Assessment of Drug Therapy Problems among Ambulatory Epileptic Patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Beshir Bedru entitled ***"Assessment of Drug Therapy Problems among Ambulatory Epileptic Patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia"*** and submitted in partial fulfilment 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 with respect to originality and quality.

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Abstract

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About 90% of epileptic patients in developing countries are not receiving appropriate treatment due to different reasons. Recurrence and breakthrough seizures can be caused by both drug and non-drug related problems such as inadequate or suboptimal antiepileptic regimens, adverse reaction and poor adherence. This may lead to reduced quality of life, increased overall health care cost and increased risk of morbidity and mortality. Management of epilepsy especially in developing country is challenging and drug therapy problems (DTPs) and poor medication adherence might be the major reasons. There is limited evidence regarding DTPs in epileptic patients thus this study aimed to asses DTPs and medication adherence among ambulatory epileptic patients at Tikur Anbessa Specialized Hospital (TASH). A hospital based cross sectional study was conducted on 291 epileptic patients who had follow up at TASH. Data collection was done through patient interview and medical charts review. Epi Info7.2.1 was used for data entry and data was analysed using SPSS version 21. Descriptive statistics, cross-tabulation, binary and multiple logistic regressions were utilized and $P < 0.05$ was used to declare association. Phenobarbital (67%) and phenytoin (33.3%) were among the frequently prescribed antiepileptic drugs both as monotherapy and combination therapy and only (18.6%) of the study participants had controlled seizure. DTP was found in 70.4 % of the study participants. Adverse drug reaction (41.5%) was the top DTPs identified followed by ineffective drugs (27.8%), drug interaction (12.8%) and inappropriate dose (11.9%). Headache, depression and epigastric pain were frequently reported adverse drug reaction. Carbamazepine was involved in majority of the drug interaction and phenobarbital in inappropriate dose (dose too high). The rate of medication adherence was 57.3% and the common reasons for non-adherence were forgetfulness, medication unavailability and fear of side effects. Number of medications taken by the patients had a significant association with occurrence of DTPs, whereas source of medication and seizure free periods were found to have significant association with poor adherence. Prevalence of DTPs among ambulatory epileptic patients was high and about half of the patients were non adherent for their medication.

Key words: Drug Therapy Problems, Epilepsy, Tikur Anbessa Specialized Hospital

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List of Abbreviations and Acronyms

AAN	American Academy of Neurology
ADR	Adverse Drug Reaction
AEDs	Anti-Epileptic Drugs
AOR	Adjusted Odds Ratio
CBZ	Carbamazepine
COR	Crude Odds Ratio
CPS	Complex Partial Seizure
DRPs	Drug Related Problems
DTPs	Drug Therapy Problems
EEG	Electroencephalograph
GTCS	Generalized Tonic Clonic Seizure
HAART	Highly Active Antiretroviral Therapy
ILAE	International League against Epilepsy
MMAS	Morisky Medication Adherence Scale
MTM	Medication Therapy Management
NICE	National Institute for health and Care Excellence
PHB	Phenobarbital
PHT	Phenytoin
PI	Principal investigator
RVI	Retroviral Infection
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences
TASH	Tikur Anbessa Specialized Hospital
VPA	Valproic acid
WHO	World Health Organization

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1. Introduction

1.1. Background

Epilepsy is a neurologic disorder characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure, which is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain (Fisher *et al.,* 2005). In 2014, the International League Against Epilepsy (ILAE) revised the definition of epilepsy as a disease of the brain defined by any of the following conditions: (i) At least two unprovoked (or reflex) seizures occurring > 24 h apart; (ii) 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 ever the next 10 years; or (iii) diagnosis of an epilepsy syndrome (Fisher *et al.,* 2014).

There are two major categories of seizure types classified by the ILAE in 1981 named as partial seizures and generalized seizures. Partial seizure is characterized by begining in a local area of the brain. This type of seizure is further subdivided into simple partial and complex partial seizures. Epilepsy characterized by generalized onset seizures usually involves the entire brain simultaneously. But individual generalized seizure types include absence, myoclonic, tonic-clonic, atonic, tonic, and clonic symptoms. Since some seizure types co-exist, it is assumed that the classifications represent the predominant seizure type and in some cases, seizure type may remain unclassifiable (Ahmed and Spencer, 2004, Banerjee *et al.,* 2009).

More than 50 million people have epilepsy worldwide, more than three quarters living in low and middle income countries and about 2.4 million new cases occur each year (WHO, 2016). It is estimated that there are 5.5 million persons with epilepsy in India, 2 million in USA and 0.3 million in UK (Network, 2003). In Ethiopia a large community-based epidemiological study revealed the prevalence of epilepsy to be 5.2/1000 population (Tekle-Haimanot *et al.,* 1997). The incidence was 64/100,000 population as reported in a community-based study conducted in Mescan and Marko districts of rural central Ethiopia (Tekle-Haimanot *et al.,* 1990).

Diagnosing epilepsy in the early stage is challenging, especially in the absence of a witnessed account. It is mandatory to identify the seizure type whether generalized epilepsies or focal epilepsies, as this affects treatment choices, investigation, prognosis and counseling (Thurman *et al.*, 2011).

The ultimate goal of treatment for epilepsy is no seizure episode and no side effects with having an optimal quality of life (Kerr *et al.*, 2009). Therefore, the management should be individualized to eliminate seizures or reduce seizure frequency, while avoiding drug interactions and side effects as well as prevent other complications and achieve the best possible quality of life.(Rout and Kar, 2010, Henry and Conway, 2012).

Treatment should be started with monotherapy using conventional antiepileptic drugs (AEDs). The dose should be slowly built up until seizure control is achieved or side effects occur. If the initial treatment is ineffective or poorly tolerated then another AED can be tried. The dose of the second drug is slowly increased until adequate or maximum tolerated dose is reached. Combination therapy is considered when two attempts at monotherapy with AEDs have not resulted in seizure freedom (Glauser *et al.*, 2006).

Among AEDs, valproic acid (VPA) is contraindicated during pregnancy. It is associated with midline birth defects including spina bifida (6-10%) and autism-spectrum disorder in children of mothers exposed during pregnancy (Harden *et al.*, 2009). It is recommended to avoid enzyme inducer AEDs to combine with highly active antiretroviral therapy (HAART) regimen that contains protease inhibitors and non-nucleotide reverse transcriptase inhibitors as pharmacologic interaction may result in virologic failure, which leads to diseases progression and drug resistance (Birbeck *et al.*, 2012). The pharmacokinetics of most AEDs is complex, which makes dosing and monitoring difficult in most of epileptic patients. The complexity of medical problems and co-medications for patients requiring AEDs can result in an increased likelihood of drug-related problems & drug interactions, which in turn can affect seizure control and toxicity (Perucca, 2006). Enzyme-inducing AEDs such as carbamazepine (CBZ) may accelerate the metabolism of many drugs including antiretroviral, anti-tuberculosis (anti TB), and hormonal contraceptives thereby reducing their concentration by up to 50%. This may increase treatment failure and the risk of unwanted pregnancy (Blume, 2003).

Drug therapy problem (DTP) is any undesirable event experienced by a patient that involves or is suspected to involve drug therapy, and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve. They are central to pharmaceutical care practice. An infinite number of drug therapy problems exist because of the rapidly expanding array of drug products available, the growing number of diseases being recognized & diagnosed and the growing number of patients entering the health care system. All patient problems involving medications can be categorized into one of the seven types of drug related problems. These include unnecessary drug therapy, need for additional drug therapy, ineffective drug, dosage too low, adverse drug reaction, dosage too high and noncompliance (Cipolle *et al.,* 2012).

It would be much better to prevent DTPs than to correct them. But this is not always possible because of the complexity of pharmacotherapy, lack of training, and knowledge of health care providers and the behavior of medicine users (Christensen *et al.,* 2011). Even though one could analyze the medication and patient related factors during a medication review before a medicine is given to the patient, the evaluation of pharmacotherapy after it has been initiated still remains necessary to detect DTPs and optimize outcomes.

1.2. Statement of the Problem

In the case of most diseases, drug therapy will enhance health-related quality of life. However, inappropriate use of drugs may be harmful and lead to DTPs (Rahmawati *et al*., 2008). DTPs also may lead to reduced quality of life, increases overall health care cost and increases risk of morbidity and mortality (Dahal *et al.,* 2013). People who are dying due to inappropriate drug treatment is more than the number of peoples dying due to breast cancer, AIDS and traffic accidents (Donaldson *et al.,* 2000). The annual cost of drug-related morbidity and mortality in the USA is estimated to be $ 177 billion which is twice as much money as used to solve drug related problems (DRPs) and adverse drug events than on the drug themselves (Ernst and Grizzle, 2001).

About 90% of epileptic patients in developing countries are not receiving appropriate treatment due to the cultural attitude, lack of prioritization, poor health care system, economic problem and inadequate supply of AEDs (Scott *et al.,* 2001). Studies in India reported that 36% of prescriptions were irrational as per the global standard ILAE guidelines (George *et al.,* 2016)**.** A study in Ethiopia, Bishoftu general hospital, revealed that only 54.4% of AED use was in accordance with the indication set in the national standard treatment guideline. According to this study there were 16.5% under dose, 1.1% over dose and 12.7% AED use was with incorrect duration and 5% potential drug-drug interactions (Rishe *et al.,* 2015).

Recurrence and breakthrough seizures can be caused by a variety of triggering factors which are related to both drug and non-drug-related problems such as inadequate or suboptimal antiepileptic regimens, poor adherence, adverse reaction and emotional stress. AED therapy is often associated with a variety of adverse effects, which may be the reason for non-adherence, leading to a poor quality of life being endured by epileptic patients. There was evidence to suggest that adherence to medications among patients with epilepsy was suboptimal (Tsiropoulos *et al.,* 2009), which might be due to DTPs including ADRs. Previous studies have shown that non-adherence to AEDs was associated with increased mortality, emergency department visits, hospitalizations, fractures and head injuries (Koshy, 2012). There was a negative correlation between adherence and frequency of seizure. Patients with poorly controlled epilepsy were more anxious, and expected a longer duration of their epilepsy (Jones *et al.,* 2006). Thus, management of epilepsy especially in developing country is challenging and assessment of adherence should be routine a practice. Further recognition

and support should be given to patients who have poor seizure control, since they are more likely to be more anxious and have wrong illness and treatment beliefs (Jones *et al.*, 2006).

However, studies regarding DTPs in ambulatory neurologic disorder like epilepsy are limited in Ethiopia. Therefore, this study attempted to assess DTPs and medication adherence that influence treatment outcome in chronic ambulatory care. Therefore, based on the study result medication therapy management (MTM) which is a distinct service or group of services that optimize therapeutic outcomes will be provided for the patients by integrating with clinical pharmacy services. In addition, the thesis may be useful to other researchers as a baseline reference material while conducting further studies on related topics. The findings of this study might also help to influence the development of treatment guidelines and policies for the prevention and management of DTPs in epilepsy care. This in turn, might improve the quality of care and treatment outcomes.

