects are less and there is no problem of drug-to-drug interactions and to yield better compliance.

- In monotherapy, (64%) subjects were mostly prescribed with single antiepileptic drug, hence

the most commonly prescribed antiepileptic drug in monotherapy is levetiracetam (38%), followed by clobazam (20%), sodium valproate (4%) and oxcarbamazepine (2%).

- In dual therapy, (27%) subjects were prescribed with 2 antiepileptic drugs, (levetiracetam + clobazam, levetiracetam + sodium valproate and levetiracetam + phenytoin) was prescribed to subjects which constitute about 5% each, followed by (clobazam + sodium valproate) was prescribed to subjects which constitute about 4%, and (sodium valproate + phenytoin, clobazam + clonazepam, brivaracetam + carbamazepine, levetiracetam + clonazepam) which constitute about 2 % each.

Under monotherapy and dual therapy, the results of the current study was contrast to the study conducted by Julie Thampi *et al.*, [2]. The mostly preferred monotherapy was with sodium valproate, clobazam, phenytoin and carbamazepine. The mostly preferred dual therapy was phenytoin + clobazam, levetiracetam + sodium valproate, and sodium valproate + phenytoin.

- In triple therapy, (7%) subjects were mostly prescribed with 3 antiepileptic drugs, out of which (levetiracetam + sodium valproate + carbamazepine) was prescribed to about 4%, followed by (levetiracetam + clobazam + sodium valproate and levetiracetam + clobazam + phenytoin) which is about 2 % each.
- In polytherapy, (2%) subject was mostly prescribed with 4 antiepileptic drugs, mostly prescribed polytherapy combination was (levetiracetam + clobazam + sodium valproate + oxcarbamazepine) which is about 2 %.

Under triple therapy and polytherapy, the results of the current study was similar to the study conducted by Sonia *et al.*, [13].

In this study, out of 166 drug products in the prescription, it was found that the most commonly prescribed dosage form is injections (44%), followed by the tablets and syrups which constitute about 28 % each. The result of the study was similar to the study conducted by Lekshmi *et al.*, [15]. The drug use pattern of AEDs was described based on WHO prescription indicators, which shows out of 55 sample size, average number of drugs per encounter was 0.5,44% of injections were encountered, antibiotics prescribed were 0%, drug prescribed based on generic name were 54% and 93% of drug was encountered based on essential drug list. The current study finding was similar to the study conducted by Sonia *et al.*, [13]. Out of 55 prescriptions, 44% indicates incorrect prescription of AEDs and not as per ILAE (International League Against Epilepsy) recommendation.

Limitations

Our study had certain limitations. The sample size for this study was less and it was conducted only for a short duration of time. Some subject-specific data were missing from the patient records.

Future Directions

- Study should be conducted in large population.
- Study should be conducted for longer duration of time.
- Drug Utilization Evaluation of Antiepileptic drugs can be conducted.
- Measure to improve medication Adherence.

CONCLUSION

In conclusion, Epilepsy is a condition which needs prolonged treatment with antiepileptics and hence the appropriateness of therapy has a great impact on the quality of life of patients. Prescription pattern monitoring studies is a tool for assessing the prescribing, dispensing and distribution of medicines. The current study has shown the different types of epilepsy prevalent in pediatric patients, drugs used among them along with useful baseline data. This study concluded that male children were more prone to seizure than female children. Based on age wise distribution, children between 3-6 years and 6-12 years of age were admitted more with the complaints of seizure. Breakthrough seizures was the most commonly observed type of seizure followed by simple febrile seizure. The most commonly prescribed antiepileptic drug was levetiracetam, followed by clobazam. Majority of the patients were prescribed with monotherapy followed by dual therapy. The most commonly prescribed dosage form was injections, followed by the tablets and the least prescribed dosage form was syrup. In this study drug use pattern of AEDs was described based on WHO prescription indicators, which shows out of 55 sample size, average number of drugs per encounter was 0.5,44% of injections were encountered, antibiotics prescribed were 0%, drug prescribed based on generic name were 54% and 93% of drug was encountered based on essential drug list. Antiepileptic prescribing in this study population is only 56% in accordance to the ILAE treatment guidelines for epilepsy.

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