Assessment of Adherence and Treatment Outcome among Epileptic Patients on Follow-up at Amanuel Specialized Mental Hospital

Melak Gedamu (BPharm)

A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy in Partial Fulfillment of the Requirement for the Degree of Master of Pharmacy in Pharmacy Practice (MPharm)

Addis Ababa University

Addis Ababa, Ethiopia

February 2015

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Melak Gedamu, entitled "Assessment of Adherence and Treatment Outcome among Epileptic Patients on Follow-up at Amanuel Specialized Mental Hospital, 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 with respect to originality and quality.

Signed by the Examining Committee:

Internal Examiner: Workineh Shibeshi (PhD, Associate professor); Signature _____Date _____

External Examine: Yonas Baheretibeb (PhD, Associate professor); Signature _____Date ____

Advisor: Ephrem Engidawork (PhD, Associate Professor); Signature _____Date_____

_____

Chair of Department

Assessment of Adherence and Treatment Outcome among Epileptic Patients on Follow-up at Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia

Melak Gedamu

Addis Ababa University, 2015

Abstract

Anti-epileptic drugs (AEDs) are the primary therapeutic modes for epileptic patients and have been demonstrated to control seizure, which decreases morbidity and mortality associated with epilepsy. There is a paucity of data on treatment outcome among epileptic patients in resource poor settings. The aim of this study was therefore to assess adherence and treatment outcome among epileptic patients. A cross-sectional study was conducted among epileptic patients on follow-up at Amanuel Specialized Mental Hospital. Patients who had follow up for at least two years were recruited in the study to evaluate adherence and treatment outcome through medical records review and patient interview. Factors affecting adherence and seizure control were determined using regression analysis.

From a total of 397 patients 61% were males. The common type of seizure diagnosed was generalized tonic clonic seizure (76.1%). Monotherapy was commonly (74.8%) used in the management of seizure, among which phenobarbitone was the most commonly utilized (60.5%) single anticonvulsant drug. About 70% patients were adherent to their treatment and only 38.6% of the patients were seizure free for at least two years. Seizure free period and year of follow up were found to have significant association with adherence. Number of drugs, side effect burden, adherence and educational levels were found to have a significant association with seizure

control status. The findings collectively indicate that health care providers should focus on adherence, treatment modality and side effect burden to control seizure. In addition, for those patients who were seizures free for at least two years, there must be a consideration of clinical assessment to withdraw AED treatment.

Key words: adherence, anti-epileptic drugs, epilepsy, treatment outcome

Acknowledgments

First and for most, I would like to thank the almighty God and His Mother, St. Virgin Marry, who gave me the forte to work through this paper starting from the commencement up to its completion. I would also like to extend my sincerest gratitude to my advisor Dr. Ephrem Engidawork who helped me with his constructive ideas and feedback throughout the work. My gratitude also goes to Amanuel Specialized Mental Hospital which sponsored my study. Furthermore, I would also like to acknowledge all participants of the study who kindly volunteered to answer to the interview questions. Finally, I am also grateful to my data collectors and staff members of Amanuel Specialized Mental Hospital for their unreserved support.

List of Abbreviations/Acronyms

AAU	Addis Ababa University
AEDs	Anti-epileptic drugs
ASMH	Amanuel Specialized Mental Hospital
CHS	College of Health Sciences
CPS	Complex partial seizure
EEG	Electroencephalograph
GTCS	Generalized tonic clonic seizure
ILAE	International League Against Epilepsy
MMAS	Morisky Medication Adherence Scale
OR	Odds ratio
PHB	Phenobarbitone
PHT	Phenytoin
SD	Standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
SPSS	Statistical Package for Social Sciences
WHO	World Health Organization

Table of Contents

List of Tables

List of Figures

1. INTRODUCTION

1.1. Background

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disorder of the brain 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 (LIAE, 2005).

Epileptic seizures are the clinical manifestations of excessive and/or hyper-synchronous, usually self-limited, abnormal activity of neurons in the brain. Signs and symptoms of seizures vary and depend on where in the brain the disturbance first starts, and how far it spreads. Temporary symptoms occur, such as loss of awareness or consciousness, and disturbances of movement, sensation (including vision, hearing and taste), mood, or other cognitive functions. All epileptic seizures, however, are not epilepsy, which requires recurrent epileptic seizures in the absence of acute pathology. Active epilepsy has been defined as epilepsy that has caused two or more unprovoked seizures on different days (WHO, 2004).