1.3. Literature Review

Even though the findings were greatly varied on prevalence of seizure type, many studies revealed that the most identified seizure type was generalized tonic clonic seizure (GTCS). Thus the highest magnitude was found in India (82%) (Sebastian *et al.,* 2013) and Bangladesh (74%) (Habib *et al.,* 2013), but relatively lower in Saudi Arabia (65%) (Gabr and Shams, 2015), in Pakistan (47 %) (Morgan *et al.,* 2004) and in Singapore (63%) (Hsieh and Huang, 2009). Studies in Ethiopia have produced different results as regards to seizure type in different areas. For example 80% of the patients were diagnosed as GTCS in Jimma referral hospital (Gurshaw *et al.,* 2014), 48.6% in Bishoftu hospital (Rishe *et al.,* 2015) and 72.91% in Gondar referral hospital (Birru *et al.,* 2016).

Studies also revealed that selection of AEDs were different in different areas. CBZ was mainly prescribed in different countries ranging from 37% to 67 %. The lowest found in UK 37% (Jones *et al.,* 2006) and the highest in Bangladesh (67%) (Habib *et al.,* 2013). However, valproic acid (VPA) was the most frequently prescribed AED in most of the countries including Saudi Arabia (60%) (Gabr and Shams, 2015) and phenytoin (PHT) in India (42%) (Sebastian *et al.,* 2013). In Ethiopia, studies showed that the commonly prescribed AED was phenobarbital (PHB) in Jimma referral hospital (55%) (Gurshaw *et al.,* 2014) and Bishoftu hospital (92.8%) (Rishe *et al.,* 2015). Similarly a study in Gondar referral hospital revealed that PHB was the most frequently prescribed monotherapy (75.95%) followed by CBZ (15.18%) even though it was not the first-line agent for any type of epileptic case as per the standard treatment guideline (Birru *et al.,* 2016).

Several lines of evidences indicate that monotherapy was the preferred treatment modality ranging from 55% to 96 %. The highest frequency was found in developed countries like UK (96%) (Jones *et al.,* 2006). Studies in Asian countries reported 77% in Saudi Arabia (Gabr and Shams, 2015), 62% in India (Sebastian *et al.,* 2013) and 63% in Singapore (Hsieh and Huang, 2009). Ethiopian studies also reported a higher prevalence of monotherapy in Bishoftu hospital (88%) (Rishe *et al.,* 2015) and Gondar referral hospital (80.4%) (Birru *et al.,* 2016), but a lower one in Jimma referral hospital (55%) (Gurshaw *et al.,* 2014).

Unlike other chronic diseases there were no accessible data regarding DTPs among epileptic ambulatory patients that includes the entire DTP components. However, there are studies which were done on parts of the DTPs. A study in India showed that forty five adverse drugs

reactions were reported during the study period. PHT 53.3% and VPA 26.7% were the major drugs implicated for ADRs (Sebastian *et al.,* 2013). According to AEDs utilization in Bishoftu hospital 54.4% was in accordance with the national standard treatment guideline, while 2.9% were inappropriate. In addition, 44% of the indications were found to be difficult to categorize as correct or incorrect indications, since the type of epilepsy was not identified & written on the patient card. There were 16.5% under dose, 1.1% over dose and 12.7% AED use was with incorrect duration. There were potential drug-drug interactions in 5% and headache was the commonest (47.8%) adverse effect followed by irritability 13.6% (Rishe *et al.,* 2015). In a similar study in Jimma referral hospital, 33.4% of the patients experienced adverse effects related to AEDs therapy. Headache was the commonest (21.6%) followed by epigastric pain (18.5%), confusion (17.5%) and weakness (12.3%) (Gurshaw *et al.,* 2014). A study in Gondar referral hospital revealed that 17.6% patients reported that they had experienced adverse effects related to their AED therapy. Hypersomnia was the commonest adverse effect reported (9.3%) (Birru *et al.,* 2016).

In Malaysia hospitalized epileptic patients, the DTPs identified were dose inadequacy (51.9%), under reporting of adverse effects (76.2%), under-utilization of therapeutic drug monitoring services (41.5%) and inappropriateness of therapy in patients with liver disease. (Manan *et al.,* 2014).

Even thought there was no accessible data on DTPs among ambulatory epileptic patients, similar studies on other chronic diseases reported that DTPs were very common among chronic ambulatory patients. The prevalence was 80.7% among hypertensive ambulatory patients in Adama hospital. In this study drug interaction (58.7%) was the commonest and numbers of drugs used and number of co-morbidities were significantly associated with DTPs (Hussein *et al.,* 2014). The prevalence among diabetic patients in Wolaita Sodo University hospital was 83.1%, in which need additional drug (56.37%) was the commonest. Age ≥ 65, comorbidity, polypharmacy and history of hospitalization were independent predictors DTPs (Hailu *et al.,* 2017). Similarly, among patient with cardiovascular disease in Gebretsadik Showa general hospital, the prevalence was 72%, in which need additional drug therapy 33% was the commonest (Kaleab and Mariam, 2017).

Medication non-adherence to antiepileptic medications is detrimental to the perceived outcome of treatment. Non-adherence to medication regimen accounts for substantial worsening of disease, death and increased health care costs (Getachew *et al.,* 2014). Previous

studies conducted to assess adherent status of epileptic patients to their medications produced varied results. Adherence was higher in India (98.6%) (Sebastian *et al.,* 2013) and Palestine (85.3%) (Sweileh *et al.,* 2011) and relatively lower in China (51.9%) (Liu *et al.,* 2013), South Africa (54.6%) (Egenasi *et al.,* 2015), Jimma referral hospital (58.5%) (Getachew *et al.,* 2014) and UK (59%) (Jones *et al.,* 2006). It was moderate in USA (71%) (Hovinga *et al.,* 2008) and Gondar referral hospital (70.8%) (Abula and Worki, 2001).

Studies investigating factors affecting adherence rate have identified knowledge of AEDs (Jones *et al.,* 2006), frequency of seizures (Jones *et al.,* 2006, Gabr and Shams, 2015), duration of illness, uncontrolled seizures and increasing treatment complexity (Sweileh *et al.,* 2011) and side effects of the drugs (Liu *et al.,* 2013) to affect adherence rate of epileptic patients. However, age, sex, educational status, income, religion and place of residence were identified as factors not affecting adherence of the patients (Johnbull *et al.,* 2011, Liu *et al.,* 2013). A similar study in Saudi Arabia on adolescent epileptic patients showed that number of administered drugs and the regularity of the relationship between patients and their healthcare providers were the most important factors that significantly affect patients' adherence to their medications. This study also revealed that forgetfulness, inability to obtain medication and fear from side effects of drugs were the most common causes of non-adherence among these group of patients (Gabr and Shams, 2015).

2. Objectives

2.1. General Objective

The general objective of this study was to assess drug therapy problems and medication adherence among ambulatory epileptic patients at neurology clinic of Tikur Anbessa Specialized Hospital

2.2. Specific Objectives

- ✓ To determine the prevalence of drug therapy problems
- ✓ To identify predictors of occurrence of drug therapy problems
- ✓ To determine the rate of adherence of patients to AEDs
- ✓ To identify factors affecting adherence of epileptic patients to AEDs

3. Methods

3.1. Study Setting

The study was conducted at TASH, which is the largest referral hospital in the country. TASH was established in 1972 with bed capacity of 700 beds and serving as a teaching specialized hospital for medical and health science students. In 1998 TASH was transferred to Addis Ababa University from the Federal Ministry of Health, and it has since become a University teaching specialized hospital. TASH is now the main teaching specialized hospital for both clinical and preclinical training of most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions throughout the country are rendered to the whole nation (AAU, 2015). Among the specialty clinics in TASH, neurology is one of them and serving for a comprehensive neurologic case including epilepsy. The clinic provides the service only for epileptic patients one day per week (every Monday). On average 65 patients are served per day and a total of 780 patients are expected to visit the clinic within the three month period.

3.2. Study Design and Study Period

A hospital based cross sectional study was done in ambulatory epileptic patients who had a follow-up at neurology clinic by patient interview and medical chart review. Data collection was done from June to August 2017.

3.3. Source and Study Population

The source population of the study was all epileptic patients attending neurology clinic of TASH for the management of epilepsy during the study period. The study population constituted all epileptic patients attending TASH and fulfilling the inclusion criteria.

3.4. Inclusion and Exclusion Criteria

3.4.1. Inclusion Criteria

- ✓ Patients who had follow-up at adult neurology clinics of TASH and diagnosed as seizure disorder or Epilepsy.
- ✓ Patients who had been on AEDs treatment for at least six months
- ✓ Patients who had complete medical records
- ✓ Patients who were willing to participate in the study

3.4.2. Exclusion Criteria

- ✓ Patients without confirmed diagnosis

3.5. Sample Size and Sampling Technique

Sample size was computed based on single population proportion formula by using the following assumption. The proportion (P) of DTP in this group is taken as 50% to get possible minimum sample size.

$$n = \frac{Z_{\frac{\alpha}{2}}^{2} \times P(1-P)}{d^2}$$

Where: Proportion of DTPs (p) = 50 %

Confidence level of 95 % chosen with z-value of 1.96

Margin of error (d) = 5%

n = 384 (sample size without adjustment and with p = 50%)

The total population of epileptic patients who have follow up at TASH (N) is around = 1100

$$\text{Corrected sample size} = \frac{n\,XN}{n+N}$$

By using the correction formula the sample size was 285 from 1100 study population. With the addition of 10% contingency 312 patients were included in the study.

Systematic random sampling method was used to recruit samples for the study in each day of the data collection process. The sampling fraction (k) was varying in the different days of data collection as the total number of study population varies in different days. It was calculated through dividing the number of study population available each day by the maximum possible number of patients' that could be interviewed on that day. Then every k^{th} patient was then interviewed following physicians' visit (usually every two or three patients).

3.6. Study Variables

3.6.1. Dependent variables

- ✓ DTPs
- ✓ Adherence of patients to their AEDs

3.6.2. Independent Variables

Demographic variables (age, sex, educational status, marital status, occupation, place of residence, source of medication)

Patient characteristics (type and number of prescribed AEDs, duration of treatment with AEDs, seizure free period and co morbid conditions)

3.7. Data Collection and Management

3.7.1. Data Collection Instrument and Collection Process

DTPs instruments

The relevant information about each patient (demographic data and patients clinical characteristics) was collected from patient interview questionnaire (annex I). Laboratory results, current medications, co-morbidities with their treatment, relevant previous medical and medication histories were collected using data abstraction format from chart (annex II). Appropriateness of medical therapy was evaluated using various references and guidelines like National Institute for Health and Care Excellence (NICE), American Academy of Neurology (AAN), ILAE guideline and Ethiopian treatment guideline for general hospital 2014. Micromedex drug interaction checker was used to identify drug-drug interactions and only absolute contraindications and major drug interaction were selected as a significant drug interaction, whereas moderate and minor interactions were omitted.

