Treatment Outcome of Epilepsy and Associated Factors among Pediatric Patients at Selected Hospitals in Addis Ababa, Ethiopia

By

Bamlak Markos (B.Pharm)

A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment of the Requirements for Masters of Science in Pharmacy Practice (M.Pharm)

June 2023

Addis Ababa, Ethiopia

Addis Ababa University

College of Health Sciences

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June 2023

Addis Ababa, Ethiopia

Addis Ababa University School of Graduate Studies

This is to certify that the thesis prepared by Bamlak Markos, entitled: **"Treatment Outcome of Epilepsy and Associated Factors among Pediatric Patients at Selected Hospitals in Addis Ababa, Ethiopia"** and submitted in partial fulfillment of the requirements for the Degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the University and meets the accepted standards concerning originality and quality.

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Abstract

Background: Anti-seizure medications (ASMs) are the mainstay for achieving remission in patients with epilepsy. A successful therapy using anti-seizure medications can eliminate or reduce symptoms, and leads to freedom of seizures.

Objective: To assess treatment outcome of epilepsy and associated factors among pediatric patients at selected hospitals.

Methods: A hospital-based cross-sectional study was conducted among 300 pediatric patients with epilepsy at selected hospitals. Data were collected by interviewing and reviewing the medical records of the patients using semi-structured questionnaires. Data were entered into Epi data version 4.6.6 then analyzed using SPSS version 25. Descriptive statistics were used to present the results. Logistic regression was used to determine the relationship between independent and dependent variables and p-value <0.05 was considered statistically significant.

Result: Males account 64.3% of the 300 patients. The mean age of patients was 8.2 ±4.2 years. The most common type of seizure (66%) was a generalized seizure followed by a mixed seizure (13.3%). Monotherapy was commonly 64.3% used in the management of seizures, with phenytoin being used in the majority (47.7%) of patients. The current study revealed that 62.3% of patients had an uncontrolled seizure. No statistically significant relationship was found between seizure control and serum level of antiseizure medications, X^2 (df=1 N=58) P= 0.920. Female gender (AOR= 0.515, 95% CI: 0.285-0.931, P=0.028), primary education of caregivers (AOR=0.436, 95% CI: 0.192-0.99, P=0.047), and family history of epilepsy (AOR=0.363, 95% CI: 0.153-0.857, P=0.021) decreased odds of uncontrolled seizures. Seizure-triggers (AOR=3.63, 95% CI: 1.99-6.614, P<0.001), and polytherapy with anti-seizure medications (AOR=6.79, 95% CI: 3.221-14.311, P<0.001) increased odds of uncontrolled seizures.

Conclusion: The finding of this study indicates that seizure control status among pediatrics was poor. Thus, Parents of children, health care providers and other concerned bodies should focus on factors that are associated with uncontrolled seizures, particularly polytheray with antiseizure medications, and seizure triggers.

Key words: Anti-seizure Medications; Epilepsy; Treatment outcome; Pediatrics

Acknowledgment

First of all, I am thankful to almighty God, for his blessings throughout this thesis work.

I would also like to acknowledge Hawassa and Addis Ababa universities for offering me the opportunity to pursue my postgraduate study.

I am very pleased to acknowledge my advisors Mr. Minyahil Alebachew and Dr. Ayalew Moges for their guidance and input in this work.

Furthermore, I would also like to acknowledge all participants of the study who kindly volunteered to answer the interview questions, data collectors, and hospitals.

Lastly, I would like to give credit to my lovely family who entirely supported me during my study period.

Table of Contents

Contents

Abbreviations and Acronyms

ADEs	Adverse Drug Events
AEDs	Antiepileptic Drugs
AEM	Antiepileptic Medication
AOR	Adjusted Odds Ratio
ASDs	Anti-seizure Drugs
ASMs	Anti-seizure Medications
BRE	Benign Rolandic Epilepsy
CAE	Childhood Absence Epilepsy
CBZ	Carbamazepine
CI	Confidence Interval
CLN	Clonazepam
CWE	Childrens with Epilepsy
EEG	Electroencephalogram
GTCS	Generalized Tonic-Clonic Seizure
ILAE	International League Against Epilepsy
JME	Juveline Myoclonic Epilepsy
LEV	Levetiracetam
LGS	Lennox Gastaut Syndrome
LTG	Lamotrigine
MRI	Magnetic Resonance Imaging
OR	Odds Ratio
PHB	Phenobarbitone

PHT	Phenytoin
SAP	Seizure Action Plan
SUDEP	Sudden Unexpected Death in Epilepsy
SPHMMC	Saint Paul's Hospital Millennium Medical College
TASH	Tikur Anbessa Specialized Hospital
TDM	Therapeutic Drug Monitoring
Y12 HMC	Yekatit 12 Hospital Medical College
VPA	Valproic Acid
WHO	World Health Organization

List of figures

Lists of tables

1. Introduction

1.1 . Background

Epilepsy is a neurological disorder caused by an abnormal connection of neurons in the brain that affects peoples of all ages in the world (1-3). A seizure is a transient occurrence of signs and/or symptoms resulting from abnormal, excessive or synchronous neuronal activity in the brain (4). It affects over 50 million people worldwide of whom 10 million are children and with high prevalence in the developing world due to pediatrics exposure to infectious diseases such as meningitis, onchocerciasis, malaria, neurocysticercosis, encephalitis, HIV infections and birth-related conditions (1, 5-8). Approximately, 4% - 10% of children experience one seizure within the first 16 years of their life from them 1% develop epilepsy (4, 9). In Ethiopia a community based-study found that the prevalence of epilepsy was 5.2/1000 people and incidence was 64/10,000 population (10).

Furthermore, low and middle-income countries are highly affected, with high severity of disease and greater years of life lost as a result of epilepsy this may be due to low socio-economic background, poor understanding of the disease condition, social stigma, and depression surrounding the illness which limits access to anti-seizure medications (1, 8, 11). It has been identified as a health priority for school-age children because of its high psychosocial morbidity, mortality, poor quality of life, and potential for control using low-cost interventions (12).

The International League Against Epilepsy (ILAE) described epilepsy in 2017 as a brain disease characterized by any of the following conditions: 1) At least two unprovoked (or reflex) seizures occurring > 24 hr apart; 2) One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring every the next 10 years; 3) Diagnosis of epilepsy syndrome (13).

The diagnosis of epilepsy may be difficult in the early stages, especially in the absence of a witnessed account. The diagnosis of epilepsy is usually clinical based on the history of epileptic seizures that is reported by the patient and caregivers and examinations like electroencephalography demonstrate the type of seizures (14). It is necessary to identify the seizure type, as this affects treatment choices, investigation, prognosis and counseling.

According to the ILAE operational classification of seizure types divides epileptic seizures into four categories based on the presumed mode of seizure onset: 1. Focal: If the first clinical and electroencephalographic (EEG) changes suggest initial activation of a system of neurons limited to part of one cerebral hemisphere, 2. Generalized: If the first clinical and EEG changes indicate synchronous involvement of all of both hemispheres, 3. Unknown onset: If there is not enough clinical information available to determine if the seizure is focal or generalized, 4. Unclassified: If the clinical characteristics of a seizure are unusual and a determination of onset cannot be made despite an adequate workup (13), 5. Mixed seizures is also considered in the category of seizures currently in different literature, particularly in pediatric populations, they are a type of seizures in which two/more types of seizures co-exist (15, 16) .

There are different types of modalities used to treat children with epilepsy such as medications, surgery, vagus nerve stimulations, and diet therapy. Anti-seizure medications are the mainstay for achieving remission in patients with epilepsy, however the response to anti-seizure drugs requires the patients' adherence to medications and pharmacotherapy knowledge of the medications (17). Additionally, the goal of treatment is to restore a near-normal life with complete seizure control using a single anti-seizure medication, by minimizing the side effects of the ASDs and maintaining psychosocial stability. As compared to multiple ASDs, monotherapy is recommended because of fewer adverse drug effects, the absence of drug-drug interactions, better compliance, and lower cost, Only one drug should be used initially, and the dose increased until complete control is achieved or until side effects prohibit further increases. Then, and only then, may another drug be added and the initial drug subsequently tapered, combination therapy should only be considered when attempts at monotherapy with the tolerated dose of AED have not resulted in seizure freedom (4, 18, 19). Due to abrupt discontinuation can result in withdrawal seizures or status epilepticus, ASMs therapy should be discontinued gradually; often over a period of 3-6 months So, successful therapy using anti-seizure medications helps to eliminate or leads to freedom of seizures, adherence to AEDs is subsequently a key to treatment success (4, 20).

However, in resource-limited countries, a large proportion of patients with epilepsy, despite being diagnosed and initiated on ASD treatment, soon discontinue the treatment (21, 22). It has been proven that the course of epilepsy and the outcome regarding seizure occurrence, both at short-term observation and after many years of follow-up vary considerably, even among

patients with the same epileptic syndrome and seizures and determinants of the individual prognosis among idiopathic childhood epilepsies remain largely unknown (23).

Sudden unexpected death in epilepsy (SUDEP) is the most common epilepsy-related cause of mortality and accounts for up to 17% of all epilepsy deaths which is most commonly associated with uncontrolled seizure (24) other risk factors have been identified including poly-therapy with more than three ASDs, male gender, young age at epilepsy onset, developmental delay, poor ASD compliance, nocturnal seizures, poorly controlled seizures (especially if > 3/year), high frequency of seizures (especially if > 50/year), and having epilepsy for > 30 year in adults (4). Therefore, the present study is aimed to assess treatment outcome of epilepsy and associated factors among the pediatric patients at selected hospitals in Ethiopia.

1.2. Statement of the problem

An estimated 10.5 million children are affected by epilepsy worldwide, of which 80% live in developing countries, often accompanied by physical and cognitive disabilities and around 6-14% of children are developing intractable epilepsy (25-27). Epilepsy in Ethiopia is also strongly associated with low levels of education and markers of poverty (28, 29).

According to studies, uncontrolled epilepsy/seizures have a great contribution to direct and indirect costs, and every year, 100,000 to 120,000 children are hospitalized due to epilepsy (30). According to the review, the mean annual cost per child was $1853 for controlled epilepsy and $4950 for uncontrolled epilepsy (31).

In Ethiopia, an estimated 1% of people live with epilepsy of which 85% are children and only less than 5% of them get adequate treatment to control the seizure due to associated stigma regarding the disease and other social and economic factors (32).

Studies have shown that insufficient access to health care services and treatment, a lack of current testing methods, social stigma, and a lack of awareness of the conditions and medications may compromise diagnosis and the provision of cost-effective care which can lead to unfavorable outcomes of epilepsy (33-35). As a result, it can degrade the quality of life and cause severe body injury, neuropsychological impairment, social stigma, future marriage rates, and inadequate schooling. It is also strongly associated with morbidity and mortality.

Anti-seizure medication therapy aims to provide patients with seizure-free lives for the rest of their lives. However, the success of treatment is determined by several criteria, including AED selection, close monitoring, identifying the underlying cause, type of seizures, and pharmacokinetic properties of the medications (36).