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; (iii) diagnosis of an epilepsy syndrome (ILAE, 2014).

Epilepsy may be difficult to diagnose in the early stages, especially in the absence of a witnessed account. The diagnosis of epilepsy is fundamentally a clinical judgment made on the basis of a clinical history. The accuracy of the diagnosis depends on the skill and experience of the physician and the quality and reliability of the information provided by witnesses. It is important to make the distinction between generalized epilepsies and focal epilepsies, as this affects treatment choices, investigation, prognosis and counseling. Electroencephalography (EEG) can aid classification of epileptic seizures and epilepsy syndromes (Epilepsy Implementation Task Force, 2015).

The two major categories of seizure type classified by the ILAE in 1981 are partial seizures and generalized seizures. Epilepsy characterized by partial (focal) seizures is that in which seizures begin in a local area of the brain. This seizure type is further subdivided into simple partial (no alteration in consciousness) and complex partial seizures (alteration of consciousness). Epilepsy characterized by generalized seizures may also be categorized as partial with secondary generalization if a clinical description of an antecedent symptom (aura) or a clear EEG signature of focality is indicated. Epilepsy characterized by generalized onset seizures conceptually involves the entire brain simultaneously. 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. This is seldom clear, however, and in some cases, seizure type may remain unclassifiable (SIGN, 2003; Ahmed & Spencer, 2004; Banerjee et al., 2009).

About 10% of the whole world population living a normal life span can expect to have at least one epileptic seizure. At least 50 million will have recurrent seizures. This could be underestimated, as partial seizures are often not recognized as such in the developing world. Out

of the 50 million, 40 million receive no treatment when 70% of these could lead seizure-free lives (WHO, 2004).

One epidemiological survey conducted in Brazil revealed that the life time prevalence of epilepsy was 9.2/1,000 people and the estimated prevalence of active epilepsy was 5.4/1,000 people(Li et al., 2007). Other studies also reported 400,000 patients with epilepsy in England and Wales (Purcell et al., 2002). Incidence as well as prevalence of epilepsy is generally lower in developed regions in comparison to developing region (Banerjee et al., 2009). In a large community-based epidemiological study, the prevalence of epilepsy in Ethiopia was reported as 5.2/1000 population (Tekle-Haimanot et al., 1999). The incidence was 64/100,000 population as reported in a community-based study conducted in Mescal and Marko districts of rural central Ethiopia (Tekle-Haimanot et al., 1997).

The mainstay of treatment for epilepsy remains symptomatic despite the rapid expansion in knowledge of its neurological disabilities. The management of epilepsy includes pharmacological, non- pharmacological (vagal nerve stimulation & ketogenic diet) and surgical (Lobectomy and lesionectomy are among several possible curative surgeries) approaches (SIGN, 2003). The principle of epilepsy management should be individualized and the selection of treatments should aim to control symptoms as well as to prevent other complications. There are a number of drugs available for treatment of epilepsy in modern therapy (Rout & Kar, 2010).

The goal in treating patients with epilepsy is a cost-effective approach to the elimination of seizures or a reduction in their number and frequency while avoiding drug interactions and side effects, so as to achieve the best possible quality of life (Garnett, 2000).

Treatment should be started with a single (monotherapy) conventional AED. 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. The first drug is then tapered off slowly. Combination therapy can be considered when two attempts at monotherapy with AEDs have not resulted in seizure freedom (Epilepsy Implementation Task Force, 2015).

When a patient, who has previously had epileptic seizures, has remained free from attacks for several years while taking anticonvulsant medication, the question arises whether the epilepsy has burnt itself out and therefore the medication can be withdrawn. Drug therapy may not be indicated in patients who have had only one seizure or those whose seizures have minimal impact on their lives. Patients who have had two or more seizures should generally be started on AEDs. Factors favoring successful withdrawal of AEDs include a seizure-free period of 2 to 5 years, complete seizure control within 1 year of onset, an onset of seizures after age 2 years and before age 35 years, and a normal EEG (SIGN, 2003; Wells et al., 2008).