Finally, DTPs were identified from the collected data using the pretested data collection abstract form from the above guidelines. The identified DTPs were recorded and classified by using DTP registration format which was taken from Cipolle *et al*, (2004) with modification (annex III).

ADRs were identified from the patient reports (experiencing undesired effects) and from medical charts which were already recorded by physician.

Adherence assessment

Adherence of epileptic patients was measured using a Morisky Medication Adherence Scale-8 (MMAS-8) (Annex I part III). The MMAS-8 is a generic self-reported, medication-taking behavior scale, used for a wide variety of medical conditions. It consists of eight items focusing on past medication use patterns with a scoring scheme of “Yes” = 1 and “No” = 0. The last item has a five-point Likert response that was used with options “never”, “once in a while”, “sometimes”, “usually”, and “always.” In this Likert scale, values ranging from 0 to 1 was given at a specified interval of 0.25 with “0” given for “never” and “1” given for

"always". The items was then summed up to give a range of scores from high adherence to low adherence with a maximum score of 8.

3.7.2. Recruitment of Data Collectors and Training

Three data collectors (nurses) were recruited for patient interview and the principal investigators (PI) and one clinical pharmacist were involved in chart review. The actual DTPs were identified by the PI. One full day training was given to the data collectors to familiarize them with the data collection instrument as well as how to collect the necessary data from charts and how to conduct patient interview.

3.7.3. Data Quality Assurance

Before the actual data collection, pretest was done on 5 % of the sample size to ensure the appropriateness of the data collection instruments and the tool was re-prepared with some modifications after a thorough and deep review of inputs obtained during the pre-test. During training of the data collectors the objective of the study and methods of data collection was explicitly discussed to avoid any ambiguity. The PI closely supervised the data collection process and the collected data was checked on daily basis during data collection.

3.8. Data Analysis

The raw data collected from all the participants was checked for appropriateness and quality before data entry. The data was then entered by using Epi Info version 7.2.1 and analyzed using Statistical Package for Social Science (SPSS) version 21.

Descriptive statistics such as frequency, percentage, mean and standard deviation (SD) was used to summarize patients' characteristics. Tables and charts were used to present the results.

Univariable binary logistic regression analysis was performed to relate each independent variable to DTPs and adherence. Among the univariable analysis, those variables with $p<0.25$ were selected for multi-variable binary logistic regression analysis. Multi-variable binary logistic regression analysis was used to assess predictability of the independent variables to DTPs and rate of medication adherence. P value < 0.05 was considered statistically significant.

3.9. Ethical Consideration

Letter of ethical clearance was obtained from College of Health Sciences, Institutional Review Board. Verbal consent from each patient was requested to participate for the interview and to extract data from their medical charts. Patients were informed about the objective of the study and they were told that they have full right to refuse their participation at any time, and this by no means affect the service they get from the institution. Privacy and confidentiality was ensured during patient interview and review of patient medical charts. Thus, name and address of the patient was not recorded in the data abstraction formats.

3.10. Operational Definitions

Adherent: If the MMAS - 8 score was ≤ 2.

Non-adherent: If the MMAS - 8 score was > 2.

Treatment outcome: It is to mean whether seizure is controlled or uncontrolled.

Controlled seizure: Seizure free period of ≥ 2 years.

Uncontrolled seizure: Seizure free period of < 2 years.

Unclassified seizure: The diagnosis was documented as epilepsy/seizure disorder without any classification

DTP: is any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve.

DRP: is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.

ADRs: any noxious, unintended, and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy and bothersome adverse effects complained by the patient, was included.

4. Results

4.1. Socio Demographic Characteristics of the Study Participants

From 312 study participants enrolled, 291 were candidate for analysis and 21 were excluded because of incompleteness of the data. Mean age of the participants was 30.2 ±11.4 years and half of them (50.2%) were young adults. Majority of them (63.6%) were single and were from Addis Ababa (81.1%). Regarding their education status, 36.1% had secondary school education, while 5.5% had no formal education. Among the study participants, 38.5% were unemployed and 17.2% were students. Almost half (48.1%) of the patients got their medication for free (Table 1).

Table 1: Socio demographic characteristics of epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Variables		Number (n)	Percentage (%)
Sex	Male	154	52.9
	Female	137	47.1
Age	Adolescent (<18)	39	13.4
	Young adult (18-30)	146	50.2
	Adult (31-60)	99	34.0
	Elderly (>60)	7	2.4
Marital status	Single	185	63.6
	Married	97	33.3
	Divorced	5	1.7
	Widowed	4	1.4
Residential area	Addis Ababa	238	81.8
	Out of Addis Ababa	53	18.2
Educational status	No formal	16	5.5
	Primary	88	30.2
	Secondary	105	36.1
	Tertiary	82	28.2
Occupation	Unemployed	112	38.5
	Employed	69	23.7
	Private/ merchant	49	16.8
	Student	50	17.2
	Daily labourer	2	0.7
	Farmer	6	2.1
	Others*	3	1.0
Source of medication	Free	140	48.1
	Payment	151	51.9

*** Pension**

4.2. Clinical Characteristics of the Study Participants

GTCS was the commonest (66.3%) seizure type in the study participants followed by focal with secondary generalization. Majority of the the study participants (83.8%) had follow up for more than 2 years. Two-third (65.6%) of the study participants had seizure free period below 1 year and only 7.7% of the patients had seizure free period of more than 5 years. Most of the patients (41.2%) had 1-5 times seizure frequency per year and 12.7% of them had seizure frequency more than ten seizure episode in the previous one year. Sixty eight (23.4%) of them had chronic comorbid conditions and Retroviral Infection (RVI) was the commonest one followed by Hypertension (HTN). The detail clinical characteristics of the participants are presented in (Table 2). Among the study participants, only 54 (18.6%) patients had controlled seizure (Figure 1).

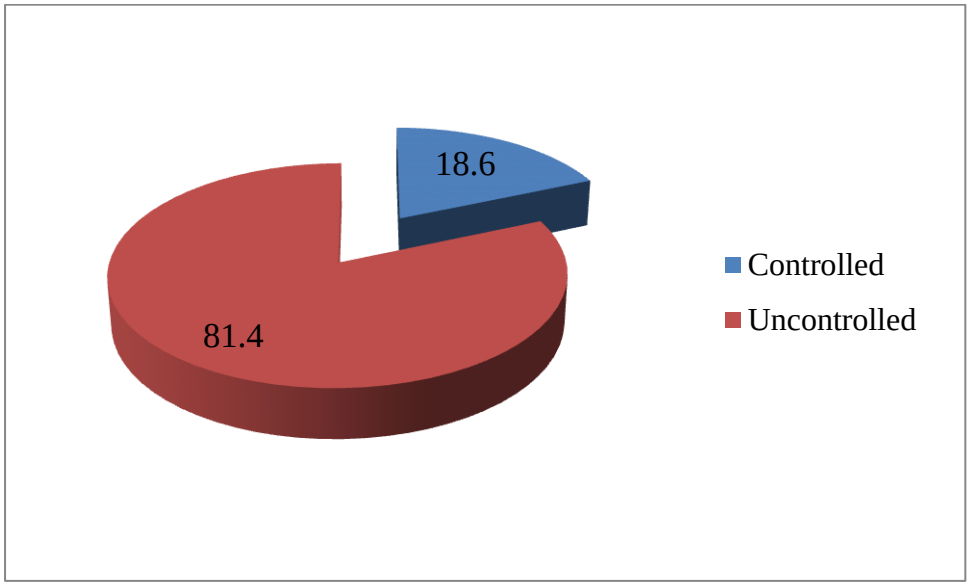

Figure 1: Seizure control status of epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Table 2: Clinical characteristics of epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Variables		Number (n)	Percentage (%)
Types of seizure	***Generalized seizure***	197	67.7
	GTCS	193	66.3
	Myoclonic	3	1.0
	Absence	1	0.3
	Partial seizure	71	24.4
	Simple partial	19	6.5
	Complex partial	23	7.9
	Focal with secondary generalization	29	10.0
	Unclassified*	23	7.9
Follow up years	< 2 years	49	16.8
	2-5 years	53	18.2
	6-10 years	69	23.7
	>10 years	120	41.2
Seizure free period	< 1 year	191	65.6
	1-2 years	46	15.8
	2-5 years	33	11.3
	>5 year	21	7.7
Number of seizure episode per year	None	102	35.1
	1-5	120	41.2
	6-10	32	11.0
	>10	37	12.7
Co-morbid conditions	RVI	20	6.9
	CRVHD/CHF	8	2.7
	Major depressive disorder	10	3.4
	Migraine headache	3	1.0
	Mental retardation	5	1.7
	HTN	12	4.1
	Stroke	7	2.4
	Others	14	4.8

"Unclassified seizure" was seizure which is diagnosed by the physician as "Epilepsy" or "seizure disorder".

GTCS: **Generalized Tonic Clonic Seizure,** ***RVI*****: Retroviral Infection,** ***CHF*****: Congestive Heart Failure,** ***CRVHD:*** **Chronic Rheumatic Valvular Heart Disease,** ***HTN:*** **Hypertension,**

4.3. Pattern of Antiepileptic Drug Uses among the Study Participants

Majority (58.8%) of them were on monotherapy regimen followed by dual (33.3%) and triple therapy (7.2%). Phenobarbital (196, 67.0%) was the most frequently prescribed AEDs among the study participants both as monotherapy and combination therapy followed by PHT (97, 33.3%), CBZ (79, 27.1) and VPA (55, 18.9%). PHB + PHT was the most frequently used dual therapy regimen. One fourth (25.1%) of the study participants were taking more than two medications with mean and SD of 2.03±1.27 medications per day (Table 3).

Table 3: Pattern of medication use among epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Variables		Number (N)	Percentage (%)
Number of AEDs used	One	171	58.8
	Two	97	33.3
	Three	21	7.2
	Four	2	0.7
AEDs use Pattern	PHB	93	32.0
	PHT	35	12.0
	CBZ	32	11.0
	VPA	17	5.8
	LAMO	1	0.3
	PHB+ PHT	30	10.3
	PHB+CBZ	17	5.6
	PHB+VPA	15	5.2
	PHB+LAMO	1	0.3
	PHT+CBZ	13	4.5
	PHT+VPA	9	3.1
	CBZ+VPA	7	2.4
	PHB+PHT+CBZ	4	1.4
	CBZ+VPA+PHB	4	1.4
	PHB+PHT+VPA	1	0.3
	PHB+PHT+CLONA	1	0.3
	Others *	11	3.8
Total number of drugs (AEDs + others)	1	120	41.2
	2	97	33.3
	>2	74	25.5

Others *: different combination of the above AEDs including quadruple therapy.