Recurrent and breakthrough seizures can be caused by a variety of triggering factors which are expected to happen in 20% of pediatric patients after ASMs withdrawal (37). Also, modern medicines being used in most developed countries to treat such conditions are either unavailable or inconsistently available in developing countries (38). Using old generations medications like carbamazepine, phenytoin, phenobarbital, and valproate as well as the prolonged use of some ASMs are frequently linked to long-term side effects that can negatively impact the outcome of treatment and patients' quality of life (39).

Patients with poorly controlled seizures should be given more attention and assistance because they are more likely to be anxious, expect their epilepsy to last longer, have false beliefs about their condition and treatment, and have higher hospital admission rates, particularly in developing countries (34, 40). Under-reporting of a seizure by parents is 49% and seizure frequency recording is mandatory which helps to improve seizure control and desirable patient outcomes through dose adjustment and appropriate selection of medications (20, 41).

Even though around 70% of people who have epilepsy are supposed to be seizure-free with optimum anti-seizure medications (ASMs) treatment around 30% remain with seizures despite receiving ASMs (42, 43) additionally sudden unexpected death in epilepsy has an incidence of between 0.22 and 1.1 per 1000 person-years in children and adolescents which is commonly associated with uncontrolled seizures (44). There is a paucity of research done on the pediatric population in the country and little is known about seizure control status in a specific area.

1.3. Significance of the study

It is known that epilepsy in children is a common occurrence resulting in a neurodevelopmental delay in children and a socio-economic burden for families. Seizure control is the main outcome measure in pediatric epilepsy treatment. Monitoring of serum drug concentration is a useful guide for effectiveness, dose adjustment, and adverse reactions and to assess compliance with the therapy, particularly in the case of phenytoin which follows non-linear kinetics and it has also been implicated by studies (45).

Early identification of patients who are likely to have poor seizure control helps predict long-term seizures, counseling patients and their families. This also helps in selecting patients for detailed investigations, intensive treatments, and timely consideration of treatment modifications (46). In addition, assessing the predicting indicators of refractory epilepsy and leads to breakthrough seizure and preventing potential disability is of great interest in light of the disability and mortality brought by the condition.

Globally, the majority of studies are focused on the adult population and studies are scarce in childrens. Thus, this research could address this gap and assess treatment outcomes and factors that lead to unsuccessful outcomes among pediatrics at follow-up clinic of Tikur Anbessa Specialized Hospital, Saint Paul's Hospital Millennium Medical College, and Yekatit 12 Hospital Medical College for epilepsy treatment.

Moreover, newly generated data on epilepsy treatment outcomes in pediatric could also help in influencing stakeholders during the development of guidelines and to strengthen the multi-disciplinary approach between families, medical professionals, pharmacists, and other healthcare providers to improve the quality of care and treatment outcomes.

2. Literature review

2.1. Magnitude and risk factors of epilepsy in pediatrics

Epilepsy incidence and prevalence vary from country to country. An incidence rate of 144/100,000 person-years in the first year of life and 58/100,000 person-years in the subsequent years up to the age of 10 (47), and Kenya (187/100,000) in children aged 6-12 years (48). The lifetime prevalence of childhood and adolescent epilepsy (children < 18 years) in Bangladesh (9/1000) (49), Upper Egypt was 9.7/1000, with a higher prevalence among children < 12 years (10.8/1000) than adolescents (7.2/1000) (50), (41/1000) (48), and slightly higher in males than females (33), active epilepsy was (11/1000)(95% CI: 5-15) (48). A review done in Ethiopia shows the highest age-specific prevalence of epilepsy was seen in the age group between 10-19 years (51).

According to a review conducted in Nigeria by Izoura, the prevalence of childhood epilepsy is 60% among children attending the pediatric neurology department (52), and University of Calabar Teaching Hospital of southern Nigeria 59.4% (1). Mortality due to epilepsy tends to be increased in Africa it is particularly related to poorly controlled seizures (17, 18, 53). A prospective longitudinal study conducted in the United States of America revealed that interventions should be tailored to the family's sociocultural context to shift attitudes toward epilepsy (54).

Previous studies implicated many causes and risk factors for epilepsy in pediatrics. A case-control study shows a significant association between developmental delay, newborn distress, significant head trauma, and family history and childhood epilepsy are risk factors for childhood epilepsy while 50% of cases of epilepsy have unknown causes (8, 55). According to a study conducted in Ethiopia, 22% had a family history of seizures, and seizures occurred in 4.8% of siblings mental retardation was the most commonly associated disorder, found in 7.9 - 21% of the people with seizures (51).

2.2. Type of epilepsy and treatment pattern of epilepsy

There are different types of epilepsy syndromes in pediatrics the most commons are benign rolandic epilepsy (BRE), childhood absence epilepsy (CAE), juvenile myoclonic epilepsy (JME), infantile spasms (West syndrome), and Lennox-Gastaut syndrome (LGS) (56). Studies show that

the most common form of epilepsy and seizures in pediatrics was generalized tonic-clonic epilepsy and seizure in Nigeria 61.1% (1), Gujarat 55% (57), in Malaysia the most common type of seizure in pediatrics was focal (47.6%) followed by generalized (38.1%) (36). A population-based cross-sectional study in rural Ethiopia also shows that generalized convulsive seizures occurred in 69% followed by partial seizures (20%) and unclassifiable (10%) (10), 61.2% of the patients were diagnosed as generalized seizure in Jimma referral hospital (58), 98.5% in Gondar referral hospital (59). Additionally, a study done in Pakistan showed generalized onset tonic-clonic seizures of 75.4% were commonly followed by mixed seizure types in 5.7% of pediatric populations (15). Also, another study reported mixed seizure to be one of the seizure type in pediatrics 4% (60).

The pattern of ASM prescription varied between studies, but the majority of them used older anticonvulsants. A study conducted in Nigeria found that over 75% of children with generalized epilepsy were treated with sodium valproate while phenobarbitone, carbamazepine, and clonazepam were used for other types of epilepsy and the preferred drug for the treatment of the partial type of epilepsy was carbamazepine (1). The retrospective cohort study conducted in Gondar University Hospital shows that the majority of pediatric epileptic patients were on phenobarbitone (71%) followed by phenytoin, valproate, and carbamazepine (33), phenytoin (48.2%) in Jimma referral hospital (58).

The burden of comorbidities in patients is high when compared to the general population with the predominance of psychiatric conditions and developmental delay which will have an impact on treatment choice and outcomes of seizure control.

2.3. Treatment outcome and associated factors

Treatment outcome depends on several factors such as disease-related factors and patient-related factors and mediation-related factors (61). A systematic review assessing the magnitude of the treatment gap of epilepsy in resource-poor countries found that an overall rate of 56% and the following region-specific Latin America (55%), Asia (64%), Africa (49%), rural populations (73%) and urban populations (47%) which shows the high rate in rural populations (22). A study in rural Kenya found that 89% of childrens with epilepsy were not diagnosed or received ASM therapy (48).

Healthcare facilities are often long distances for patients to reach, the supply of ASMs tends to be unreliable, and compliance is often poor based on a combination of limited access to AEDs, cost, and lack of understanding of the nature of the disease (62). Thus, in only 70% of children and 60% of adults, the seizure was completely controlled with ASDs. To withdraw ASD patient has to be seizure free for 3-4 years since sudden withdrawal increased seizure frequency and severity (63).

A cross-sectional study done in adult patients shows that patients diagnosed at less than 15 years of age show poor treatment outcomes (63.4% uncontrolled seizure) (64). A Sudanese cohort study found that 7.4% of patients were fully recovered, where 81.7% were well-controlled, 9.8% had partial control, and 1.0% were uncontrolled seizure patients on monotherapy (65). In astudy that followed patient seizure control status over a 6-month period around 60.4% of the study participants had poor seizure control (66). On the other hand a study done in Pakistan reported different figure on poorly controlled seizures which were (74%) (67), According to Norwegian study 30% of CWE had Drug resistant epilepsy, 59% had achieved ≥1 year of seizure freedom, and the remaining 12% had intermediate seizure outcomes (68).

Numerous factors are either positively or adversely associated with seizure control. Patients with generalized seizures and those with normal MRI brain imaging did positively affect seizure control (65), a study conducted in Gonder referral hospital showed that females had a 2.21 times greater chance of a successful treatment outcome than males (AOR = 2.21; 95% CI: 1.11, 4.41) (33).

Another study identified early seizure start, multiple seizure types, children on multiple anti-seizure medications, status epilepticus, treatment abandonment, spontaneous improvement in seizure symptoms, distance to clinics, poor access to prescribed medicines, inaccessible second-line medications, severe poverty, and seeking alternative treatments are prognostic factors for poor response to treatment in children (18, 23, 69). Furthermore, studies also identified triggers such as watching television, fever, playing video games, emotional stress, sleep deprivation, menstruation, and non-compliance to anti-seizure medications as precipitating factors that leads to breakthrough seizure after remission (70-72).

A study done in Australia shows significant side effects occurring in 15% of the drug category; 7% due to behavioral changes such as irritability, aggression or hyperactivity and 8% due to other factors such as a rash, headache, gastrointestinal disturbance or drowsiness (73). In another

cross-sectional study done in India, behavioral problems and somnolence were the most common ADRs with poly-therapy significantly increasing the likelihood of ADRs in children resulting in poor seizure control (60). A study conducted to identify risk factors in adolescents and young adults for long-term outcomes of epilepsy psychosocial and health-related long-term problems revealed by their study that an unsupportive and unstable family environment had a higher risk factor for poor psychosocial and health-related outcomes (74).