The advantages are evident: a dose reduction means fewer side effects and less risk of teratogenesis; successful discontinuation eliminates the risk of idiosyncratic reactions, helps to remove the stigma of epilepsy and confers greater social freedom. Some patients may be unwilling to risk further epileptic seizures particularly if they have a driving license and choose to continue medication, possibly at a reduced dose. Others find the drugs so troublesome that they would prefer to stop them, if at all possible (Overweg, 1995).

Seizure control is the main outcome measure in epilepsy treatment. Treatment efficacy, achieved by AEDs or surgery, is counterbalanced by drug related or surgical adverse effects. Chronic

AED use is not particularly well tolerated. Drug-related adverse effects occur in 40-80% of individuals, especially in those on poly therapy. A better understanding of the contributive role of these individual perspectives and needs in epilepsy treatment outcomes is, however, needed. In addition to the traditional, clinical pharmacological determinants may hold important information and possibilities to reduce seizure load, adverse effects or the impact on daily life. Their relation to treatment outcomes warrants further research. Quality of life measures do incorporate these individual perspectives of health and well-being, as well as seizure control and adverse effect, and can be regarded the optimal and most comprehensive outcome measure (Suurmeijer et al., 2001).

1.2. Statement of the problem

Medication non-adherence is defined as patient's failure to engage in a therapeutic regimen because of deficit in one or more of these pre-requisites: comprehension of the regimen, regard for the value of medical advice, or skills required for self-management. In both developed and developing countries, non-adherence to medication remains a significant concern for health care providers as well as patients because of its adverse consequences on therapeutic outcomes. It is significant most especially in those with chronic illnesses that involve complex and long-term medical regimen (Harold, 2000; Munger *et al*., 2007).

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 (Faught *et al*., 2009; Getachew *et al*., 2014) .

Longer-term adverse events are a concern with the use of certain AEDs, and older drugs such as carbamazepine, phenytoin, and phenobarbital and valproate are associated with long-term side effects (Privitera, 2011).

The capability to identify people with epilepsy and provide cost-effective care is compromised by widespread poverty, illiteracy, inefficient and unevenly distributed health-care systems, and social stigma and misconceptions surrounding the disease. Several studies have reported that a large proportion of patients with epilepsy in resource-poor countries never receive appropriate treatment for their condition, and many, although diagnosed and initiated on treatment, soon discontinue treatment. The high cost of treatment, a lack of availability of antiepileptic drugs,

and superstitious and cultural beliefs contribute to a large epilepsy treatment gap (Radhakrishnan, 2009).

Although some epileptic patients are seizure free for many years, they could still be on AED treatment. This may lead to unnecessary drug treatment which exposes the patients to drug side effect, drug expenses, psychological dependence and social stigma.

There is a paucity data on adherence and treatment outcome of AED in Ethiopia. Hence, this study would attempt to assess treatment outcome by taking seizure control as a factor. In addition, adherence would also be assessed as it could determine treatment outcome. The findings could be used to uncover the practices rendered at the hospital, improve the service and serve as a baseline for further studies.

1.3. Literature review

Studies investigating adherence to medications in epileptic patients have produced different rates ranging from 33-99%. Studies done in the western countries revealed an adherence rate of 71% in the US (Hovinga *et al*., 2008) and 59% in the UK % (Jones *et al*., 2006). The rate appeared not to be that different in China (51.9%) (Liu *et al*., 2013), but was higher in India (98.6%) (Sebastian *et al*., 2013) and Palestine (85.3%) (Sweileh *et al*., 2011). However, lower adherent rate was found in Nigeria (32.6%) (Johnbull *et al*., 2011) and South Africa (54.6%) (Egenasi *et al*., 2015). The result was not different in Gondar, Ethiopia (70.8%) (Abula *et al*., 2001) and Jimma, Ethiopia (58.5%) (Getachew *et al*., 2014).