PHB: phenobarbital, PHT: phenytoin, CBZ: carbamazepine, VPA: Valproic acid LAMO: lamotrigine, CLONA: clonazepam

Regarding AEDs use based on seizure type, while PHB followed by PHT were frequently used for generalized seizure, CBZ followed by PHB were frequently prescribed AEDs for partial seizure. PHB was the most frequently used AEDs for unclassified seizure and the use of VPA was low for all seizure type (Table 4).

Table 4: Types of antiepileptic drugs prescribed with corresponding seizure type among epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Medication pattern	Types of seizure			
	Generalized seizure	Partial seizure (focal)	Unclassified	Total
PHB	69	14	10	93
PHT	25	10	0	35
CBZ	12	18	2	32
VPA	14	3	0	17
LAMO	1	0	0	1
PHB+ PHT	25	1	4	30
PHB+CBZ	8	5	4	17
PHB+VPA	13	2	0	15
PHB+LAMO	1	0	0	1
PHT+CBZ	3	10	0	13
PHT+VPA	5	2	2	9
CBZ+VPA	3	4	0	7
CBZ+VPA+PHB	3	1	0	4
PHB+PHT+CBZ	4	0	0	4
PHB+PHT+VPA	1	0	0	1
PHB+PHT+CLONA	1	0	0	1
Others*	9	1	1	11
Total	197	71	23	291

Others* Different combinations of the above drugs including four drug combination.

PHB: phenobarbital, PHT: phenytoin, CBZ: carbamazepine, VPA: Valproic acid
LAMO: lamotrigine, CLONA: clonazepam

4.4. Drug Therapy Problems

A total of 352 DTPs were identified from 205 (70.4%) of the study participants. Among these patients 1 DTP was identified in 102(49.8%), 2 DTPs in 73(35.6%) and more than two DTPs in 30(14.6%) (Figure 2).

ADRs followed by inappropriate drug selection and drug interaction were the major DTPs found in the present study (Table 5). Average number of DTPs per patient was 1.2.

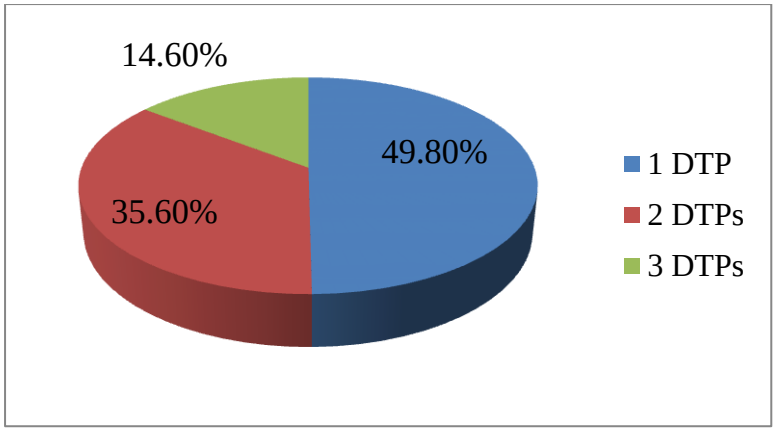

Figure 2: Number of drug therapy problems among epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Table 5: Types of drug therapy problems identified from epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

DTPs		No. of DTPs	Total	(%)
Drug interaction		45	45	12.8
Adverse drug reaction	Undesired effect	144		
	Contraindications	2	146	41.5
Ineffective drugs	Inappropriate drug selection	80		
	Condition refractory to the drug	18	98	27.8
Need additional therapy	Untreated medical condition	13		
	Need synergistic/potentiating	5	18	5.1
Inappropriate dose	Dose too low	24		
	Dose too high	18	42	11.9
Unnecessary drug therapy	No medical indication	2		
	Duplicate therapy	1	3	0.9
Total			352	100

A total of 45 significant drug interactions were identified in 38 (13.1%) study participants among them CBZ+ PHT had the highest frequency (Figure 3).

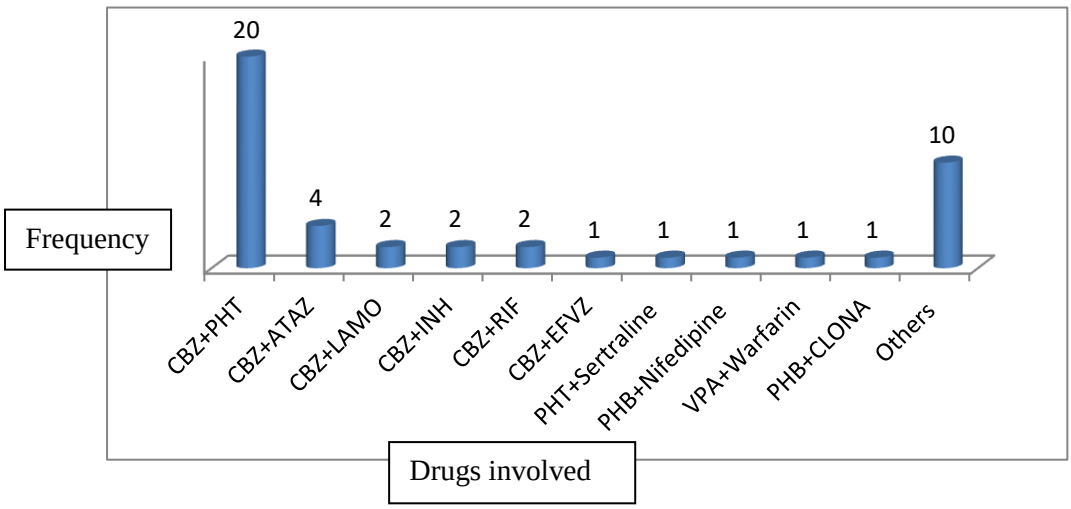

Figure 3: Type of drugs involved in drug interaction and their frequency from epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

ATAZ: Atazanavir, EFAZ: Efavirenz, INH: Isoniazid, RIF: Rifampicin, CLONA: clonazepam

About half (49.5%) of the participants experienced ADRs that could possibly associated with AEDs. Headache, depression and epigastric pain were the top three ADRs encountered (Table 6).

Table 6: Types and prevalence of ADRs identified from epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Types of adverse drug reaction	Frequency (N)	Percentage (%)
Headache	39	27.1
Depression	36	25.0
Epigastric pain	35	24.3
Gingival hyperplasia	16	11.1
Hypersomnia	28	19.4
Forgetfulness	18	12.5
Weight gain	9	6.3
Confusion	15	10.4
Skin rash	4	2.8
Blurring of vision	7	4.9
Weakness	16	11.1
Others *	10	6.9
Total	144	100

***Others include irritability, ataxia, tremor**

DTPs appeared to be common in patients with uncontrolled seizure (Figure). While a quarter of patients did not have DTPs in patient with uncontrolled seizure, this rate was nearly half in those with controlled seizure (r = -0.264, P= 0.000).

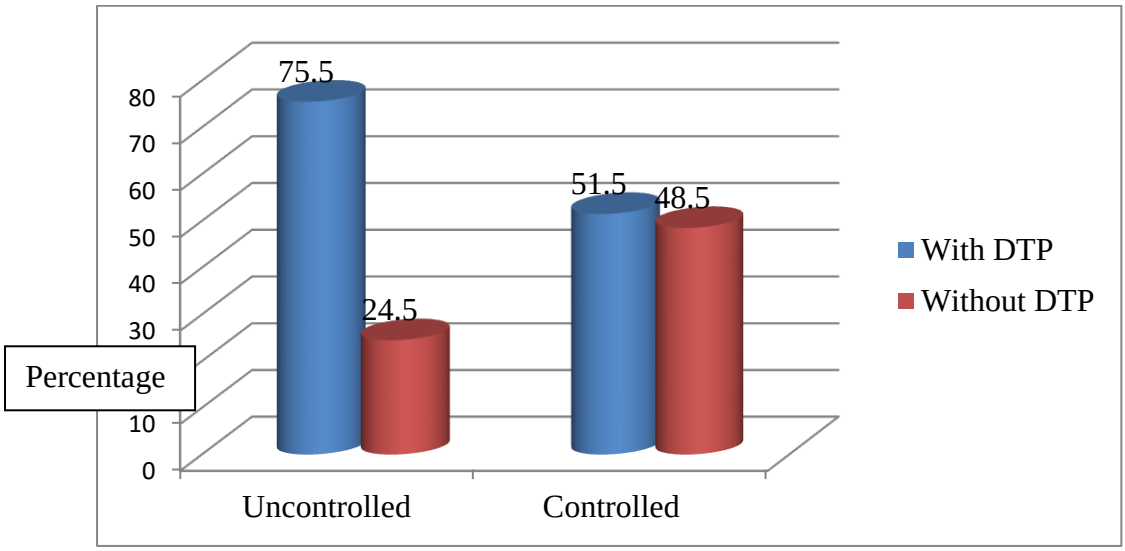

Figure 4: Distribution of DTPs based on seizure control status among epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

4.5. Adherence Status and Possible Reasons for Non-Adherence

Determination of adherence using the Morsky scale revealed that 129 (44.3%) of the participants had poor adherence, while 123(42.3%) and 39(13.4%) of them had medium and good adherence, respectively. For the purpose of data analysis, the original three categories of adherence were recategorized in to two and thereby participants were dichotomized. Accordingly, high and medium adherence were re-assigned as adherent with a score of less than or equal to two and low adherence was regarded as non-adherent with a score of greater than two (Figure 5). The major reason for poor adherence was forgetfulness followed by patient feeling as cured, medication unavailability, patient disbelief on drug effectiveness and fear of drug side effects (Table 7).