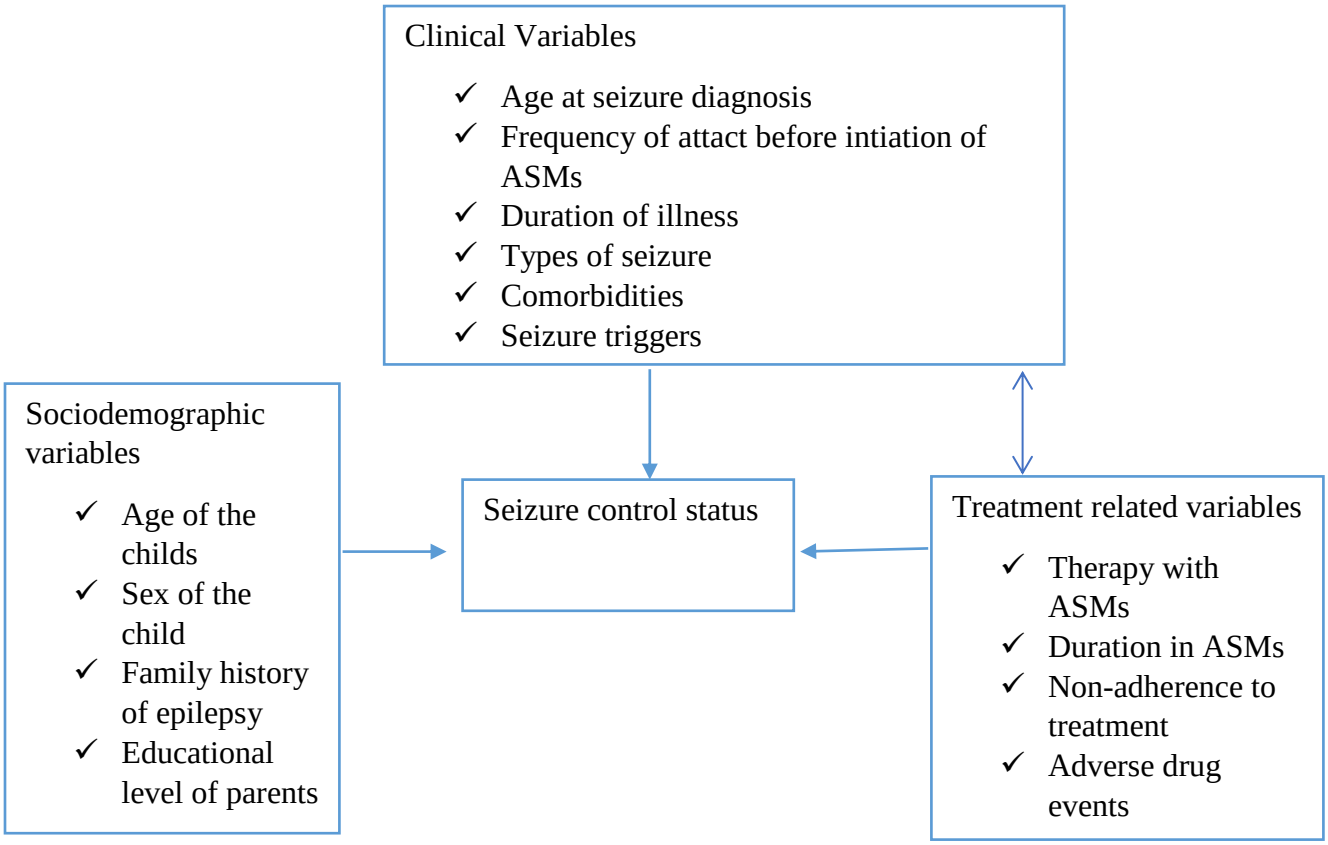


Figure 1: Conceptual framework that shows the association between independent and dependent variables (18, 33, 59, 67, 70).

3. Objectives

3.1. General objective

- ✓ To assess treatment outcome of epilepsy and associated factors among pediatric patients at Tikur Anbessa Specialized Hospital, Saint Paul's Hospital Millennium Medical College, and Yekatit 12 Hospital Medical College.

3.2. Specific objectives

- ✓ To assess seizure control status.
- ✓ To identify commonly used anti-seizure medications.
- ✓ To determine factors associated with treatment outcomes of epilepsy.

4. Methods

4.1. Study setting

The study was conducted at Tikur Anbessa Specialized Hospital (TASH), Saint Paul's Hospital Millennium Medical College (SPHMMC), and Yekatit 12 Hospital Medical College (Y12HMC).

TASH was established in 1972 and is the largest referral and tertiary specialized hospital in Ethiopia that gives service to the community in common. It has more than 700 beds and provides patient care service for over 400,000 patients/year. It is also an education center for undergraduate and postgraduate students. Among the clinics pediatric neurology clinic is the one that provides service for around 240 epileptic patients/month.

SPHMMC was established in 1969 and also the largest hospital and teaching center. It has more than 392 beds and 1300 clinical and non-clinical staff who are providing medical services for over 200,00 patients/year who are referred from all over the country in over 13 departments and teaching medicine and nursing. It has its pediatric outpatient clinic which provides service for children with epilepsy.

On the other hand, Yekatit 12 Hospital was established in 1923 as one of the modern medical service delivery centers in our country and became a medical college by the decision of the city government of Addis Ababa, then renamed Yekatit 12 Hospital Medical College. The hospital has its pediatric outpatient clinic and provides service for children with epilepsy.

4.2. Study design and period

A hospital-based cross-sectional study was conducted among pediatric patients with epilepsy at TASH, SPHMMC, and Y12HMC through medical record review and patient interviews. The study was conducted from September 2021 to February 2022.

4.3. Population

4.3.1. Source population

All pediatric patients visiting the pediatric clinics of TASH, SPHMMC, and Y12HMC were the source population for the study.

4.3.2. Study population

All pediatric epileptic patients who are available during the data collection period.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

- ✓ Pediatric patients who were diagnosed with epilepsy were included.
- ✓ Patients aged 1 to 18 years with the diagnosis of epilepsy/seizure disorders.
- ✓ Patients who have been taking at least one ASMs for a minimum of 1 year.

4.4.2. Exclusion criteria

- ✓ Medical records with incomplete data
- ✓ Patients/caregivers who are unable to respond or unwilling to participate.

4.5. Sample size and sampling techniques

The required sample size was calculated based on a single population proportion formula assuming a prevalence (p) of uncontrolled seizure, 23% from the study conducted on this topic in Ethiopia(33).

$$n = \frac{Z\alpha/2^2 \mathrm{p}(1-\mathrm{p})}{d^2}$$

$$n = \frac{(1.96)^2 0.23(0.77)}{(0.05)^2}$$

$$n = 273$$

With adjustment for contingency 10%, the total sample size was 300, the confidence level of 95% chosen with a z-value of 1.96, Margin of error (d) = 5%

Participants were selected using systematic sampling technique. The sampling fraction was calculated by dividing the total number of study population in each hospitals over 6 months period by total sample size. (TASH, K^{th} =N/n K^{th} = 1290/300 = 4), (SPHMMC, K^{th} =N/n K^{th} = 960/300 = 3) and (Y12HMC, K^{th} =N/n K^{th} = 750/300 = 2)

Table 1: Proportionate sample size

S.no	Hospitals	Total population	Proportional sample size
1	TASH	1290	300*1290/3000=129
2	SPHMMC	960	300*960/3000=96
3	Y12MHC	750	300*750/3000=75
	Total	3000	300

4.6. Study variables

4.6.1. Dependent variable

Treatment outcome (seizure control status)

4.6.2. Independent variables

- ✓ Socio-demographic variables (age, sex, residence, religion, primary caregiver, marital status of caregivers, caregivers educational level, occupation of caregivers, source of medications, parents' income level, family history of epilepsy)
- ✓ Clinical related variables (investigations, age at diagnosis of epilepsy, seizure triggers, seizure types, duration of illness, comorbidities, frequency before intiation of treatment, frequency of seizure, seizure free period)
- ✓ Medication and treatment outcomes related variables (types of ASMs, treatment duration with ASMs, treatment modalities, adverse drug effects related to ASMs, serum level of ASMs)

4.7. Data collection and management

4.7.1. Instrument and techniques

A semi-structured questionnaire was prepared and respective medical and medication information was reviewed from patient’s medical record using a data abstraction checklist.

A questionnaire was developed after reviewing different types of literatures done on the pediatrics (18, 33) and using checklists from the Epilepsy Foundation (SAP), and guidelines (ILAE 2017) then it was translated into the local language (Amharic) by professional translator who has knowledge of both languages and then translated back to English.

The questionnaire contains socio-demographic characteristics of patients and caregivers/parents of childrens, questions related to clinical characteristics, medication and treatment outcome informations about patients and information from medical records of the patients and Amaharic version questionnaire. Primary caregivers were asked questions related to seizure triggers. ADEs were identified from patient/parents' reports and medical records which were already recorded by the physician. Only single and recent blood sample data were taken for ASMs serum level reports from the medical record of the patients.

For the analysis of the chi-square test only patients with 1 ASMs level performed were considered because one patients with two ASM concentrations with different result had normal for one and abnormal for another.

4.7.2. Recruitment of data collectors and training

Data were collected by a trained health professionals (5 nurses) using interview and medical records. The training was given on all aspects of data collection (tools, interviewing techniques, how to collect data from the medical records, and ethical issues) by principal investigators. Data was collected by data collectors using pre-tested questionnaires to ensure completeness of the data.

4.7.3. Data quality assurance

A pretest was done at Amanuel Specialized Mental Hospital in 5% (15 patients) of the sample with similar characteristics before starting patient recruitment and data collection to check the completeness of the instruments. Based on the finding obtained from the pre-test, an amendment was made to the assessment tool for instance (adherence test was considered in pre-test due to non-validity of tools it was removed, comorbid disease category has been modified, and TDM data has been added). The pre-tested data were excluded from the analysis. The principal investigator closely supervised the data collection process and the collected data were checked daily during data collection to ensure accuracy and consistency.

4.7.4. Data interpretation and analysis

Data were checked for completeness and then coded, entered, and cleaned using Epi data version 4.6.6 and then analyzed using statistical science for social science (SPSS) version 25 (IBM Corp, NY, USA).

Descriptive statistics (frequency, percentage, mean, and standard deviation (SD) were used to summarize socio-demographic, disease-related characteristics, and medications related information. To present the results tables and charts were used. Those variables with continuous nature were transformed into categorical variables in the logistic regression.

The chi-square test of independence was used to see the relationship between serum drug concentrations and seizure control status and it was used because of small sample size. Univariate analysis was used to determine the existence of an association between treatment outcome and each independent variable. All variables with $p<0.25$ in the univariate analysis were included in the multivariate logistic regression, which was performed to determine associated factors with treatment outcome. Adjusted Odds Ratio (AOR) with its p-value and confidence interval (95%) were reported in logistic regression analysis and p-value <0.05 was considered statistically significant.

4.8. Ethical consideration

Ethical approval was obtained from the Ethical Review Committee of the School of Pharmacy, Addis Ababa University (Ref no: ERB/SOP/247/13/2021/) and Ethical Review Committee of each hospital; TASH (Ref no: ሕፃ/ህት/529/13), SPHMMC (Ref no: PM 23/416) and Y12HMC (Ref no: የካ-337/300/1394). Verbal consent from caregivers and assent were requested to participate in the interview and to extract data from their medical records. Patients were informed about the objective of the study and that their participation was completely voluntary. Confidentiality and privacy were maintained. Thus, individual identifiers like names were not recorded in the data collection tool instead card numbers and I-Care numbers were accessed and used by the data collectors.

4.9. Operational definition

Treatment outcomes: - it is interpreted as a seizure control status in terms of controlled or uncontrolled.

Uncontrolled seizures: - If the patient/child experiences greater than or equal to one episode of seizure in the last 1 year after the start of treatment despite taking anti-seizure medications (68, 75).

Controlled seizures: - If the patient/child experiences no seizure episode in the last 1 year after the start of treatment despite taking anti-seizure medications (68, 75, 76).

Pediatrics: - According to the WHO the age group is between births to 18 years.

5. Result

5.1. Sociodemographic and clinical characteristics of the patients

A total of 300 patients were included in the analysis, of which 64.3% were males. The mean age of patients was 8.2 ±4.2 years. Around three/fourth (72.7%) of the patients reside in Addis Ababa. More than half (61.7%) of the subjects got their medication with payment. The majority (87.3%) of pediatrics have a negative family history of epilepsy.

Around 217 (72.3%) of children had EEG tracings or reports, with 84 (28%) having normal EEG findings and 72 (24%) having generalized epileptiform discharge, 23 (7.7%) having focal epileptiform discharges and 38 (12.7%) having abnormal result without epileptiform discharge, 21(7%) had no EEG tracing with 62 (20.7%) missing cases. Brain imaging study (MRI and CT Scan) was done in 27.4 % of these patients half (13.7%) have an abnormal result. Generalized seizures were the most common 198 (66%) seizure type among patients followed by mixed seizures 40 (13.3%), focal seizures 36 (12%), and unclassified 26 (8.7%).