Studies investigating factors affecting adherence rate have produced different associated factors. Knowledge of AED and frequency of seizures (Jones *et al*., 2006), duration of illness (Sweileh *et al*., 2011; Liu *et al*., 2013), side effects of the drugs (Liu *et al*., 2013; Egenasi *et al*., 2015), uncontrolled seizures and increasing treatment complexity (Sweileh *et al*., 2011; Ferrari *et al*., 2013) were factors affecting adherence rate of epileptic patients. However, age, sex, educational status, income, religion and place of residence (Jones *et al*., 2006; Johnbull *et al*., 2011; Liu *et al*., 2013) were identified as factors not affecting adherence of the patients.

Classifying the type of seizures requires well trained expertise and availability of diagnostic tools. Different studies found the most identified seizure was generalized tonic clonic seizure (GTCS). The magnitude ranges from 47 to 82 %. The highest magnitude found in India (82%) (Sebastian *et al*., 2013) and sizable magnitude in Bangladesh (74%) (Habib *et al*., 2013), but lower in Saudi Arabia (65%) (Gabr & Shams, 2015), 47 % in Pakistan (Morgan *et al*., 2004) and

63% in Singapore (Hsieh & Huang, 2009). However, 80% of the patients were diagnosed as GCTS in Jimma, Ethiopia (Gurshaw *et al*., 2014).

AEDs were prescribed to control seizure; however the selection of drugs were different in different studies. Carbamazepine was mainly prescribed in different countries ranging from 37 to 67 %. The lowest found in UK (37%) (Jones *et al*., 2006), the highest in Bangladesh (67%) (Habib *et al*., 2013). However, VPA was the most frequently prescribed AED in Saudi Arabia (60%) (Gabr & Shams, 2015) and phenytoin in India (42%) (Sebastian *et al*., 2013). But, studies showed the commonly prescribed AED was phenobarbitone in Jimma, Ethiopia (55%) (Gurshaw *et al*., 2014) and in Gondar, Ethiopia (62 %) (Hailu *et al*., 2012).

Different literatures found monotherapy was the preferred treatment modality ranging from 55 to 96 %. The highest frequency of monotherapy found in developed countries. Such as 96% in UK (Jones *et al*., 2006), 77% in Saudi Arabia (Gabr & Shams, 2015), 78% in Pakistan (Morgan *et al*., 2004), but lower in India (62%) (Sebastian *et al*., 2013) and Singapore (63%) (Hsieh & Huang, 2009). However, the lowest rate of monotherapy treatment modality was found in Jimma, Ethiopia (55%) (Gurshaw *et al*., 2014) and ASMH, Ethiopia (62%) (Tegegne *et al*., 2015).

Many clinical features in epilepsy have been assessed for their association with long-term epilepsy outcome. These factors include gender, age of seizure onset, type and duration of epilepsy, neurological examination finding, seizure frequency, duration between epilepsy onset and treatment initiation, duration between treatment initiation and response, response to the first antiepileptic drug (AED), and number of AED tried or needed for seizure control. The most consistent factor associated with long-term epilepsy outcome is the ease of controlling seizures

(Elson, 2011). Most of the studies conducted to identify the effect of adherence on seizure control showed a positive association (Jones *et al*., 2006; Tefera *et al*., 2015; Ipingbemi, 2015), but there were some studies that showed adherence status of the patients didn't have no significant association with seizure control status of the patients (Hovinga *et al*., 2008; Egenasi *et al*., 2015). The complexity of drugs and side effect burden were found to have a significant association with seizure control (Louis *et al*., 2009). However, seizure type didn't affect seizure control status of the patients (Ipingbemi, 2015)

2. OBJECTIVES

2.1. General objective

The general objective of the study was to assess adherence and treatment outcome among epileptic patients on follow-up at ASMH

2.2. Specific objectives

- ✓ To determine treatment outcome of the patients
- ✓ To identify factors affecting treatment outcome of epileptic patients
- ✓ To determine the rate of adherence of patients using Morisky Medication Adherence Scale-8 to AEDs
- ✓ To identify factors affecting adherence of epileptic patients to AEDs
- ✓ To determine the most commonly prescribed AEDs

3. METHODS

3.1. Study Setting

The study was conducted at ASMH which is the only public specialized mental hospital in the country. It gives service for mentally ill patients and also serves as a rehabilitation center for substance abuse patients. ASMH is located in Addis Ababa, Ethiopia, and has 280 beds. The hospital also offers post-graduate program in psychiatry in collaboration with University of Gondar. The staff profile of the hospital comprised of psychiatrists, general practitioners, health officers, nurses, pharmacists and support staff.