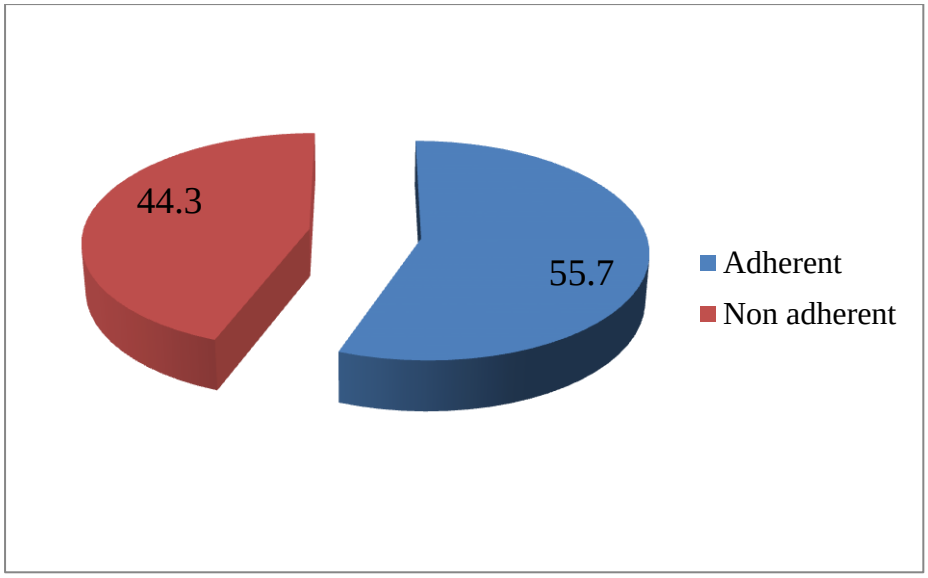

Figure 5: Adherence status of epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Table 7: Possible reasons for non-adherence reported by epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

		Number (N)	Percentage (%)
Reason for non adherence	Forgetfulness	141	48.5
	Unavailability of the medication	20	6.9
	Fear of side effect	18	6.2
	Patient felt as cured	22	7.6
	Patient disbelief on drug effectiveness	19	6.5
	Drug was expensive	3	1.0
	Others*	29	10.0

Others* include starting other alternative and traditional treatment (holly water and quranic medicine), patient prefers not to take, regimen complexity, dispensing error, unawareness of patient for medication changes.

4.6. Predictors of Occurrence of Drug Therapy Problems

The identification of risk factors for DTPs may be helpful in finding patients at risk. These patients could then be given special attention, with the hope of avoiding overt DTPs. Age, gender, total number of medication and co-morbidity fulfilled the criteria for multi-variable logistic regression analysis. Number of medication was shown to be the only risk factor for the occurrence of DTPs. Patients who took more than 2 medications were 3.8 times more likely to develop DTPs as compared to patients who took one medication (AOR= 3.810 CI 1.409-10.30) (Table 8).

Table 8: Predictors of occurrence of drug therapy problems in epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Variables	**category**	**DTPs (%)**		**COR (95% CI)**	**AOR (95% CI)**	**P-Value**
		Yes	No			
Gender	Male	106(73.6)	48(32.7)	1.00	1.00	
	Female	38(23.6)	99(67.3)	1.18(0.711-1.957)	1.19(.667-2.13)	0.552
Age	<18	33(16.1)	6(7.0)	1.00	1.00	
	18- 30	104(50.7)	42(48.8)	0.450(0.176-1.153)	0.371(0.129-1.068	0.066
	30-60	65(31.7)	34(39.5)	0.348(0.133-0.911)	0.256(0.089-0.790	0.057
	>60	3(1.5)	4(4.7)	0.136(0.024-0.770)	0.135(0.017-1.081	0.059
Number of	1	73(35.6)	47(54.7)	1.00	1.00	
medications	2	71(34.6)	26(30.2)	1.758(0.985-3.140)	1.350(0.687-2.652)	0.383
	>2	61(29.8)	13(15.1)	3.273(1.594-6.719)	3.810(1.409-10.30)	0.008*
Co-	No	155(75.6)	68(79.1)	1.00	1.00	
morbidities	Yes	50(24.4)	18(20.9)	1.22(0.662-2.242)	1.475(0.286-1.607)	0.378

4.7. Determinant Factors of Non-Adherence

Educational status, seizure free years, source of medication, number of medication and occurrence of ADRs fulfilled the criteria for multi-variable binary logistic regression. Source of medication and seizure free period were shown to be determinant factor for non-adherence. The odds of being non adherent for patients who got their medication for free were increased by 2.3 times (AOR = 1.360-3.943) as compared to patients who pay for their medication. Being non adherent for patients with seizure free period of 1-2 years and 2-5 years were decreased by 64% and 54% respectively as compared to patients with seizure free period of below one year. But it was not statistically significant for patients who have seizure free period above five years (Table 9).

Table 9: Multivariable logistic regression analysis of factors associated with medication adherence among epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Variable	Category	Adherence N (%)		COR (95% CI)	AOR (95% CI)	P-Value
		Non adherent	Adherent			
Educational status	No formal	4 (3.1)	12 (7.4)	1.00	1.00	
	Primary	40(31.0)	48(29.6)	2.500(0.748-8.358)	2.848(0. 824-9.839)	0.098
	Secondary	46(35.7)	59(36.4)	2.339(0.708-7.730)	3.266(0. 939-11.355)	0.063
	Tertiary	39(30.2)	43(2 6.6)	2.721(0.810-9.141)	5.177(1.412-18.584)	0.013*
Seizure free years	< 1	98(76.0)	93(57.4)	1.00	1.00	
	1-2	14(10.9)	32(19.8)	0.415(0.208-0.827)	0.359(0.170-0.761)	0.007*
	2-5	11(8.5)	22(13.6)	0.474(0.218-1.032)	0.455(0.198-1.044)	0.043*
	>5	6(4.6)	15(9.2)	0.380(0.141-1.020)	0.368(0.129-1.050)	0.062
Source of medication	Paying	55(42.6)	96(59.3)	1.00	1.00	
	Free	74(57.4)	66(40.7)	1.957(1.224-3.128)	2.316(1.360-3.943)	0.002*
Number of mediations	1	45(34.9)	75(46.3)	1.00	1.00	
	2	45(34.9)	52(32.1)	1.442(0.837-2.485)	1.295(0.731-2.298)	0.098
	>2	39(30.2)	35(21.6)	1.912(1.060-3.449)	1.728(0.939-11.355)	0.063
Occurrence of ADRs	No	60(46.5)	87(53.7)	1.00	1.00	
	Yes	69(53.5)	75(46.3)	1.334(0.839-2.121)	1.273(0.784-2.080)	0.327

4.8. Examples of Drug Therapy Problems Identified in the Study Subjects

Table 10: Examples of drug therapy problems identified from epileptic patients attending at neurology clinic of Tikur Anbessa specialized Hospital, 2017

Sr. No.	Description of the drug therapy problem	Type of DTPs
1.	A 30 years old female patient with GTCS was on VPA 500 mg po daily and she became pregnant. She was taking the medication until 26 weeks of her pregnancy and then replaced by PHB 100 mg po daily.	VPA is contra indicated in pregnancy
2.	A 22 years old patient with uncontrolled GTCS (more than three attacks per week) was taking CBZ 200/ 400 mg po and VPA 1gm po bid for the past two years and serum concentration of VPA was 147.1 µg/ml (50-100 ug/ml). The patient was also experiencing ADRs like ataxia.	High dose Condition refractory to the medication ADRs
3.	A 14 years old female patient having uncontrolled partial seizure (seizure attack every other day) was taking VPA and PHB for more than three years however, CBZ and PHT are first line for partial seizure but they were not considered.	In appropriate drug selection
4.	A 55 years old patient with GTCS and HTN (uncontrolled BP=160/110 mm Hg) was taking PHB 100 mg daily and nifedipine 20 mg bid. PHB significantly decrease serum concentration of nifedipine which is thought to be the risk factor for uncontrolled BP.	Drug interaction between PHB and nifedipine.
5.	24 years old, 55 kg male patient with GTCS (uncontrolled and frequent seizure) was taking PHB 100/100/130 mg (330 mg po daily). The patient was complaining for side effects. Instead of vey high dose PHB it is recommended to add second AEDs as synergistic (add on therapy)	High dose of PHB Needs synergistic (second AEDs) In appropriate drug selection
6.	A 44 years old patient with GTCS, CRVHD and DVT. Thus the patient was taking VPA 500 mg po daily and warfarin prophylaxis 5 mg po daily. VPA can increase risk of bleeding by increasing serum concentration of warfarin and INR was 3.6 which is above the recommended range (2-3)	Drug interaction between VPA and wrfarin.
7.	A 27 years old male patient with uncontrolled GTCS (at least three episodes per week) was tried with different AEDs so far but no response. Currently he is on VPA 500/1500 mg , CBZ 600 mg bid and lamotrigen 25 mg bid and he claimed he is adherent for AEDs but still no improvement.	Condition refractory to the drugs Drug interaction (LAMO, VPA and CBZ)

8.	A 36 years old patient with uncontrolled GTCS (morethan three episodes per week) was taking VPA, CBZ and clonazepam. Serum concentration of these drugs were: CBZ 1.8 (4-12ug/ml and clonazepam 14ng/ml (20-70). The serum concentration was below the lower limit of therapeutic range and their dose was not increased. Further more CBZ decrease serum concentration of clonazepam.	Low dose of CBZ and clonazepam Drug interaction
9.	A 30 years old female patient with partial seizure and RVI was taking CBZ, zidovudine, lamivudine and atazanavir/ritonavir. CBZ is contra indicated in patients taking atazanavir/ritonavir due to their interaction	Drug interaction
10.	A 42 years old, 56 kg female patient with controlled (5 years seizure free period) was taking PHB 200 mg po bid (400 mg po daily). The patient didn't have recent EEG result but still continued with such high dose.	High dose of PHB
11.	A 23 years old female patient with controlled GTCS (seizure free period of 6 years) and normal EEG result was taking PHB 100/200 mg (300 mg daily). The patient was taking the PHB just for insomnia but she was experiencing other ADRs associated with PHB.	No medical indication ADRs
12.	A 23 years old female patient with GTCS, RVI and anaemia (RBC= 2.9, Hgb =7.9 and Hct = 18.6) was on 3TC/EVZ/atazanavir/ritonavir but no any treatment for anaemia (needs atleast iron supplementation).	Untreated medical condition (anaemia)
13.	A 22 years old female patient was taking PHB and CBZ. The patient has very poor adherence because of ADR (GI irritation) and refuse to take the medication appropriately.	Untreated medical condition(GI irritation) Poor adherence
14.	A 44 years old female patient with controlled seizure (seizure free period of 20 years) was taking PHT 100 mg po daily. She was told to tapper down and to stop it but she refused to do so.	No medical indication (dependency)

5. Discussion

The goal of drug therapy is to achieve defined therapeutic outcomes and improve the patient's quality of life while minimizing drug related complications. But inappropriate use of drugs during disease management may lead to DTPs. Identification of common types of DTPs is an important component of drug therapy and contributes to reduction of drug related morbidity and mortality. Therefore this study was carried out to asses DTPs and medication adherence in epileptic ambulatory patients in one of a tertiary care teaching hospital in Ethiopia.

In this study, GTCS (66.3%) was the commonest seizure type encountered, which is in line with a study conducted in Saudi Arabia (65%) (Gabr and Shams, 2015) and Bangladish (74%) (Habib *et al.,* 2013). But the prevalence is lower compared to a study in Jimma referral hospital in which GTCS was (80%) (Gurshaw *et al.,* 2014). This might be due to difference in qualification of expertise and availability of diagnostic tools used for classification of seizure type. Choice of the most appropriate AEDs depends on the proper classification of seizures type. Lack of proper classification of seizure type affects selection of drugs and treatment outcome (Azar and Abou-Khalil, 2008, Gurshaw *et al.,* 2014). In this study, 7.9% of the patients were not categorized to a specific seizure type that could possibly contributed to inappropriate drug selection and poor treatment outcomes.