The common age group at epilepsy diagnosis was 1-5 years (48.7%), and the majority of patients (42%) had 1-2 times the frequency of seizure events before to commencement of ASMs therapy. Around two-thirds 62.3% of the study patients had a seizure-free period below 1 year/greater than or equal to one episode of seizure in the last 1 year after the start of treatment from them 31.3% of patients experienced 1-5 times seizure attacks. Comorbid conditions were found in 40.3% of patients with intellectual disability (12.7%) found to be the most common comorbid condition in children with epilepsy followed by developmental delay (11.3%) (Table 2).

Table 2: Sociodemographic and clinical characteristics of the pediatric epileptic patients in Addis Ababa, Ethiopia

Variables	Category	TASH	SPHMMC	Y12HMC	Total (%)
Sex	Male	78 (26.0)	65 (21.7)	50 (16.7)	193 (64.3)
	Female	50 (16.7)	31 (10.3)	26 (8.7)	107 (35.7)
Age of the child (yrs.)	1-5 years	35 (11.7)	30 (10.0)	24 (8.0)	89 (29.7)
	5-10 years	52 (17.3)	35 (11.7)	30 (10.0)	117 (39.0)
	10-15 years	36 (12.0)	26 (8.7)	17 (5.7)	79 (26.3)
	15-18 years	6 (2.0)	5 (1.7)	4 (1.3)	15 (5.0)
Residence	Addis Ababa	98 (32.7)	62 (20.7)	58 (19.3)	218 (72.7)
	Out of Addis Ababa	31 (10.3)	34 (11.3)	17 (5.7)	82 (27.3)
Source of medications	Free	52 (17.3)	40 (13.3)	23 (7.7)	115 (38.3)
	Payment	77 (25.7)	56 (18.7)	52 (17.3)	185 (61.7)
Family monthly income	>/=1500	105 (35.0)	78 (26.0)	60 (20.0)	243 (81.0)
(ETB)	</=1500	24 (8.0)	18 (6.0)	15 (5.0)	57 (19.0)
Family history of epilepsy	Yes	13 (4.3)	18 (6.0)	7 (2.3)	38 (12.7)
	No	116 (38.7)	78 (26.0)	68 (22.7)	262 (87.3)
Age at diagnosis	<1 year	52 (17.3)	25 (8.3)	23 (7.7)	100 (33.3)
	1-5 years	60 (20.0)	46 (15.3)	40 (13.3)	146 (48.7)
	5-10 years	16 (5.3)	15 (5.0)	10 (3.3)	41 (13.7)
	≥10 years	1 (0.3)	10 (3.3)	2 (0.7)	13 (4.3)
Frequency of attack before	None	37 (12.3)	15 (5.0)	18 (6.0)	70 (23.3)
initiation of treatment	1-2 times	44 (14.7)	53 (17.7)	29 (9.7)	126 (42.0)
	3-5 times	18 (6.0)	18 (6.0)	16 (5.3)	52 (17.3)
	6-10 times	18 (6.0)	4 (1.3)	12 (4.0)	34 (11.3)
	>10 times	12 (4.0)	6 (2.0)	0 (0)	18 (6.0)
Types of seizures	Focal	24 (8.0)	7 (2.3)	5 (1.7)	36 (12.0)
	Generalized	83 (27.7)	63 (21.0)	52 (17.3)	198 (66)
	Mixed	21 (7.0)	10 (3.3)	9 (3.0)	40 (13.3)
	Unclassified	1 (0.3)	16 (5.3)	9 (3.0)	26 (8.7)
Duration of illness (yrs.)	1-5 years	62 (20.7)	74 (24.7)	47 (15.7)	183 (61.0)

	5-10 years	45 (15.0)	19 (6.3)	22 (7.3)	86 (28.7)
	≥10 years	22 (7.3)	3 (1.0)	6 (2.0)	31 (10.3)
Seizure free period	<1 years	88 (29.3)	53 (17.7)	46 (15.3)	187 (62.3)
	1-2 years	32 (10.7)	35 (11.7)	25 (8.3)	92 (30.7)
	2-5 years	9 (3.0)	8 (2.7)	4 (1.3)	21 (7.0)
Frequency of seizures/year	None	40 (13.3)	43 (14.3)	30 (10.0)	113 (37.7)
	1-5 times	41 (13.7)	29 (9.7)	24 (8.0)	94 (31.3)
	6-10 times	32 (10.7)	11(3.7)	11 (3.7)	54 (18.0)
	>10 times	16 (5.3)	13 (4.3)	10 (3.3)	39 (13.0)
Comorbidities	Intelletual disability	19 (6.35)	11 (3.7)	8 (2.67)	38 (12.7)
	Global developmental delay	15 (5)	9 (3)	10 (3.32)	34 (11.3)
	Psychiatric conditions	9 (3)	9 (3)	6 (2)	24 (8)
	Cerebral palsy	10 (3.3)	5 (1.68)	5 (1.68)	20 (6.7)
	Malnutrition	0 (0)	4 (1.3)	0 (0)	4 (1.3)
	Cardiac conditions	1 (0.33)	1 (0.33)	1 (0.33)	3 (1)
	Others*	12 (4)	8 (2.66)	4 (1.33)	24 (8)
	None	72 (24)	61 (20.3)	46 (15.4)	179 (59.7)

Abbrevations: ETB=Ethiopian Birr TASH-Tikur Anbessa Specialized Hospital SPHMMC-Saint pauls Hospital Mellinium Medical College Y12HMC-Yekatit 12 Hospital Medical College

** Hemiparesis, HIV/AIDS, Anemia, Rickets, Migraine headache, Chronic kidney disease, Asthma, Scabies, Enuresis, Obesity, Benign neck cyst, Tuberculosis, Conjunctivitis, Mycosis*

5.2. Characteristics of caregivers

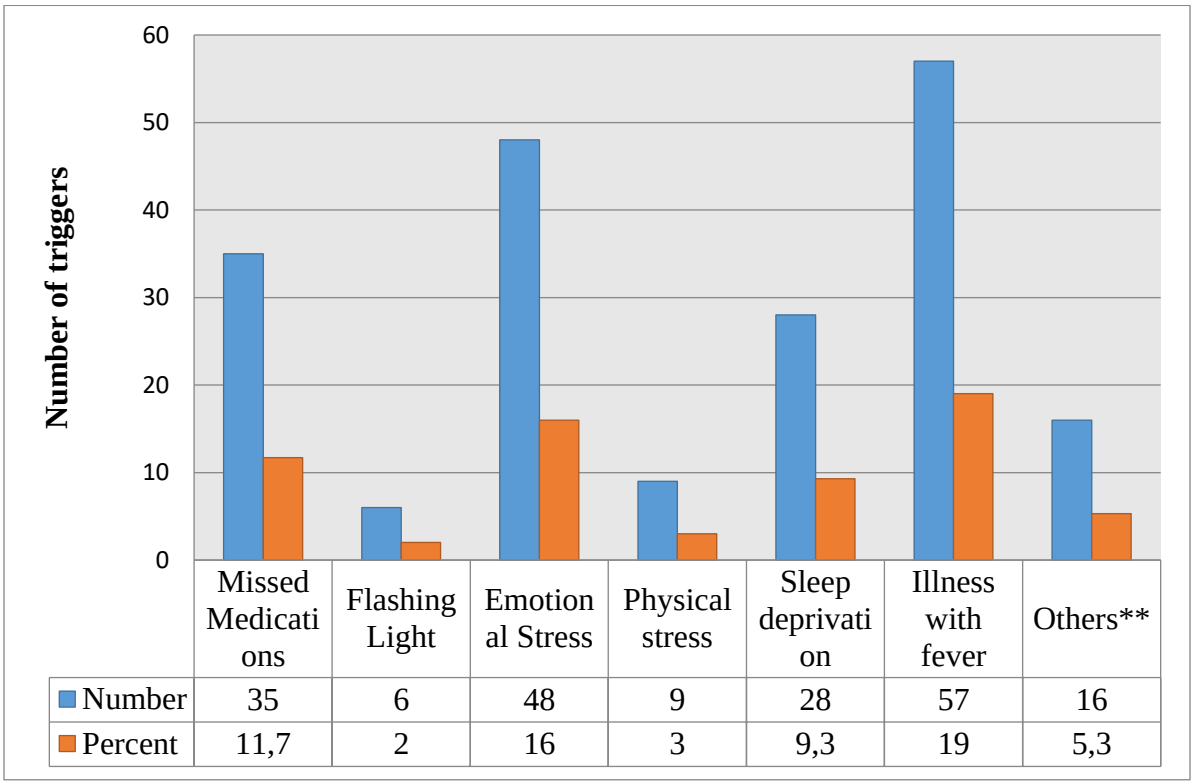
In regards to the caregivers of the children, more than half (58%) of the caregivers were mothers. More than three-fourth of caregivers 82.3% were married while 9.0% were single, 30.3% had finished primary school, and nearly half (49.3%) of the caregivers of the children were unemployed (Table 3).

Table 3: Characteristics of the caregivers in Addis Ababa, Ethiopia

Variables	Category	Number (n)	Percent (%)
Primary caregiver	Father	104	34.7
	Mother	174	58.0
	Brother	4	1.3
	Sister	5	1.7
	Others*	13	4.3
Religion	Orthodox	166	55.3
	Protestant	45	15.0
	Muslim	86	28.7
	Others**	3	1.0
Caregivers marital status	Married	247	82.3
	Single	27	9.0
	Divorced	15	5.0
	Widowed	11	3.7
Caregivers educational level	No formal education	72	24.0
	Primary school	91	30.3
	Secondary school	76	25.3
	College and Above	61	20.3
Occupation of caregivers	Not employed	148	49.3
	Government employee	40	13.3
	Private employee	22	7.3
	Self-employed	88	29.3
	Others***	2	0.7

Aunt, Uncle, Grandfather/mother Adventist, catholic ***Student, pastor*

More than half (56%) of caregivers/patients reported seizure triggers that can increase seizure attacks illness with high fever (19%) was mostly reported followed by emotional stress (16%) (Figure 2).



	Missed Medications	Flashing Light	Emotional Stress	Physical stress	Sleep deprivation	Illness with fever	Others**
Number	35	6	48	9	28	57	16
Percent	11,7	2	16	3	9,3	19	5,3

***Hunger, Noisy sounds, Drinking coffee, Cold weather*

Figure 2**:** Seizure triggers among pediatric epileptic patients in Addis Ababa, Ethiopia

5.3. The Pattern of anti-seizure medication use

Overall, 7 types of ASMs were used. Of them phenytoin was prescribed in 142 (47.7%) of patients followed by valproic acid in 140 (46.2%). Around two-third (64.3%) of patients were on monotherapy. Phenytoin (28.7%) was the most frequently prescribed ASM monotherapy, followed by valproic acid (21.3%), phenobarbitone (11.0%), carbamazepine (2.7%) and clonazepam (0.7%). Among the ASM combination therapies, VPA+PHB (10.3%) was the most frequently prescribed dual therapy while VPA+PHB+PHT (2%) was mostly used as triple therapy. The maximum number of ASM prescribed was three/patients. The mean duration in ASMs was 4.2 ± 3.21 years (Table 4).