3.2. Study design and period

The study was a hospital-based cross sectional study that had two components. The first component was a patient interview and the second one was a retrospective patient chart review. The study was conducted from 1 July to 31 August 2015.

3.3. Source and study population

The source population of the study was all epileptic patients attending at ASMH. The study population constituted all epileptic patients attending ASMH fulfilling the inclusion criteria.

3.4. Inclusion and exclusion criteria

i) Inclusion criteria:

- Patient's chart with complete records.
- Patients who were on AEDs treatment for at least the last two consecutive years
- The age of the patients' ≥13 years

- Voluntary epileptic patients for interview

ii) Exclusion criteria:

- Juvenile myoclonic epilepsy

3.5. Sample size & Sampling methods

The sample size was calculated using the following single population proportion formula, where 1.96 used for Z α/2, 50% for P and 5% for d. where: d is margin of error, p is proportion of treatment outcome and Z α/2 is the 95 % confidence interval.

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

The total sample size required for the study was 385. By adding 10 % contingency, a total of 423 patients were sampled.

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. Hence, it was calculated through dividing the number of study population available each day by the maximum possible number of patients' that could be interviewed the same day. Every k^{th} patient was then interviewed following physicians' visit.

3.6. Data collection Process

3.6.1. Instruments

a) Adherence assessment:

In the absence of any pre-existing gold standard measure, adherence of epileptic patients to their AEDs was measured using a Morisky Medication Adherence Scale-8 (MMAS-8) (Annex III). The MMAS-8 is a generic self-reported, medication-taking behavior scale, validated for hypertension but used for a wide variety of medical conditions (Riccardo and Vietri, 2014). MMAS-8, which is the latest version of the scale, has a good internal consistency (Cronbach's $\alpha = 0.83$) (Morisky, 2008). It consists of eight items focusing on past medication use patterns with a scoring scheme of "Yes" = 0 and "No" = 1 for the first seven items except item number five in which the values "Yes" and "No" were reversed and for the last item a five-point Likert response was used with options "never", "once in a while", "sometimes", "usually", and "always." In this Likert scale, values ranging from 0 to 1 were given at a specified interval of 0.25 with "0" given for "never" and "1" given for "always". The items were then summed to give a range of scores from low adherence to high adherence with a maximum score of 8. For the purpose of data analysis, the original three categories of adherence were re-categorized 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.

b) Chart review

A data abstraction form (Annex IV) was developed to extract pertinent information from patients' chart in order to determine seizure control. The form contains information on diagnosis, prescribed drugs, years of follow up, adverse effects, tapering and planning to taper.

3.6.2. Data collectors recruitment and training

Data was collected by one nurse and two health officers. The data collectors were trained for one day on how to collect the necessary data from charts as well as how to conduct patient interview.

3.6.3. Data quality assurance

The data abstraction format was pre-tested in 5% of the sample size to check the validity of the data abstraction tool. The final tool was developed with some modifications after a thorough and deep review of inputs obtained during the pre-test. The pre tested patients were excluded from the analysis. The Principal investigator closely supervised the data collection process to make sure quality of data was maintained. During data analysis, incomplete data were discarded.

3.7. Study variables

3.7.1. Independent variables

- Demographic variables (age, sex, educational qualification, monthly income, marital status, occupation, place of residence, source of medication)
- Patient characteristics (type and number of prescribed AEDs, duration of treatment with AEDs)
- Types of seizure

- Adherence rate to medications

3.7.2. Dependent variables

- Seizure control status
- Adherence rate to medications

3.8. Data analysis

The filled-in forms were checked for completeness of data, cleaned prior to data entry and then entered using Epi Info™ version 3.5.3. In order to minimize data-entry errors, data were double entered and checked for discrepancies. Data analysis was carried out using Statistical Package for Social Sciences (SPSS®Statistics) program version 20 (SPSS; Chicago, IL, USA).