The present study revealed that monotherapy (58.8%) was the preferred treatment modality. This finding is in concordance with the findings of Jimma referral hospital (54.5%) (Gurshaw *et al.,* 2014), India (62%) (Sebastian *et al.,* 2013) and Singapore (63%) (Hsieh and Huang, 2009). But it was lower than the findings in Bishoftu hospital (88%) (Rishe *et al.,* 2015) and in Gondar referral hospital (80.35%) (Birru *et al.,* 2016). The reason might be due to differences in the settings. This study was conducted in a tertiary care hospital, where complicated and uncontrolled seizures are referred, that might need combination therapy.

In this study, PHB (67.0%) was the most frequently prescribed drug both as monotherapy and combination therapy. PHB appears to be the most commonly used agent used in Ethiopia, as various local studies produced a proportion ranging from 55%-92.8% (Hailu *et al.,* 2012, Gurshaw *et al.,* 2014, Rishe *et al.,* 2015). However, the most frequently prescribed AEDs was VPA (60%) in Saudi Arabia (Gabr and Shams, 2015), CBZ (67%) Bangladesh (Habib *et al.,*

2013) and PHT (42%) India (Sebastian *et al.*, 2013). This might be due to cost of the drugs and their availability in resource limited settings.

According to this study, 65.6% of the study participants had a seizure free period of below one year and 81.4% of the patients had uncontrolled seizure. This finding showed the treatment is still suboptimal similar to other developing countries (Scott *et al.*, 2001) due to many reasons but DTPs like non-adherence to AEDs and inappropriate drug selection might be among the crucial reasons to compromise the treatment outcomes.

About 70% the study participants on a follow up at neurology clinic for the management of epilepsy had at least one DTP. This is in line with a finding in other chronic disease, which was 72% among patients having chronic cardiovascular disease in Gebretasik Showa General Hospital (Kaleab and Mariam, 2017). But this finding was lower than the findings obtained from hypertensive patients in Adama hospital (80.7%) (Hussein *et al.*, 2014) and diabetic patients in Wolaita Soddo University Hospital (83%) (Hailu *et al.*, 2017). The discrepancy might be due to hypertensive and diabetic patients have a number of other co-morbid conditions and use large number of medication that could possibly increase prevalence DTPs.

ADR (41.5%) was the number one frequently encountered DTP. An adverse effect retrieved from patient medical records is usually under-estimated. A study in Malaysia illustrated that most of the patients (31%) claimed to have at least one adverse effect but only 5% of the cases were documented in medical records (Manan *et al.*, 2014). Therefore, most accurate data had been obtained by questioning the patient directly in addition to adverse effects mentioned in medical records. A higher prevalence (82%) was obtained in a community based cohort study in Netherland (Wassenaar *et al.*, 2013) and 31% in Malaysia hospitalized epileptic patients (Manan *et al.*, 2014). The discrepancy could be due to difference in study design in which the higher prevalence was obtained from a cohort study where patients were followed for longer time. Among 144 patients complaining of ADRs, headache (27.1%), depression (25.0%), epigastric pain (24.3.0%) and hypersomnia (19.4%) were the most common adverse effect faced by patients. Gingival hyperplasia due to PHT was reported in 16 (11.1%) of the patients complaining for adverse effects. Similar findings were obtained, in which headache was the commonest (21.6%) in Jimma referral hospital (Gurshaw *et al.*, 2014) and (47.8%) in Bishoftu hospital (Rishe *et al.*, 2015) followed by epigastric pain (18.5%) and confusion (17.5%) (Gurshaw *et al.*, 2014).

Generally, AEDs are known for their frequent ADRs and most of them have overlapping cognitive and neurologic side effects. Other systemic adverse effect like epigastric pain was usually associated with CBZ and VPA, whereas gum hyperplasia was due to PHT. Most of the ADRs were not life threatening but there were patients experiencing toxicity due to high dose of PHB. Most of the ADRs are dose related and may be reason for poor adherence, therefore ADR should be assessed and possible intervention should be taken to improve medication adherence and treatment outcomes.

The second most common DTP identified in this study was in-effective drug (27.8%). According to Cipolle *et al,* (2004) DTP classification, this category has two major components (inappropriate drug selection and condition is refractory to the drug). Similarly in India teaching hospital, the treatment was inappropriate in 24.5% as per NICE guideline and 37% in appropriate as per ILAE guideline (George *et al.,* 2016). A study in Bishoftu hospital, on AEDs utilization, only 54.4% of AED use was in accordance with the national standard treatment guideline, while 2.9% were inappropriate and 44% were found to be difficult to determine since the type of epilepsy was not identified (Rishe *et al.,* 2015).

Appropriateness of AED selection was made based on established guidelines like NICE, AAN, ILAE and Ethiopian standard treatment guideline for general hospital. The use of PHB in monotherapy and combination therapy was very high whereas, that of VPA was very low. One of the common reasons for inappropriateness was drug selection problem with regard to seizure type. For example patients were taking PHB for focal seizure, while PHT and CBZ are first line according to the guidelines. The other one was the use of narrow spectrum AEDs for unclassified seizure type instead of VPA, as it is the AEDs of choice for unclassified seizure. The physicians working in neurology clinic justified the reason for high prevalence of inappropriate drug selection in different ways. Major reasons were cost and availability problems, thus the cost of PHB is low as compared to VPA and CBZ that made the physicians to prescribe PHB for most of epileptic patients regardless of seizure type. The other reason cited was influence of previous trends. PHB and PHT were the most commonly prescribed drugs and unavailability of treatment guidelines for tertiary hospital. Fear of side effects from CBZ and VPA and once daily dosing of PHB were also among the justifications.

Forty five drug interactions were identified in 13.8% of the study participants. The most frequently involved AED was CBZ because of its liver enzyme inducing activities. AEDs have a wide range of drug interactions among themselves and with other drugs commonly by

liver enzyme induction (CBZ, PHT and PHB) or inhibition (VPA). Such drug interaction is a major factor that might cause ADRs, therapeutic failure and drug related harm to patients (Blume, 2003).

The most common drug interactions were between CBZ + PHT, CBZ with anti TB drugs (isoniazid and rifampicin), and CBZ with HAART medications (efavirenz and ritonavir/atazanavir). These drug interactions are likely to cause treatment failure or drug resistance. Thus, changing the medication or dose adjustment is recommended especially for anti TB and HAART medications. Furthermore, PHB + nifedipine and VPA + warfarin were another potential drug interaction that could result in uncontrolled HTN and increase in INR value, respectively. The judgment to identify major drug interaction was based on theoretical consideration. In clinical practice, some of these combinations may still be used, but the patient should be closely monitored for manifestations such as lack of therapeutic efficacy or presence of toxicity.

Inappropriate dosing (dose too low and dose too high) accounted for 11.9% of all DTPs. This was in line with a finding among epileptic patients taking PHT in Thailand, in which dose inappropriateness was 13.67% (Kanjanasilp *et al.*, 2008). The principle of seizure treatment is starting with low dose and escalating to a maximum dose based on treatment response and occurrence of toxicity (unable to tolerate). The most common drug encountered as high dose was PHB in which patients were taking above the maximum recommended dose or serum concentration was above the maximum range whenever available. In contrary, CBZ was frequently encountered as too low dose usually daily dose of 400 mg or below with patients having uncontrolled seizure and yet it was not escalated until the optimal treatment was achieved. There were patients taking combination of AEDs below the recommended serum concentration that might be due to their pharmacokinetic interaction. Since most of neurologic side effects are dose related, AEDs don't have acceptable safety profile. Therefore, patients on high dose of AEDs should be monitored for toxicity and serum concentration should be considered for patients with uncontrolled seizure.

Need of additional therapy accounted for 5.1% of all DTPs. The most common untreated conditions were epigastric pain, migraine headache, anaemia and psychiatric illness like already diagnosed major depression. Epigastric pain was also associated with poor adherence and it should be treated, so that it could help to improve patient quality of life and medication adherence.

The identification of risk factors for DTPs may be helpful in finding patients at risk. These patients can then be given special attention, with the hope of avoiding overt DTPs. In the attempt to identify risk factors, this study showed number of medication taken by a patient was an important risk factor for DTPs. However, gender and age did not have significant correlation with the occurrence of DTPs. This finding is supported by studies that number of medications used was found to be a risk factor for increasing DTPs (Hussein *et al.,* 2014, Ayalew *et al.,* 2015).

Adherence to AEDs can be measured in several ways. The experience of using MMAS-8 suggests that it is useful as an objective measure. According to Cipolle *et al, (*2014*),* adherence is one of the categories of DTPs but in this study it was done separately by using MMAS-8 as one core objective.

The rate of adherence to AEDs observed in the present study was 55.7%, which is in line with the findings in Jimma university (58.5%) (Getachew *et al.,* 2014), China (51.9%) (Liu *et al.,* 2013), UK (41%) (Jones *et al.,* 2006) and Saudi Arabia (62.7%) (Gabr and Shams, 2015). But lower than the findings in Palestine (85.3%) (Sweileh *et al.,* 2011), India (98.6%) (Sebastian *et al.,* 2013) and USA (71%) (Hovinga *et al.,* 2008). The probable reason for these discrepancies could be due to differences in culture, belief, education and physicians approach to their patients that could bring differences in patients' attitudes for their medication.

According to the patients' response, the major reason for poor adherence was forgetfulness followed by patients feeling that they were cured (patients with seizure free period of above five years), lack of confidence on medication effectiveness and fear of side effects. Similar findings were reported elsewhere (Gabr and Shams, 2015).

Source of medication was significantly associated with poor adherence. Patients who got their medication for free were 2.3 times more non-adherent than those who paid for their medication. This might be due to medication supply in the hospital is inadequate and not persistent and most of free patients cannot afford to pay for their medication. The findings also showed that seizure free year was found to have statistically significant association with adherence of patients. Non-adherence was decreased by 64% and 54% for patients with seizure free period of 1-2 years and 2-5 years respectively as compared to patients with seizure free period of below one year. This finding strongly suggests that longer seizure free

years would make patients to be more adherent to their medications possibly by increasing patients belief on medication effectiveness and this is in line with other studies (Liu *et al.,* 2013). In contrary, the association was not statistically significant for patients who have seizure free period above five years. This might be due to most of these patients perceived that they were cured that will hinder their adherence. Age, gender, occupation, and place of residence were not significant factors for medication adherence, which is supported by other studies (Johnbull *et al.*, 2011, Liu *et al.,* 2013).