Table 4: Anti-seizure medications use pattern among pediatric epileptic patients in Addis Ababa, Ethiopia

Variables	Category	Number (n)	Percent (%)
Type of ASMs	PHB	32	11.0
	VPA	65	21.3
	PHT	86	28.7
	CBZ	8	2.7
	CLN	2	0.7
	VPA+PHT	23	7.7
	VPA+PHB	31	10.3
	PHB+PHT	23	7.7
	PHB+CBZ	3	1.0
	PHB+CLN	2	0.7
	PHT+CLN	1	0.3
	VPA+CLN	9	3.0
	VPA+LTG	3	1.0
	CBZ+LEV	1	0.3
	VPA+PHB+PHT	6	2.0
	PHB+PHT+CLN	2	0.7
	VPA+PHB+CLN	1	0.3
	VPA+PHT+CLN	1	0.3
	VPA+CLN+LEV	1	0.3
ASMs treatment modality	Monotherapy	193	64.3
	Dual therapy	96	32.0
	Triple therapy	11	3.7

Abbrevations: ASMs- Anti-seizure medications CBZ-Carbamazepine CLN-Clonazepam LTG-Lamotrigine LEV-Levetiracetam PHB-Phenobarbitone PHT-Phenytoin VPA-Valproic acid

5.4. Distribution of anti-seizure medications and modality based on type of seizures

The majority of patients with generalized and focal seizures were treated with monotherapy on the other hand, majority of patients with mixed seizures were treated with dual-therapy.Regarding ASMs used based on seizure type, phenytoin was the most frequently used medication for generalized and unclassified types of seizures, followed by valproic acid. Valproic acid was a frequently used medication for focal seizures and followed by phenytoin. A combination of VPA+PHB was the most commonly used dual ASM therapy and this combination was used for all types of seizure followed by a combination of VPA+PHT and PHB+PHT. Among the triple-therapy ASMs, VPA+PHB+PHT was the most commonly used combination and prescribed for all types of seizures (Figure 3).

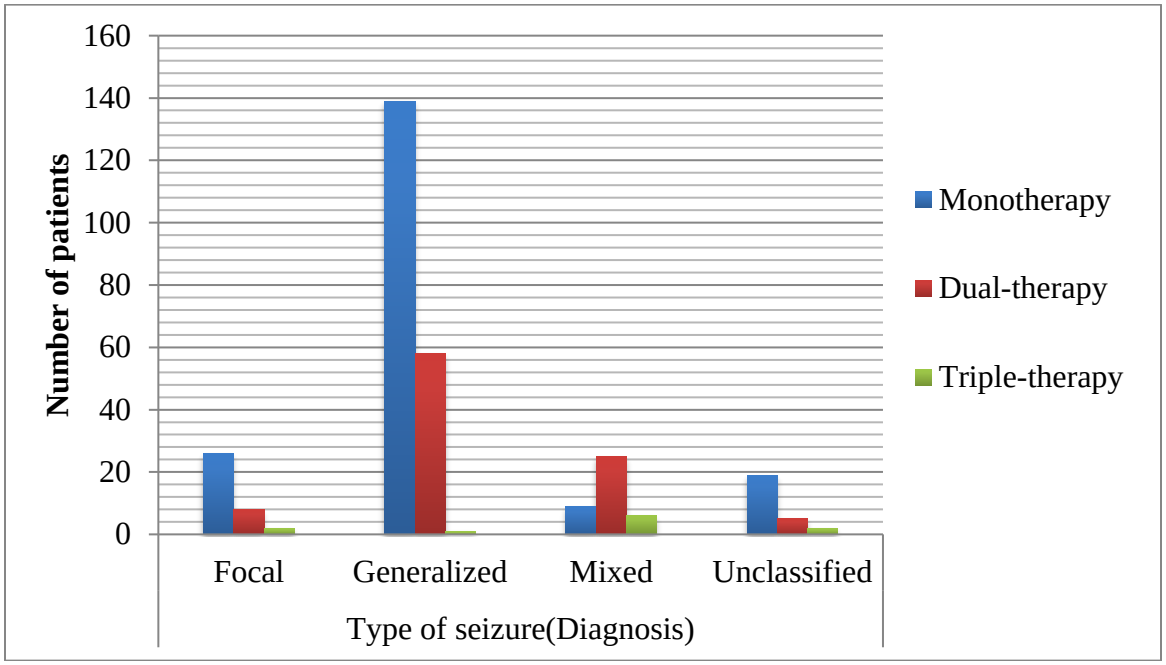


Figure 3**:** Distribution of mode of anti-seizure medications therapy based on the type of seizure among pediatric epileptic patients in Addis Ababa, Ethiopia

5.5. Prescribed drugs other than anti-seizure medications

The most prescribed medication other than anti-seizure medication among patients was calcium with vitamin D (42.1%) followed by risperidone (21%) (Table 5).

Table 5: Prescribed drugs other than ASMs among pediatric epileptic patients in Addis Ababa, Ethiopia

Medications	**Number (n)**	**Percent (%)**
Calcium with vitamin D	16	42.1
Risperidone	8	21
HAART	3	7.9
Iron sulfate	2	5.3
Terbinafine	2	5.3
Others*	8	21

Abbreviation: HAART- Highly active anti-retroviral therapy

**Nifedipine, Imipramine, Levothyroxine, plumpynut, Salbutamol, Enalapril, Benzyl benzoate, Ciprofloxacin Eye drop*

5.6. Adverse drug events related to anti-seizure medications

About 50% of patients experienced adverse drug events, while on ASMs out of which gingival hyperplasia (11.3%) was most common followed by vitamin D deficiency/insufficiency (9%) and skin rash (7.7%) (Table 6).

Table 6: Adverse drug events related to anti-seizure medications among pediatric epileptic patients in Addis Ababa, Ethiopia

Variables	**Number (n)**	**Percent (%)**
Gingival hyperplasia	34	11.3
Vitamin D deficiency/insufficiency	27	9.0
Skin rash	23	7.7
Weight gain	20	6.7
Behavioral changes	20	6.7

Weakness	9	3.0
Others*	33	10.9

**Forgetfulness, Headache, Blurring of vision, Drowsiness, Irritability, Epigastric pain, Appetite loss, Weight loss, Numbness, Cough*

5.7. Serum level and chi-square test of independence between seizure control status and serum drug concentrations

Therapeutic drug monitoring (TDM) was performed in 27% of patients and measured for 4 types of ASMs involving valproic acid 41 (13.7%), phenytoin 35 (11.7%), phenobarbitone 26 (8.7%), and carbamazepine 4 (1.3%). The result from the chi-square test of independence shows there is no statistically significant relationship between seizure control status and serum level of ASMs, X^2 (df=1 N=58) P= 0.920. (Table 7).

Table 7: Relationship between seizure control status and serum drug concentrations among pediatric epileptic patients in Addis Ababa, Ethiopia

Variable		**Seizure control status**		**P-value**
		Uncontrolled	**Controlled**	
Serum drug level	Within the reference range	78.3%	21.7%	0.920
	Out of the reference range	77.1%	22.9%	

5.8. Seizure control status

In this study, nearly two third 62.3% of patients had uncontrolled seizures (Figure 4).

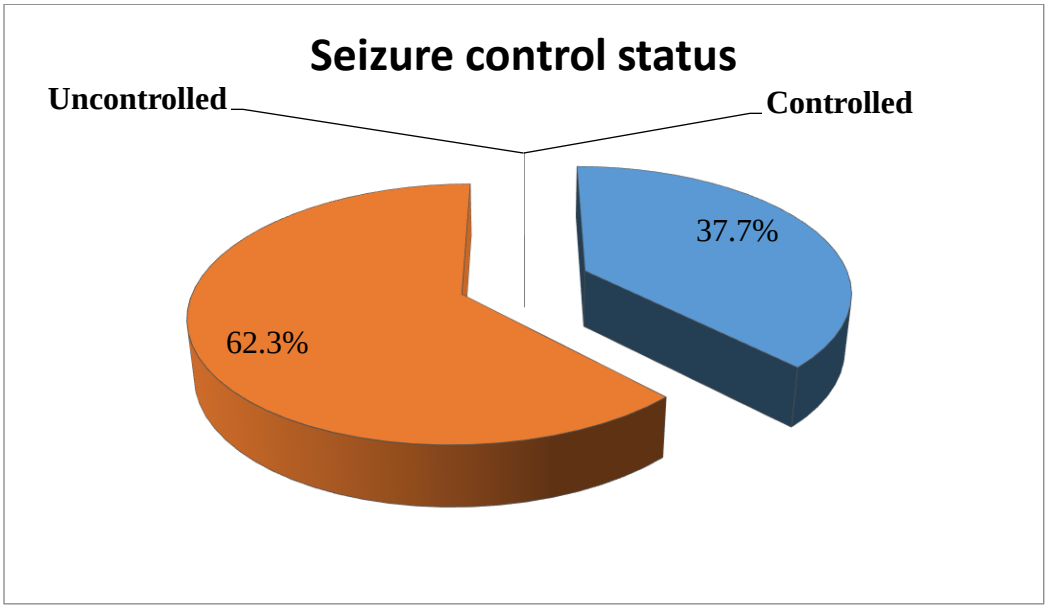


Figure 4: Seizure control status among pediatric epileptic patients in Addis Ababa, Ethiopia

5.9. Predictive factors of uncontrolled seizures

All clinically relevant variables were entered into the univariate model. Those variables with P value <0.25 were taken into the multivariable logistic regression model.

The omnibus test of the model coefficient shows that overall the model is statistically significant $\chi 2$ (22) = 100.876, $p < .05$. Hosmer-Lemeshow tests of the null hypothesis that predictions made by the model fit perfectly with observed group memberships. Therefore, the value in the model shows no statistically significant value which shows a good fit. The model explained 38.9% variation in uncontrolled seizures based on nagelkerke R square. The model classified 76% of cases correctly and with the independent variable added 85.6% of patients with uncontrolled seizure were predicted correctly and 60.2% of patients with controlled seizures were predicted correctly.

Multivariate logistic regression revealed a significant association between the sex of the child (females), educational status of caregivers (primary education), and family history of epilepsy were found to be protective for uncontrolled seizures where as seizure-triggers and type of therapy (polytherapy with ASMs) were positively associated with uncontrolled seizures.

However, no statistically significant association was found between uncontrolled seizures and the age of the child, source of medication, frequency of attack before initiation of ASM therapy, age at seizure diagnosis, type of seizure, duration of illness, and comorbidities.