Descriptive statistics such as frequency, percentage, mean and standard deviation (SD) were employed to summarize patients' characteristics and other related information. Univariable binary logistic regression analysis was performed to relate each variable to adherence and seizure control status. From the univariable analysis, those variables with $p<0.2$ were selected for multivariable binary logistic regression analysis. Multivariable binary logistic regression analysis was used to assess predictability of the independent variables of adherence and seizure control status and to estimate the odds ratios (OR), 95% confidence intervals (CI) and p-values. The association was declared significant at $p<0.05$.

3.9. Ethical considerations

Ethical clearance and approval of the study protocols was granted from the Ethical Review Board of School of Pharmacy, AAU and ASMH Ethical Review Committee. Prior to data collection, informed written consent was obtained from the study participants. Each patient was informed about the objective of the study, procedures of selection and assurance of confidentiality (Annex II). Individuals were told that they had a right to withdraw from the study at any time and this would not affect the service they get from the hospital. Confidentiality was ensured during patient interview and review of charts. Thus, name and address of the patient were 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.

4. RESULTS

4.1. Socio-demographic Characteristics

Out of the total of 423 study participants enrolled, 397 were candidate for analysis. The demographic data (Table 1) revealed that about two- third of the patients were male. Almost half of the patients were adult. The mean age of the study population was 33.33 years (SD ±11.67 years; range: 14 to 81 years). Educational background of majority of the study participants was found to be primary and secondary school, 32% for both. The larger proportion of patients responded that they were urban dwellers. Around a third of the study participants were unemployed and a sizable proportion of them had very low (<445) monthly income. Evidently, significant proportions of the participants were free patients.

Table 1: Socio-demographic characteristics of epileptic patients on follow-up at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Variables		Number	Percentage (%)
Sex	Male	242	61.0
	Female	155	39.0
	Total	397	100.0
Age	Adolescent (<18)	14	3.5
	Young adult (18-30)	178	44.8
	Adult (31-60)	194	48.9
	Elder (>60)	11	2.8
	Total	397	100
Age at the time of first seizure	1-15	155	39.0
	16-30	185	46.6
	31-45	48	12.1
	46-60	8	2.0
	>60	1	0.3
	Total	397	100.0
Marital status	Single	215	54.2
	Married	164	41.3
	Divorced	14	3.5
	Widowed	4	1.0
	Total	397	100.0
Residence	Rural	79	19.9
	urban	318	80.1
	Total	397	100.0
Educational status	Illiterate	70	17.6
	Primary	127	32.0
	Secondary	127	32.0
	Tertiary	73	18.4
	Total	397	100.0
Occupation	Unemployed	116	29.2
	Housewife	54	13.6
	Farmer	38	9.6
	Student	41	10.3
	Daily laborer	13	3.3
	Employed	94	23.7
	Merchant	26	6.5
	Others***	15	3.8
	Total	397	100.0
Monthly income (ETB)	Very low (<445)	164	41.4
	Low (446-1200)	66	16.6
	Average (1201-2500)	43	10.8
	Above average (2501-3500)	22	5.5
	High (>=3501)	13	3.3
	Missing	89	22.4
	Total	397	100.0
Source of medication	Free	260	65.5
	Payment	137	34.5
	Total	397	100.0

ETB-Ethiopian birr * Catholic, Adventist ** Siltie, Hareri, Somali and Afar *** Pension, Broker

4.2. Clinical characteristics

Among the study participants, majority of the patients were diagnosed with GTCS, which accounted for almost three-quarter of the participants. This was followed by unclassified type of epilepsy, accounting for about a fifth of the patients (Table 2).

Table 2: Distribution of types of epileptic seizures at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Type of seizure	Frequency, N (%)
GTCS	302 (76.1)
CPS	5 (1.3)
Absence	7 (1.8)
Unclassified	83 (20.9)
Total	397 (100)

GTCS-generalized tonic clonic seizure CPS-complex partial seizure

The number of respondents to clinical factors of interest for the present study is depicted in Table 3. Accordingly, majority of the study participants had seizure free periods of less than two years and from those not seizure free, almost 95% of them had experienced seizure attack 1-5 times. With regards to follow up, respondents were evenly distributed across the interval years, with those followed up for more than 10 years tending to account for a slightly higher proportion. Whilst adverse effect was experienced by the majority, co-morbidity was found in less than a fifth of the participants.