6. Limitations of the Study

- The cross-sectional nature of the study didn't allow a follow up, and it was a non-interventional study.
- Self-reported measure of adherence was used to measure adherence, which could have caused overestimation of adherence.
- ADRs was considered based on patients' complains and/or from medical records without establishment of causal relationship.
- The result of the study may not be generalizable to all hospitals because it was a single centred study conducted in a tertiary referral hospital that serves patients having severe illnesses and multiple co morbidities.

7. Conclusion

In conclusion, findings of this study showed that GTCS was the commonest seizure type and PHB and PHT were the most prescribed AEDs as monotherapy and combination therapy as well. Only 18.6% of the study participants had controlled seizure. Drug therapy problems were common (70.4%) among epileptic patients. Adverse drug reaction was the top ranking DTP followed by in appropriate drug selection, drug insteraction and inappropriate dose. Headache, depression and epigastric pain were the commonest ADRs. CBZ was the most frequently encountered AEDs for drug interaction and PHB was the common agent used in high dose. The rate of medication adherence was 57.3% and the common reason for non-adherence was forgetfulness, medication unavailability and fear of side effects. Number of medications taken by the patients had a significant association with occurrence of DTPs. Source of medication and seizure free periods were found to have significant association with poor adherence.

8. Recommendations

- Guideline should be developed and implemented on treatment of seizure based on the drug selection parameters.
- There should be a regular patient education program similar to other chronic diseases to improve medication adherence and attitude towards the diseases and its treatment.
- Therapeutic drug monitoring of AEDs should be considered for patients who have uncontrolled seizure and experiencing ADRs to monitor dose related toxicity and sub therapeutic dose.
- Clinicians should assess and monitor patients for signs of adverse drug effects and appropriate management should be sought and the safest possible alternative should also be chosen.
- Potential drug-drug interactions should be checked before starting a new drug especially for RVI patients.
- Further studies with a follow up of patients and with intervention should be considered. This may be achieved with the involvement of clinical pharmacists in MTM typically for patients with other comorbidities and uncontrolled seizure.
- Sustainable AEDs availability should be ensured within the hospital to improve medication adherence.

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Annexes

Annex I: Data abstraction format from patient interview

Part I. Patients socio-demographic characteristics (Use "X" in the Boxes)

Card/code #:_____	Age:_____	Gender: □M □ F	Pregnancy: □ Yes □ No	
Marital status:	□ Single	□ Married	□ Widowed	□ Divorced
Educational level:	□ No formal	□ Primary school	□ High school	□ College & above
Place of residence	……			
Occupation:	□ Unemployed	□ Employed	**d**aily laborer	□ Merchant
	□ Student	□ Farmer	Others----------	

Part II Clinical characteristics (supplementary to the information obtained from medical chart)

Weight (kg) _____ Height (cm) _____Body mass index (BMI)[kg/m2] _____

1. When did the first seizure episode occur? _____
2. When did he/she encounter the recent seizure episode? _____
3. How many seizure attacks you encountered in one year period? _____
4. When did you start your AEDs? _____
5. How many AEDs you are taking currently? _____
6. Diagnosis other than epilepsy (comorbidity)_____
7. Do you have any medications including non-prescription and traditional medications that you are taking currently? Yes ☐ No ☐
   If yes please list them _____
8. Total number of medications you are taking currently _____
9. Source of your AEDs With payment ☐ Free ☐

Part-III: Assessment of adherence (MMAS-8)

No	Items	Yes 1	No 0
1	Do you sometimes forget to take your pills?	1	0
2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	1	0
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	1	0
4	When you travel or leave home, do you sometimes forget to bring along your medicine?	1	0
5	Did you take all your medicine yesterday?	0	1
6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?	1	0
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	1	0
8	How often do you have difficulty remembering to take all your medicine? Never ☐ Rarely ☐ Once in a while ☐ Sometimes ☐ Usually ☐ All the time ☐		
	Total score		

If you have any problems that challenges your medication adherence please the select your reason (more than one answer is possible)

- ☐ Fear of adverse events
- ☐ Disbelief in drug effectiveness
- ☐ Directions not understood
- ☐ Patient forgets to take
- ☐ Patient felt better
- ☐ Patient felt better worse
- ☐ Drug product too expensive
- ☐ Patient cannot swallow/ administer

- Drug product not available
- Regimen complexity

Others, specif----------

Part IV. Assessment of adverse drug reaction (undesirable effect)

Have you experienced any undesirable, unusual adverse drug events /allergic reaction to the prescribed medicines? Yes No:

If yes would you describe the manifestation of the events ----------

Depression	Head ache	Forgetfulness	Weight gain
Blurred vision	Gingival hyperplasia	Weakness	Hypersomnia
Confusion	Loss of hair	Epigastric pain	Skin rash
Irritability	Others please specify---------- -		

Annex II: Data abstraction format from patient medical records

1. Provisional diagnosis of seizure type _____
2. Diagnosis other than epilepsy (comorbidity)_____
3. Past medical conditions and medications

Medical condition/ Indication	Drug product (Generic Name)	Dosage regimen (dose, route, frequency, duration)	Date (dd/mm/yy)		Response Effectiveness/ safety profile
			Started	Stopped	

4. Physical Examination(PE)/**vital** signs: Consecutive record of visits

Parameters	**Date(dd/mm/yy**									
BP										
PR										
RR										
T^0										
Others:										

5. Relevant **laboratory** series results (Findings, at least for three consecutive results).

Parameters	Date(dd/mm/yy										
Lipid profiles	Total chol.										
	LDL: mg/dl										
	TG: mg/dl										
	HDL: mg/dl										
Liver function test	AST										
	ALT										
	ALP										
	PTT										
	PT										
	INR										
Rena function test	BUN										
	Sr. Cr										
	Cr. Clearance										
CBC	WBC										
	RBC										
	PLT										
	Hgb										
	HCT										
	MCV										
	MCHV										
	Neu.										
	Lymph.										
Serum Electrolyte	K										
	Na										
	Ca										
	Cl										
Blood glucose (RBS) or FBS											
Therapeutic drug monitoring if any											

Summary of any other investigations/Diagnostic imaging results	**EEG**	
	MRI	
	CT	
	Others	

6. Current medical conditions and medications

	For the current medical diagnosis (including Comorbid and complications)				
Medical condition/ Indication	Product name (Generic Name)	Dosage regimen (dose, route, frequency, duration)	Date(dd/mm/yy)		Response Effectiveness/ safety profile
			Started	Stopped	

7. Is there any drug interaction ? yes ☐ No ☐

If drug interaction is there, specify it

_____

_____

8. Was there any experienced adverse effect of the drugs? Yes ☐ No ☐

If yes would you describe the manifestation of the events ----------

Depression	Head ache	Forgetfulness	Weight gain
Blurred vision	Gingival hyper plasia	Weakness	Hypersomnia
Confusion	Loss of hair	Epigastric pain	Skin rash
Irritability	Others please specify---------- -		

Annex III: Modified DTPs Registration Format

DTPs Categories	Common Cause(s) of Drug therapy problem
1. Unnecessary drug therapy	☐ There is no valid medical indication for the drug therapy at this time Duplicate therapy ☐ Multiple drug products are being used for a condition that requires single drug therapy ☐ The medical condition is more appropriately treated with nondrug therapy ☐ Drug therapy is being taken to treat an avoidable adverse reaction associated with another medication ☐ Drug abuse, alcohol use, or smoking is causing the problem
2. Needs additional drug therapy	☐ Untreated medical condition (a medical condition requires the initiation of drug therapy) ☐ Preventive/ prophylactic(preventive drug therapy is required to reduce the risk of new condition) ☐ Synergistic/ potentiating (a medical condition requires additional pharmcotherapy to attain synergistic or additive effect) _____
3. Ineffective drug product	☐ The drug product is not the most effective for the indication being treated (In appropriate drug selection) ☐ Condition refractory to drug ☐ Dosage form inappropriate
4. Adverse drug reaction	☐ The drug product causes undesired effect ☐ The drug product is unsafe drug for patient ☐ The drug product causes allergic reactions ☐ The drug product is contraindications due to safety issues ☐ Others, specify_____
5. In appropriate dose	☐ Dose too high ☐ Dose too low ☐ The duration of drug therapy is too short to produce the desired response
6. Drug interaction	☐ Presence of major drug interaction among the medications

Annex IV: English version of information sheet

Card No…… code No…… date…….

Addis Ababa University, College of Health Science

School of Pharmacy

Department of Pharmacology and Clinical Pharmacy

Dear participant, Good Morning/Afternoon

Introduction

My name is_____. I am a member of the study that is carried out at TASH, Addis Ababa, Ethiopia entitled, "Assessment of drug therapy problems among ambulatory epileptic patients at TASH". The study is being conducted by Mr. Beshir Bedru from Addis Ababa University, school of Pharmacy, department of clinical Pharmacy and Pharmacology, post graduate program.

The main purpose of this study is to assess drug therapy problems and patient adherence and its possible reasons among epileptic patients at ambulatory clinics of TASH.

Expected Outcomes and/or Benefits

At the end of the study, drug therapy problems and adherence will be evaluated. Therefore, the study will identify and investigate the main gaps associated with drug therapy problems, adherence, factors are associated with drug therapy problems and adherence. Feasible recommendations will be proposed and may benefit you directly or indirectly by improving the treatment of epilepsy in the hospital.

Thanks for your time

Annex V: English version of informed consent form

The study will be conducted through recording medical findings from your medical chart 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 20-30 minutes'.

If you have any question or suggestion you can communicate the principal investigator, Beshir Bedru, Cell phone: +251-941166346

_____ _____

Signature of respondent Signature of interviewer

Thanks for your time

Address of the principal investigator: Mr. Beshir Bedru

Addis Ababa University, CHS, School of Pharmacy, Department of Pharmacology and Clinical

Pharmacy

Cell phone: +251-941166346

E-mail: beshir.bedru@aau.edu.et

Annex VI: Questionnaire, Amharic version (የአማርኛ መጠይቅ ቅፅ)

Card number---------- Code number---------- ቀን፦_____

አዲስ አበባ ዩኒቨርሲቲ፣ ጤና ሳይንስ ኮሌጅ፤ ፋርማሲ ት/ቤት፤ ፋርማኮሎጅና ክሊኒካል ፋርማሲ ትምህርት ክፍል

ቅጽ 1: የጥናቱ መረጃ ቅጽ

ውድ የቃለ መጠይቅ ተሳታፊ፤ እንደምን አደሩ/ዋሉ?