Females were less likely to develop uncontrolled seizure compared to males (AOR= 0.515, 95% CI: 0.285-0.931). The odds of developing an uncontrolled seizures among parents/caregivers of patients with primary education decreased by 56.4% as compared to those patients who didn't have formal education (AOR=0.436, 95% CI: 0.192-0.99). But it was not statistically significant for patients whose educational level was secondary school and above. The odds of developing uncontrolled seizures among patients with a family history of epilepsy decreased by 63.7% as compared to those patients without a family history (AOR=0.363, 95% CI: 0.153-0.857). The odds of developing uncontrolled seizures among patients with seizure triggers were increased by 3.63 times than those without seizure triggers (P<0.001, 95% CI: 1.99-6.614). Patients on polytherapy with ASMs were 6.79 times more likely to develop uncontrolled seizures compared to patients on monotherapy (P<0.001, 95% CI: 3.221-14.311) (Table 8).

Table 8: Factors associated with uncontrolled seizures among pediatric epileptic patients at Addis Ababa, Ethiopia

Variables	Categories	Seizure control status n(%)		COR(95% CI)	AOR(95% CI)	p-value
		Controlled	Uncontrolled			
Sex of child	Male	63 (32.6)	130 (67.4)	1	1	
	Female	50 (46.7)	57 (53.3)	0.552 (0.340-0.897)	0.515 (0.285-0.931)	**0.028***
Age of child	1-5yrs	29 (32.6)	60 (67.4)	1	1	
	5-10yrs	49 (41.9)	68 (58.1)	0.671 (0.377-1.193)	1.13 (0.471-2.71)	0.784
	10-15yrs	30 (38)	49 (62)	0.789 (0.419-1.489)	1.558 (0.398-6.092)	0.524
	15-18yrs	5 (33.3)	10 (66.7)	0.967 (0.303-3.088)	4.946 (0.643-38.017)	0.124
Educational status	No formal Education	26 (36.1)	46 (63.9)	1	1	
of the caregiver	Primary	44 (48.4)	47 (51.6)	0.604 (0.321-1.137)	0.436 (0.192-0.99)	**0.047***
	Secondary	26 (34.2)	50 (65.8)	1.087 (0.553-2.135)	0.751 (0.321-1.759)	0.51
	College and Above	17 (27.9)	44 (72.1)	1.463 (0.699-3.060)	1.803 (0.713-4.564)	0.213
Family history of	No	91 (34.7)	171 (65.3)	1	1	
epilepsy	Yes	22 (57.9)	16 (42.1)	0.387 (0.194-0.773)	0.363 (0.153-0.857)	**0.021***
Source of	Free	36 (31.3)	79 (68.7)	1	1	
medication	Payment	77 (41.6)	108 (58.4)	0.639 (0.391-1.044)	0.585 (0.317-1.081)	0.087
Age at onset of	<1years	33 (33)	67 (67)	1	1	
seizure	1-5 years	55 (37.7)	91 (62.3)	0.815 (0.477-1.391)	0.823 (0.398-1.702)	0.6
	5-10 years	19 (46.3)	22 (53.7)	0.570 (0.272-1.198)	0.391 (0.116-1.320)	0.13
	>10 years	6 (46.2)	7 (53.8)	0.575 (0.179-1.847)	0.508 (0.072-3.571)	0.496
Frequency of	None	23 (32.9)	47 (67.1)	1	1	
attack before	1-5 times	81 (45.5)	97 (54.5)	0.586 (0.328-1.046)	0.746 (0.361-1.542)	0.429

initiation of ASM therapy	>5 times	9 (17.3)	43 (82.7)	2.338 (0.975-5.606)	2.271 (0.819-294)	0.115
Duration of illness	1-5 years	67 (36.6)	116 (63.4)	1	1	
	5-10 years	38 (44.2)	48 (55.8)	0.730 (0.433-1.229)	0.528 (0.223-1.247)	0.145
	>10 years	8 (25.8)	23 (74.2)	1.661 (0.703-3.920)	0.842 (0.176-4.024)	0.83
Seizure triggers	No	70 (53)	62 (47)	1	1	
	Yes	43 (25.6)	125 (74.4)	3.282 (2.017-5.340)	3.63 (1.99-6.614)	**<0.001***
Type of seizures	Focal	10 (27.8)	26 (72.2)	1	1	
	Generalized	85 (42.9)	113 (57.1)	0.511 (0.234-1.117)	0.446 (0.174-1.146)	0.094
	Mixed	10 (25)	30 (75)	1.154 (0.415-3.206)	0.305 (0.083-1.126)	0.075
	Unclassified	8 (30.8)	18 (69.2)	0.865 (0.286-2.618)	1.139 (0.307-4.227)	0.846
Type of ASM therapy	Monotherapy	96 (49.7)	97 (50.3)	1	1	
	Polytherapy	17 (15.9)	90 (84.1)	5.240 (2.904-9.453)	6.79 (3.221-14.311)	**<0.001***
Comorbidity	Yes	74 (41.3)	105 (58.7)	1	1	
	No	39 (32.2)	82 (67.8)	1.482 (0.914-2.403)	1.056 (0.569-1.961)	0.863

*COR=Crude Odds Ratio, AOR=Adjusted Odds Ratio 1=reference group *Significance at <0.05*

6. Discussion

The purpose of this study was to assess treatment outcome of epilepsy and associated factors among pediatric patients at Tikur Anbessa Specialized Hospital, Saint Paul's Hospital Millennium Medical College, and Yekatit 12 Hospital Medical College. The findings of this study revealed that 62.3% of patients had uncontrolled seizures with seizure triggers and polytherapy with ASMs were strong predictors.

In the current study, the majority (39%) of children fell into age category of 5-10 years which is in agreement with studies done in Gujarat (40%) (57), Gondar (39%) (33), Sudanese study (40.1%) (77) which is between 5-10 years, approximate with Malaysian (45.7%) which ranges between 6-10 years (36) and different from a study done in India (25.7%) which is between 1-3 years (78). The difference might be due to the study setting, the cause of epilepsy and the age category included in the studies being different. And males (64.3%) were more predominately affected than females (35.7%) which is in agreement with the study done in India (78).

According to the current study, the generalized seizures was the most common (66%) type of seizure followed by a mixed type of seizures (13.3%) which is in concordance with the study done in Malaysia comparing seizure type in adults and pediatrics, which shows that the most commonly reported seizure type among the pediatric population was generalized tonic-clonic seizures (75.4%) followed by mixed (5.7%) (15). This study is also in line with other studies that reported generalized seizures as the most common type of seizure in India (67%) (60), Southern Nigeria (64%) (79), Egypt (63.6%) (37), and Jordan Sudan (61.90%) (20)**.** However, a higher prevalence was reported as compared to the **s**tudies conducted in Sudan 17.3% (65), Srilanka (32%) (80) and less than the studies done in Gondar (98.5%) (59) and Wuhan City China (98%) (81) and also different from another Malaysian study which shows focal (47.2%) as most common followed by generalized (40%) (36). This disparity may be attributable to differences in professional qualifications and the availability of diagnostic instruments used for seizure type classification, as well as the fact that focal epilepsy is the most frequent epilepsy in early childhood but the age group included in this study is up to 18 years.

Most pediatric epileptic patients respond to one of the first-line ASMs; second-line agents may be useful in patients who do not respond to one or more of the first-line agents. In this study, the majority (64.3%) of children were on monotherapy followed by dual (32%) and triple (3.7%)

which aligns with the study done in Jimma monotherapy (63%), dual therapy (35.9%), and triple therapy (0.7%) (58), Jordan monotherapy (67%), dual (23%), triple (7.5%) (82), but lower than studies done in Gondar (73.3%) (33), Sudan (84.2%) (65), Derbyshire (75%) (83), India (87%) (60) which reported monotherapy as most common type of ASMs therapy. The difference might be attributed to the fact that this study was conducted at tertiary care and teaching hospitals where uncontrolled and complicated cases are managed which needs combination therapy. Another reason could be difference in the study design and methodology.

The majority of patients were put on phenytoin (47.7%), which is in line with a studies done in India (35.5%) (60), Jimma (48.2%) (58), and Gondar (42.9%) (33). The reason could be the availability and cost of the medications. It differs from WHO recommendations in developing countries where the most usually recommended first-line ASM is phenobarbitone due to availability and affordability particularly in pediatric populations the difference might be due to fear of adverse effects including behavioral disturbance and drowsiness from phenobarbitone even though these two drugs are equally effective and preferred medications in pediatrics. A study done in Uganda found that sodium valproate was the most commonly prescribed ASMs (5).

In the present study about 50% of patients experienced adverse drug events which is in line with a study done in Gondar (47.6%) (33). This might be due to majority of patients in both studies being put on old generations ASMs and multiple ASMs therapy whereas higher than the study done in Gondar (17.6%) (59). In the current study gingival hyperplasia (11.7%) is the most common ADE, which is inline with the study done in Jimma (58). The possible reason could be the most commonly prescribed drug in both studies was phenytoin. However, data were collected through patient self-report and from caregivers which may result in over/under-reporting of the side effect as well as the bias of side effects of other medication they used while on ASMs.

Comorbidities were found in 40.3% of the patients with intellectual disability being the most common which is in line with a study done in Southeastern Nigeria (45.8%) (1) whereas it was in contrary to a study done in Uganda which reported developmental delay was most common (84%) (18).

In the present study serum concentration of ASMs level was obtained 35.5% of ASMs from medical records of the patients, majority (19.7%) were out of reference range whereas 15.8%

were within reference range. Due to few samples chi-square test with two-two table was done accordingly chi square test of independence between seizure control status and serum drug concentrations it was found to be no statistically significant X^2 (df=1 N=58) p= 0.920. This result is supported by a study done in Indian childrens aged 2-12 years which shows there is no association between serum anti-seizure level and breakthrough seizures (84). This could be due to small sample size and retrospective nature, and we have to assess pre and post intervation outcome to draw conclusion. On the other side the result could implicate that measuring serum level could be done when it is necessary because of individual variation.

According to this study, 62.3% of the patients had a seizure-free period of below one year (uncontrolled seizures) and 37.7% of the patients had a seizure free-period of 1 and more years (controlled seizures) which is in line with the study done in south-west Uganda (60.4%) (66) while it was lower than the studies done in Norway (59%) of patients have seizure-free period of one and more years (68), Eastern Nepal (80%) (46). A possible reason could be a lack of qualified medical personnel, the unavailability of medications, poor community knowledge and awareness, and poor health system infrastructure in our setting where resources are limited as well as short-term follow-up period in the latter study. In addition, lower than the study done in Jimma (54.1%) have controlled seizures with a 3-month follow-up period (58). A possible reason could be the follow-up period was short in the latter study.

In this study being female, parents' educational level, family history of epilepsy, seizure triggers, and poly-therapy with ASM were found to have a significant association with uncontrolled seizures. Females are less likely to develop uncontrolled seizure than males this could be due to females' high likelihood to adhere than males due to fear of the outcome of not taking the medications, which is supported by studies done in Gondar, Iran, and Pakistan (33, 67, 85). This might be because females are more attentive than males and think about everything critically. As a result, they may be adherent to their medications, which may be related to successful outcomes.

In this study, a positive family history of epilepsy reduces the chances of experiencing an uncontrolled seizures. The majority of studies reported the reverse result, no association was found (59). The possible explanation for family history to be protective factor against uncontrolled seizures could be that families of patients/children who understand the nature of the disease or have awareness about medical conditions (epilepsy) take their children to a healthcare center as soon as possible and resulting in decreased delayed presentations to the health facilities

this is not surprising because in developing countries such as Ethiopia families with little knowledge of disease conditions take their childrens to alternative treatment areas rather than taking to health care facilities particularly in the case of epilepsy which could lead to delayed presentations to the health facilities. Another reason could be due to a history of prior response to specific ASMs, the selection of anti-seizure medications may be better than family without disease condition.

In the relation to the aforementioned idea in the present study, the odds of developing uncontrolled seizures among patients whose parents with primary education decreased by 56.4% as compared to those patients whose parents didn’t have formal education. The reason could be illiterate parents may not query their children's health care providers about their sickness and treatments, and they may be unaware of the disease's progression. A study reported parents who had not completed high school (P = 0.08 for maternal education and P = 0.004 for paternal education) (68).

The odds of developing uncontrolled seizures among patients with seizure triggers were increased by 3.63 times as compared to those without seizure triggers (P<0.000, 95% CI: 1.99-6.614) which is supported by study conducted in pediatrics (70). This might be due to parents of childrens and the childs lack of awareness about seizure triggers, identifying and handling those factors that have an impact in the control of seizures.

Patients who were put on polytherapy 6.79 times were more likely to develop uncontrolled seizures compared to monotherapy which is in congruent with different studies (37, 46, 59). This could be because patients who are exposed to more than two anti-seizure medications are more prone to side effects, which leads to medication discontinuation (non-adherence to therapy), which influences the treatment outcome indirectly. Another reason that is specific to children and adolescents could be pill burden and refusal to take drugs, which becomes worse as the number of medications increases.

7. Strengths and limitations of the study

7.1. Strengths of the study

- The main strength of our study is multi-center which includes the largest referral hospital (TASH) and teaching hospitals (SPHMMC and Y12MMC).
- Additionally our research was conducted in childrens which is an area of interest and needs to be addressed due to the complex response of pediatrics to anti-seizure medications.

7.2. Limitations of the study

- The cross-sectional nature of the study didn't allow a follow-up of the patients.
- Adverse drug events were considered based on patients'/parents' report and medical records without the establishment of a causal relationship, we have to know the baseline level and follow after the intiation of ASMs. There might be recall bias particularly in assessment of seizure frequency.
- Adherence to anti-seizure medications was not measured due to not getting validated tool in childrens.
- We cannot generalize the results on therapeutic drug monitoring due to retrospective nature of data collection, few sample included in correlation analysis and the fact that some medications tend to decrease/increase the plasma level of another when two medications are used concurrently.
- Due to the above limitations, we might not generalize the result to all hospitals in our country even though it is multi-center.

8. Conclusions

In conclusion the findings of present study showed that around two third (62.3%) of patients had uncontrolled seizures. Generalized seizures was the most common seizure type and phenytoin was mostly commonly used anti-seizure medication. Sex of the child, educational level of parents, family history of epilepsy have increased odds of uncontrolled seizures. However seizure triggers, and polytherapy with antiseizure medications have increased odds of uncontrolled seizures. Overall seizure control status among pediatrics was found to be poor thus health care providers should give emphasis on those factors that are associated with uncontrolled seizures.

9. Recommendations

- Taking careful history could help to identify triggers and emphasis should be given to awareness and education of caregivers/childrens on seizure triggers.

- Health care providers should assess and monitor for adverse drug events due to anti seizure medications for betterment of treatment outcomes.

- Another modality should be considered for those patients with refractory seizures.

- Therapeutic drug monitoring with large sample, followup and interventions should be done for patients with uncontrolled seizures and adverse drug events.

- Further prospective and interventional studies with adherence measurement should be done.

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Appendix

Annex I: Information sheet

Hello. My name is _____ and I am data collector of the study conducted by Bamlak markos student at Addis Ababa University College of health sciences, conducting this research for partial fulfillment of masters of Science degree in pharmacy practice. We would very much appreciate your participation in this study. The information you provide will help us to know/assess epilepsy treatment outcome and associated factors among pediatrics.

Name of advisors: - Minyahil Alebachew (B.pharm, MSc, Ph.D. Fellow) and Ayalew Moges (MD, Pediatrician, Pediatric neurologist)

Name of the organization: Addis Ababa University, College of Health Sciences, School of Pharmacy

Title: - Treatment outcome of epilepsy and associated factors among pediatric patients at Tikur Anbessa Specialized Hospital, st Paul's hospital Millennium Medical College and Yekatit 12 Hospital Medical College in Addis Ababa, Ethiopia.

Introduction: Information sheet, consent and assent form will be prepared for parents of children's and children's who attending neurologic clinic who were volunteer to participate in research.

Purpose: The purpose of this study is to assess treatment outcome of epilepsy and associated factors among pediatric patients at TASH, SPHMMC and Y12HMC, Addis Ababa, Ethiopia. Your input will be extremely valuable as the information will be used to assess the medication use and to identify gaps in treatment.

Expected outcomes: The information that you provide are very essential, not only for the successful accomplishment of the study but also for producing relevant information which will help and may benefit you and your child directly or indirectly in improving the provision of the service to children's with epilepsy. We will provide research results to concerned bodies for intervention.

Annex II: Consent and assent form

1. Consent form

The study will be conducted through recording medical findings from your medical record and interviewing. Everything from your information and records would be completely confidential to the research and the data are stored without your name and only used for the purpose of this study. Additionally, taking part in this study is completely voluntary. It is your choice whether to participate or not. You may skip any questions that you do not want to answer. Please ask me to stop as we go through the information and I will take time to explain. I would like to thank in advance for your willingness to stay with me for the interview that will take 10-30minutes.

1. Name of interviewer_____ Signature_____ date_____/_____/____

2. Assent form

Your parent has agreed that you take part in our study where we are looking at epilepsy treatment outcomes among pediatrics. Your participation in the study is fully voluntary. Any information you provide not be given to anyone else. You can stop at any time. If the respondent does not agree to be interviewed, lets them thanks and go to the next respondent. If the respondent say “YES” continues.

1. Name of interviewer_____ Signature_____ date_____/_____/____

If you have questions, complaints or concerns about this study, you can contact the principal investigator **Bamlak Markos**; Phone: +251916554566

Email address: Bamlakmarkos@gmail.com

Annex III: English version questionnaires from patient interview

Title: Treatment outcome of epilepsy and associated factors among pediatric patients at Tikur Anbessa Specialized Hospital' St paul's Hospital Mellinnium Medical College and Yekatit 12 Hospital Medical College in Addis Ababa, Ethiopia.

Code # _____ Date of data collection _____

Name of health facility_____

Part I: - Socio-demographic characteristics

S.no	Questions	Response
1	Age of child	_____years
2	Sex of child	Male ☐ Female ☐
3	Residence	Urban ☐ Rural ☐
4	Address	Oromia region ☐ Amhara region ☐ Tigray region ☐ SNNPR ☐ Others (specify)_____
5	Religion	Orthodox ☐ Protestant ☐ Muslim ☐ Catholic ☐ Others (specify)_____
6	Caregiver/s	Father ☐ Mother ☐ Sister ☐ Brother ☐ Other/s (specify)_____
7	Marital status of caregivers	Married ☐ Single ☐ Divorced ☐ Widowed ☐
8	Educational level of caregivers/parents	No formal education ☐ Primary school ☐ Secondary school ☐ College and above ☐
9	Occupation of caregivers/parents	Not employed ☐ Governmental employee ☐

		Private-employed ☐ Student ☐ Other (specify)_____
10	Source of medication	Free ☐ Payment ☐
11	Income level of parents	_____(monthly)

Part II. Clinical characteristics, Medication and Treatment outcome related questionnaires

S.no	Questions	
1	Age of the child when seizure occurs	_____
2	Duration of illness (years)	1-5 years ☐ 6-10years ☐ Greather than 10 years ☐
3	Does he/ she have any family with epilepsy?	Yes ☐ No ☐
4	How many times does the seizure occur before intiation of treatment?	_____
5	How long has your child been in anti-seizure medications?	_____
6	Seizure triggers	Missed medications ☐ Lack of sleep ☐ Emotional stress ☐ Flashing light ☐ Physical stress ☐ Menstrial cycle ☐ Hunger ☐ Illness with fever ☐ Other/s (specify)_____
7	Have you ever developed side effects/ did your child have side effects with ASMs?	Yes ☐ No ☐
8	If question number 7 is yes, what side effect was it?	Ataxia ☐ Drowsiness ☐ Weight gain ☐ Skin rash ☐ Gingivial hyperplasia ☐ Behavioral abnormality ☐ Others (specify)_____

Annex IV: Amaharic version questionaries (የአማርኛ መጠይቅ ቅፅ)

የመረጃ ወረቀት

ጤና ይስጥልኝ የእኔ ስም _____ ይባላል፡፡ እኔ የጥናቱ መረጃ ሰብሳቢ ነኝ፡፡

እኔ በአዲስ አበባ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ የፋርማሲ ትምህርት ክፍል ውስጥ ተማሪ የሆኑት ባምላክ ማርቆስ በሚያካሄዱት ጥናት እና ምርምር ላይ መረጃ ሰብሳቢ ነኝ፡፡ በዚህ ጥናት እና ምርምር ላይ እንዲሳተፉ በጣም እናበረታታለን፡፡ እርስዎም ሆኑ ልጆዎ የሚሰጡት መረጃ የሚጥል በሽታ ያለባቸውን ልጆች የህክምና ውጤቶችን ለመገምገም ለማወቅ እና ለማሻሻል ይረዳናል፡፡ ቃለ-መጠይቁን ለመጨረስ ከ10-30 ደቂቃዎች ይወስዳል፡፡ ልጅዎም ቃለ መጠይቁ ላይ እዲሳትፍ የእርሶን ፍቃድ ይፈልጋል፡፡

የአማካሪ ስም፡- ምንያህል አለባቸው (ሁላተኛ ድግሪ ፣ ፒኤችዲ ዕጩ) እና አያሌዉ ሞገስ (ሀክም፣ የህፃናት ሀክም፣ የህፃናት ኒውሮሎጂት)

የድርጅቱ ስም፡- አዲስ አበባ ዩኒቨርሲቲ ፣ የጤና ሳይንስ ኮሌጅ ፣ ፋርማሲ ትምህርት ክፍል

የጥናትና ምርምር ፕሮጀክት ርዕስ፡- አዲስ አበባ ፣ ኢትዮጵያ ውስጥ በጥቁር አንባሰ, ቅዱስ ጳውሎስ እና የካቲት 12 ሆስፒታል ሜድካል ኮሌጅ በተመላለሽ ክፍል በሚጎበኙ የህፃናት ታካሚ ህመምተኞች መካከል የሚጥል በሽታ ህክምና ውጤቶች ::

መግቢያ፡- በሚጥል በሽታ ወደ መንግስት ሆስፒታሎች በኒውሮሎጂ ክሊኒክ ውስጥ ለአገልግሎት ወይም ለክትትል የሚመጡ እና ጥናቱ ላይ ለመሳተፍ ፈቃደኛ የሆኑ ወላጆች እና ልጆች የመረጃ ዝርዝር የፍቃድ እና የመስማማት ፎርም ተዘጋጅቶል ::