ስሜ_____ ይባላል። “በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል በሚጥል በሽታ ታካሚዎች ላይ በመድሀኒት ህክምና ተያያዥ ችግሮች ዳሰሳ” በተሰኘ የድህረ ምረቃ ጥናት አባል ነኝ። ጥናቱ የሚካሄውም በ አቶ በሽር በድሩና በጥናቱ ዋና አማካሪ ዶ/ር ኤፍሬም እንግዳወርቅ ከአዲስ አበባ ዩኒቨርሲቲ፣ ጤና ሳይንስ ኮሌጅ፤ ፋርማሲ ት/ቤት የድህረ ምረቃ ፕሮግራም ነው።

የጥናቱ አላማ

የዚህ ጥናት ዋና አላማው ከመድሀኒት ህክምና ጋር ተያያዥነት ያላቸው ችግሮችን ለመለየት፣ በታዘዘው መሰረት በአግባቡ እንዴት መድኃኒትዎን እንደሚወሰዱት፣ መድኃኒትዎን ሁል ጊዜ እንዳይወሰዱ የሚያደርጉ ዋና ዋና ክፍተቶችን በመለየትና የመፍትሄ ሀሳቦችን ማቅረብ ነው።

ከጥናቱ የሚጠበቁ ውጤቶች/ጥቅሞች

በዚህ ጥናት ላይ በመድኃኒት ህክምናዎ ላይ የሚከሰቱ ችግሮች ፤ በታዘዘው መሰረት በአግባቡ የአወሳሰድና የአጠቃቀም ክህሎትና ። በተጨማሪም ከጥናቱ በሚገኙ ግኝቶች የሚጥል ህክምና ዉጤትን በተወሰነ መልኩ ለማሻሻል እንደሚቻል በመገመት፤ እርስዎ የጥቅሙ ተቋዳሽ ይሆናሉ ብለን እናምናለን። ጥናቱ የሚካሄደው የህክምና ካርድዎንና በመከለስና በቃለ መጠይቅ ነው። ስለዚህ የእርስዎ ቅንና ሓቀኛ መረጃ ለጥናቱ እጅግ በጣም ወሳኝ ነው።

የተከበረ ጊዜዎ ስለሰጡን እጅግ በጣም እናመሰግንዎታለን።

ቅጽ 2፡ በቃለ መጠይቅ ለመሳተፍ የፈቃደኝነት ቃል መቀቢያ ቅጽ

በዚህ ጥናት የእርስዎ መረጃ ሙሉ በሙሉ በምስጥር የተጠበቀና ለምርምሩ አላማ ብቻ የሚውል ነው። በተጨማሪም የእርስዎ ተሳታፊነት በፈቃደኝነት የተመሠረተ ነው። የጥናቱ አላማውን ተረድተውና ጊዜዎን ሰውተው፤ ከ 20-30 ደቂቃዎች ለሚፈጅ ቃለ-መጠይቅ እውተኛው መረጃ ለመስጠት ፍቃደኛ በመሆንዎ በቅድሚያ አመሰግናለሁ።

በየትኛውም ጊዜ ጥያቄ ካለዎት በሽር በድሩ በ ስ.ቁ +251 941166346 ወይም

በ ኢ-ሜይል፡ beshir.bedru@aau.edu.et ይጠይቁን።

የቃለ መጠይቅ የቀረበለት ሰው ፊርማ ----------

የቃለ መጠይቅ አቅራቢ ፊርማ ----------

የተከበረ ጊዜዎ ስለሰጡን እጅግ በጣም እናመሰግንዎታለን።

ዋና አጥኚ:

አዲስ አበባ ዩኒቨርሲቲ፣ ጤና ሳይንስ ኮሌጅ፤ ፋርማሲ ት/ቤት፤ ፋርማኮሎጅና ክሊኒካል ፋርማሲ ትምህርት ክፍል

E-mail: beshir.bedru@aau.edu.et

ስ/ቁ: +251 941166346

ቅፅ 3: *ቃለ-መጠይቅ ከታካሚው*

ክፍል 1. ስለ ታካሚው አጠቃላይ መገለጫዎች

1.1. *ዕድሜ*:---------- (በቁጥር ይፃፍ)

1.2. *ፆታ* ወንድ☐ ሴት☐ እርጉዝ ኖት? አዎ☐ አይደለሁም ☐

1.3. የጋብቻ ሁኔታ፡ ያላገባ/ያላገባች☐ ያገባ/ያገባች ☐ የፈታ/ች ☐

ባል የሞተባት /ሚስት የሞተችበት☐

1.4. የትምህርት ደረጃ:- ———— (በቁጥር ይፃፍ)

ያልተማረ/ች ☐ አንደኛ ደረጃ (ከ 1-8 ክፍል) ☐ ሁለተኛ ደረጃ (ከ9-12 ክፍል) ☐

ዲፕሎማ እና ከዛ በላይ☐

1.5. *መኖሪያ ቦታ*.....

1.6. የስራ ሁኔታ፡ ስራ አጥ ☐ ተቀጣሪ ☐ የግልስራ/ነጋዴ ☐ ተማሪ ☐

የቀን ሰራተኛ ☐ ግብርና ☐ ሌላ/ሌሎች (ይገለፅ)

1.7. ይህን ህመምዎት ተመርምረው ካወቁ ምን ያህል ጊዜ ሆኖታል ?----------

1.8. ይህን ህመም ለመጨረሻ ጊዜ ካጋጠምዎት ምን ያህል ጊዜ ነው? ----------

1.9. በዚህ አመት ስንት ጊዜ ህመም አጋጠምዎት? (ይብራራ)----------

1.10 ለዚህ ህመምዎ መድኃኒት መውሰድ ከጀመሩ ምን ያህል ጊዜ ነው; ----------

1.11. ለዚህ ህመምዎ የሚወስዱት የመድሃኒት ብዛት ስንት ነው? (ይዘርዝሩት)----------

1.12. ተጨማሪ ወይም ሌላ ተያያዥ ህመም አለብዎት? አዎ☐ የለብኝም☐

ካለ እባክዎን ይግለጹት----------

1.13. *ለህመምዎ* ከሚወስዱት ሌላ ተጨማሪ ቋሚ መድኃኒቶች ወይም (የባህል ወይም ያለሓኪም ትእዛዝ የሚወሰዱት መድኃኒቶችን) አሉ; አዎ☐ የለም☐

ካለ እባክዎን ይግለጹት----------

1.14. በአሁኑ ሰአት የሚውሰዱት ጠቅላላ የመድኃኒት አይነት (ብዛት) ስንት ነው; ----------

---

1.15. *መድሃኒት* የሚያገኙት በምን መልኩ ነው; በግዢ☐ በነጻ ☐

ክፍል 2: ሞሪስኪ" መድኃኒትን በታዘዘው መሰረት በአግባቡ ስለመውሰድ" መለኪያ- 8

ክፍል 2: ሞሪስኪ" መድኃኒትን በታዘዘው መሰረት በአግባቡ ስለመውሰድ" መለኪያ- 8			
	ጥያቄዎች	አዎ 1	አይደለም 0
1	አንዳንድ ጊዜ መድኃኒትዎን ረስተው ሳይወሰዱ ቀርተው ያውቃሉ?	1	0
2	ሰዎች አንዳንድ ጊዜ ከመርሳት በተጨማሪ ባሉት የተለያዩ ምክንያቶች መድኃኒታቸውን ሳይወስዱ ይቀራሉ፡፡ ባለፉት ሁለት ሳምንታት፣ መድኃኒትዎን ሳይወስዱ የቀሩበት ቀናቶች ነበሩ?	1	0
3	መድኃኒትዎን እየወሰዱ ህመምዎ ባለመቆሙ ሐኪምዎን ሳያማክሩ መድኃኒትዎን አቋርጠው ያውቃሉ?	1	0
4	በጉዞ ወይም በሌላ ምክንያት ከቤትዎ አርቀው ሲጓዙ አንዳንድ ጊዜ መድኃኒትዎን ረስተውት ሳይወስዱት ያውቃሉ?	1	0
5	በትላንትናው ዕለት ሁሉንም መድኃኒትዎን ውጠዋለ?	0	1
6	ህመምዎ ጋብ ሲልሎት (የህመምዎ ስሜቶች ሲጠፉ) አንዳንድ ጊዜ መድኃኒትዎን አቋርጠው ያውቃሉ?	1	0
7	በየቀኑ መድኃኒት መዋጥ፣ ለአንድ አንድ ሰዎች አይመችም፡፡ እርስዎ በየቀኑ እንድሁም አንድም ሰዓት ሳያዛንፉ መድኃኒትዎን መዋጥ የመሰላቸት ስሜት ተሰምቶት ያውቃል?	1	0
8	መድኃኒትዎን አስታውሰው ለመዋጥ ምንያክል ይቸገራሉ? ጭራሽ አይቸግረኝም ☐ በጣም አልፎ አልፎ ከስንት አንድ ጊዜ ይቸግረኛል ☐ አንዳንድ ጊዜ ይቸግረኛል ☐ አብዛኛው ጊዜ ይቸግረኛል ☐ ሁል ጊዜ ይቸግረኛል ☐		

2.1. መድሃኒቱን በአግበቡ ካልወሰዱ እባክዎ ምክንያት ይግለጹ (ከ አንድ በላይ መልስ መምረጥ ይቻላል)

☐ የጎኒዮሽ ጉዳትን (ሳይድ ኢፌክት) በመፍራት

☐ ያድነኛል ብዬ ስለ ማላስብ

☐ ስለመድሃኒቱን አወሳሰድ በቂ መረጃ ስለሌለኝ

☐ ምድሃኒቱን ስወስድ ህመሜ ስለሚባባስበኝ

☐ መድሃኒቱን ማግኘት ስላልቻለኩ

☐ መድሃኒቱን ስውጠው ስለሚያስቸገረኝ

☐ ስለምረሳው

☐ ምወስዳቸው መድሃኒቶች ብዙና ግራ የሚያጋቡ ስለሆኑ

☐ ተሽሎኛል ብዬ ስላሰብኩ

☐ መድሃኒቱ ውድ ስለሆነ

ሌላምካለይግፁት…….....

<u>ክፍል 3. ከመድኃኒትዎ የጎኒዮሽ ጉዳት ወይም (ሳይድ ኢፌክት) ግምገማን በተመለከተ</u>

3.1. በአሁን ሰዓት ወይም መድሃኒትዎን መውሰድ ሲጀምሩ ከመድሃኒቱ ጋር የተያያዙ ያልተለመዱ ሁኔታዎች/ የጎኒዮሽ ጉዳት አጋጥሞዎት ያውቃል?

አዎ ☐ አላጋጠመኝም ☐

3.2 መልስዎ አዎን ከሆነ የመድሃኒቱን ስሙና የነበረው ሁኔታ ይግለጹ (ከ አንድ በላይ መልስ መምረጥ ይቻላል)

ድብርት☐	የራስ ምታት ☐	መርሳት ☐	የክብደት መጨመር ☐
የዐይን ብዥታ ☐	የድድ ማበጥ☐	የድካም ስሜት☐	ከመጠን ያለፈ እንቅልፍ☐
ግራመጋባት☐	የፀጉር መሳሳት☐	የጨጓ ራህመም ☐	የቆዳ ላይ ሽፍታና ማሳከክ☐
ራስን ማዞር (<u>ብዥታ</u>)☐		ሌላም ካለ ይግፁት----------	