ዓላማ፡- የዚህ ጥናት ዋና ዓላማ የህፃናትን በሚጥል በሽታ ህመምተኞች መካከል የህክምና ውጤቶችን ለመገምገም ነው በጥቁር አንባሰ, ቅዱስ ጳውሎስ እና የካቲት 12 ሆስፒታል ሜድካል ኮሌጅ ፣ አዲስ አበባ ፣ ኢትዮጵያ :: መረጃው በሕክምና ውስጥ ያሉ ክፍተቶችን ለመለየት እና ለመገምገም ጥቅም ላይ ስለሚውል የእርስዎ አስተዋዎ እጅግ ጠቃሚ ይሆናል

::

ከጥናቱ የሚጠበቁ ውጤቶች/ጥቅሞች: በዚህ ጥናት ላይ የእርስዎ/ልጆ የሚጥል የህክምና ዉጤቶች እና ተየያዥ ምክንያቶች በድንብ ይጠናሉ። በተጨማሪም ከጥናቱ በሚገኙ ግኝቶች የሚጥል ህክምና ዉጤትን በተወሰነ መልኩ ለማሻሻል እንደሚቻል በመገመት፤ እርስዎናልጆ የጥቅሙ ተቋዳሽ ይሆናሉ ብለን እናምናለን። ስለዚህ የእርስዎ ቅንና ሓቀኛ መረጃ ለጥናቱ እጅግ በጣም ወሳኝ ነው።

የፈቃድ እና የስምምነት መግለጫ ቅፅ

1. የወላጅ ፈቃድ

በዚህ ጥናት የእርስዎ መረጃ ሙለ በሙለ በምስጥር የተጠበቀና ለምርምሩ አላማ ብቻ የሚዉል ነው። በተጨማሪም የእርስዎ ተሳታፉነት በፋቃድኝነት ላይ የተመሠረተ ነው። የጥናቱን አላማ ተረዲተውና ጊዜዎን ሰውተው፤ ከ 10-30 ደቂቃዎች ለሚፈጅ ቃላ-መጠይቅ እውተኛው መረጃ ለመስጠት ፈቃደኛ በመሆንዎ በቅድሚያ አመሰግናለሁ።

የቃለ መጠይቁ የጠያቂው ስም _____ _____ ፊርማ _____

ቀን _____ / _____ / ____

2. የልጆች የስምምነት ቅፅ

የሚጥል በሽታ ያለባቸው ህፃናት እና ልጆች በሚኖሩበት ጊዜ ከጤና ጋር የተዛመደውን ጥናታችን ላይ እዲካፈሉ ወላጅዎ ተስማምተዋል። በጥናቱ ውስጥ የሚያደረጉት ተሳትፎ ሙሉ በሙሉ በፈቃደኝነት ነው። የሚሰጡት ማንኛውም መረጃ ለሌላ ሰው ለማንም አይሰጥም። በማንኛውም ጊዜ ማቆም ይችላሉ።

የቃለ መጠይቁ የጠያቂው ስም _____ _____ ፊርማ _____

ቀን _____ / _____ / ____

በዚህ ጥናት ውስጥ ጥያቄዎች, አቤቱታዎች ወይም ስጋቶች ካሉዎት በሚከተለው ስልክ መደወል ይችላሉ።

ባምላክ ማርቆስ የስልክ ቁጥር: +251916554566

የኢሜል አድራሻ: Bamlakmarkos@gmail.com

አመሰግናለሁ!!

ክፍል 1. ማህበራዊ እና ግላዊ ጥያቄዎች

ተ/ቁ	ጥያቄዎች	
1	የልጆዎ ዕድሜ ስንት ነው	_____ በወር/ዓመት
2	የልጆዎ ጸታ	ወንድ ☐ ሴት ☐
3	የሰዉነት ክብደት	_____ኪ.ግ
4	መኖሪያ ቦታ	ገጠር ☐ ከተማ☐
5	አድራሻ	ኦሮሚያ ክልል ☐ አማራ ክልል ☐ ትግራይ ክልል ☐ ደቡብ ክልል ☐ አዲስ አበባ ☐ ሌላ/ሌሎች (ይግለጹ)_____
6	ሃይማኖት	ኦርቶዶክስ ☐ ፕሮቴስታንት ☐ ሙስሊም ☐ ካቶሊክ ☐ ሌላ/ሌሎች (ይግለጹ) _____
7	የልጁ/ጅቱ ሕክምና የሚከታተል(አሳካሚ)	አባት☐ እናት☐ እህት☐ ወንድም☐ ሌላ/ሌሎች (ይግለጹ) _____
8	የልጁ/ጅቱ አሳካሚ የጋብቻ ሁኔታ	ያገባ/ች ☐ ያላገባ/ች ☐ የተፋታ/ች ☐ ባልየሞተባት/ሚስት የሞተችባት ☐
9	የልጁ/ጅቱ አሳካሚ የትምህርት ደረጃ	መደበኛ ትምህርት የሌለዉ/ላት ☐ የመጀመሪያ ደረጃ ☐ ሁለተኛ ደረጃ ☐ ኮሌጅ እና ከዚያ በላይ☐
10	የልጁ/ጅቱ አሳካሚ የስራ ሁኔታ	ያልተቀጠረ/ች(ስራ የለውም) ☐ የመንግስት ስራተኛ ☐ የግል ስራ ☐ የግል ድርጅት ተቀጠሪ ☐ ሌሎች የተገለጹ _____
11	የመድሃንት ምንጭ	በነፃ ☐ በግዥ ☐
12	የቤተሰብ ገቢ ስንት ነው	_____በወር ውስጥ አማካይ

ክፍል ፪: ከሕክምና ጋር የተገናኙ ጥያቄዎች

ተ/ቁ	ጥያቄዎች	
1	ልጆዎ የመጀመሪያ የመንቀጥቀጥ ችግር ስከሰት ዕድሜ ስንት ነበር	_____
2	የሕመም ላይ የቆየበት/ችበት ጊዜ (በዓመት)	1- 5 ዓመት ☐ 6-10 ዓመት ☐ ከ 10 ዓመት በላይ ☐
3	ልጆዎ በፀረ-የሚጥል በሽታ መድኃኒቶች ላይ ለምን ያህል ጊዜ ቆየ/ች	_____
4	የሚጥል በሽታ ያለበት የቤተሰብ አባል ይኖራል/?	አላ ☐ የለም☐
5	ሕክምና ከመጀመሩ በፊት መንቀጥቀጥ/መጣል በሳምንት ስንት ጊዜ ይከስት ነበር	_____
6	በልጆዎ የመንቀጥቀጥ/መጣል ችግር መቀስቀስ መንስኤ ሊሆን የሚችለዉ ምንድን ነዉ	መድሃኒት ሰይወስድ መቅረት ☐ እንቅልፍ ማጣት ☐ የብርሃን ብልጭታ ☐ ስሜታዊ ዉጥረት ☐ የወር አበባ ☐ ኣካለዊ ዉጥረት ☐ በቂ ምግብ አለመዉሰድ ☐ ከፍተኛ ትኩሳትያለበት በሽታ ☐ ሌላ/ሌሎች (ይግለጹ) _____
7	መንቀጥቀጥ/መጣል ከመከሰቱ በፊት የማስጠንቀቅያ ምልክቶች አሉ	አዎ አሉ ☐ የሉም ☐
	ለጥያቄ መልሱ አዎ ከሆነ እባክዎን ያብራሩ	_____
8	ልጆዎ ሌሎች ተጎዳኝ ሕመም አሉት/ላት	አዎ አሉት/ላት ☐ የሉትም/ለትም ☐
	ከሉት/ላት(ይግለጹ)	_____
9	ልጆዎ የመንቀጥቀጥ/መጣል መች ነበር	_____
10	የመጣል/መንቀጥቀጥ ችግር ስንት ጊዜ ይከሰታል?	በየቀኑ ☐ በየሳምንቱ ☐ በየወሩ ☐ በዓመት ከአንድ ጊዜ ያነሰ ☐ በዓመት ከአንድ ጊዜ በላይ ☐
11	በፀረ-የሚጥል በሽታ መድኃኒቶች	አዎ ☐ አያዉቅም ☐

	የጎንዮሽ ጉዳት አጋጥመው/ልጅዎ አጋጥሞት ያውቃሉ/ል?	
12	ጥያቄ ቁጥር 11 አዎ ከሆነ የጎንዮሽ ጉዳቱ ምን ነበር?	የሰዉነት መዛል ☐ ራስን ማዞር ☐ የክብዳት መጨመር ☐ የቆዳ ላይ ሽፍታና ማሳከክ ☐ የድድ መበጥ ☐ ያልተለመደ የባህርይ ለዉጥ ☐ ሌላ/ሌሎች (ይገለጹ) _____
13	የተወሰዱት እርምጃዎች ምን ነበሩ?	_____

Annex V: Data extraction format from patients medical records

1. Weigth of the child_____

2. Investigations

EEG ☐ Normal ☐ Epileptiform discharge (focal/generalized)

☐ Abnormal but no definite epileptiform discharge

MRI ☐ Normal ☐Abnormal (specify) _____

CT scan ☐ Normal ☐Abnormal (specify) _____

3. Therapeutic drug monitoring Yes ☐ No ☐

If yes, for which anti-seizure medication/s	Serum level of ASMs
1. Carbamazepine ☐	
2. Phenobarbitone ☐	
3. Phenytoin ☐	
4. Valproic acid ☐	
5. other (specify)_____	

4. When did the first seizure episode occur? _____

5. How old was the patient when he/she encountered the first seizure episode? _____

6. When did he/she encounter the recent seizure episode? _____

7. Diagnosis (seizure type)_____

8. When did anti-seizure medication(s) treatment started? _____

9. How long has your child been in anti-seizure medications?_____

10. How many anti-seizure medications do he or she takes?

11. Type of ASM(s) therapy Monotherapy ☐ Poly-therapy ☐

12. Prescribed anti-seizure medication(s)

Regimens of anti-seizure medication(s)	Dose/route/frequency

13. Comorbidities Yes ☐ No ☐

If yes, what are the comorbid conditions?	
Psychiatric conditions ☐	Cerebral palsy ☐
Malnutrition ☐	Hypertension ☐
Heart failure ☐	Diabetes mellitus ☐
Intelletually disability ☐	
Any (specify)_____	

14. Drugs prescribed other than anti-seizure medication(s)?

☐ Yes ☐ No

15. If yes for question 14 specify_____

16. Was there any experienced adverse effects related to ASM(s)? Yes ☐ No ☐

If yes,what type of adverse effects occurred?

Depressed mood ☐ Vitamin D deficiency ☐ Bone pain and fracture ☐

Epigastric pain ☐ Confusion ☐ Weakness ☐

Weight gain ☐ Blurring of vision ☐ Headache ☐

Nightmare ☐ Forgetfulness ☐ Skin rash ☐

Irritability ☐ Gingivial hyperplasia ☐

other/s (specify)_____

17. Seizure free period_____

18. Seizure control status Controlled ☐ Uncontrolled ☐

If it is uncontrolled, what is the frequency of seizure during last one year

None ☐ 1-5 times ☐ 6-10 times ☐ greater than 10 times ☐

Name and signature of principal investigator_____