Table 3: Distribution of respondents by clinical factors of epileptic patients on follow-up at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Variables		Number	Percent (%)
Seizure since last visit (within three months)	No	265	66.8
	Yes	132	33.2
	Total	397	100.0
Frequency of seizure	1-5x	125	94.7
	6-10x	4	3
	>10x	3	2.3
	Total	132	100.0
Follow up years	2-5years	125	31.5
	6-10years	132	33.2
	>10years	140	35.3
	Total	397	100.0
Seizure free period	<2 years	244	61.4
	2-5 years	109	27.5
	>5 years	44	11.1
	Total	397	100.0
Adverse effects	No	93	23.4
	Yes	304	76.6
	Total	397	100.0
Type of adverse effect	Depressed mood	41	10.3
	epigastric pain	36	9.1
	confusion	9	2.3
	weakness	16	4.0
	blurring of vision	13	3.3
	Headache	63	15.9
	nightmare	14	3.5
	forgetfulness	44	11.1
	skin rash	5	1.3
	Irritability	36	9.1
	gingival hyperplasia	5	1.3
	bone pain and fracture	22	5.5
	none	93	23.4
	Total	397	100.0
Types of comorbidity	Psychosis	21	5.3
	Depression	11	2.8
	Migraine headache	2	0.5
	Others	22	5.5
	None	341	85.9
	Total	397	100.0

4.3. Pattern of antiepileptic drugs use

Treatment with AEDs was found to involve monotherapy as well as combination therapy (Table 4). Monotherapy was found to be the most frequently prescribed treatment modality, with phenobarbitone seemed to be the preferred. Among the combination therapy, dual appeared to be more commonly used than triple therapy, with phenobarbitone and carbamazepine combination leading the rank order of frequency.

Table 4: Anti-epileptic drugs utilization pattern among epileptic patients at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Variables		**Frequency**	**Percent (%)**
Type of AED(s)	PHB	240	60.5
	VPA+CBZ	8	2.0
	PHB+PHT+CBZ	2	0.5
	VPA+CBZ+PHB	2	0.5
	VAP+CLONA	3	0.8
	PHT	14	3.5
	CBZ	30	7.6
	VPA	13	3.3
	PHB+PHT	31	7.8
	PHB+CBZ	43	10.8
	PHT+CBZ	5	1.3
	VPA+PHB	5	1.3
	VPA+PHT	1	0.3
	Total	397	100.0
Number of AED(s)	One	297	74.8
	Two	96	24.2
	Three	4	1.0
	Total	397	100.0

PHB-phenobarbitone VPA-valproic acid CBZ-carbamazepine PHT-phenytoin CLONA-clonazepam

As GTCS was the most commonly diagnosed seizure type, the variety treatment modalities were used for managing this seizure in majority (76%) of the cases. Phenobarbitone was the most commonly used single agent to control GTCS (77.1%). Indeed, it was also found to be the most frequently used single agent (61.4%) for controlling unclassified seizure. Carbamazepine either alone (13.3%) or in combination with phenobarbitone (11.6%) was the second most commonly used (13.3%) agent for controlling unclassified seizure. Phenobarbitone was commonly used to control GTCS and this was followed by use to control unclassified seizure (21.2%) (Table 5).

Table 5: Types of antiepileptic drugs prescribed by the type of seizure for epileptic patients at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Anti-epileptic drugs	**Seizure type**				**Total**
	GTCS	CPS	Absence	unclassified	
PHB	185	3	1	51	240
VPA+CBZ	4	0	1	3	8
PHB+PHT+CBZ	2	0	0	0	2
VPA+CBZ+PHB	2	0	0	0	2
VAP+CLONA	3	0	0	0	3
PHT	13	0	0	1	14
CBZ	17	2	0	11	30
VPA	5	0	4	4	13
PHB+PHT	28	0	0	3	31
PHB+CBZ	35	0	1	7	43
PHT+CBZ	4	0	0	1	5
VPA+PHB	3	0	0	2	5
VPA+PHT	1	0	0	0	1
Total	302	5	7	83	397

PHB-phenobarbitone VPA-valproic acid CBZ-carbamazepine PHT-phenytoin CLONA-clonazepam

GTCS was mainly treated with monotherapy followed by dual therapy and complex partial seizure was treated with only monotherapy (Figure 1).

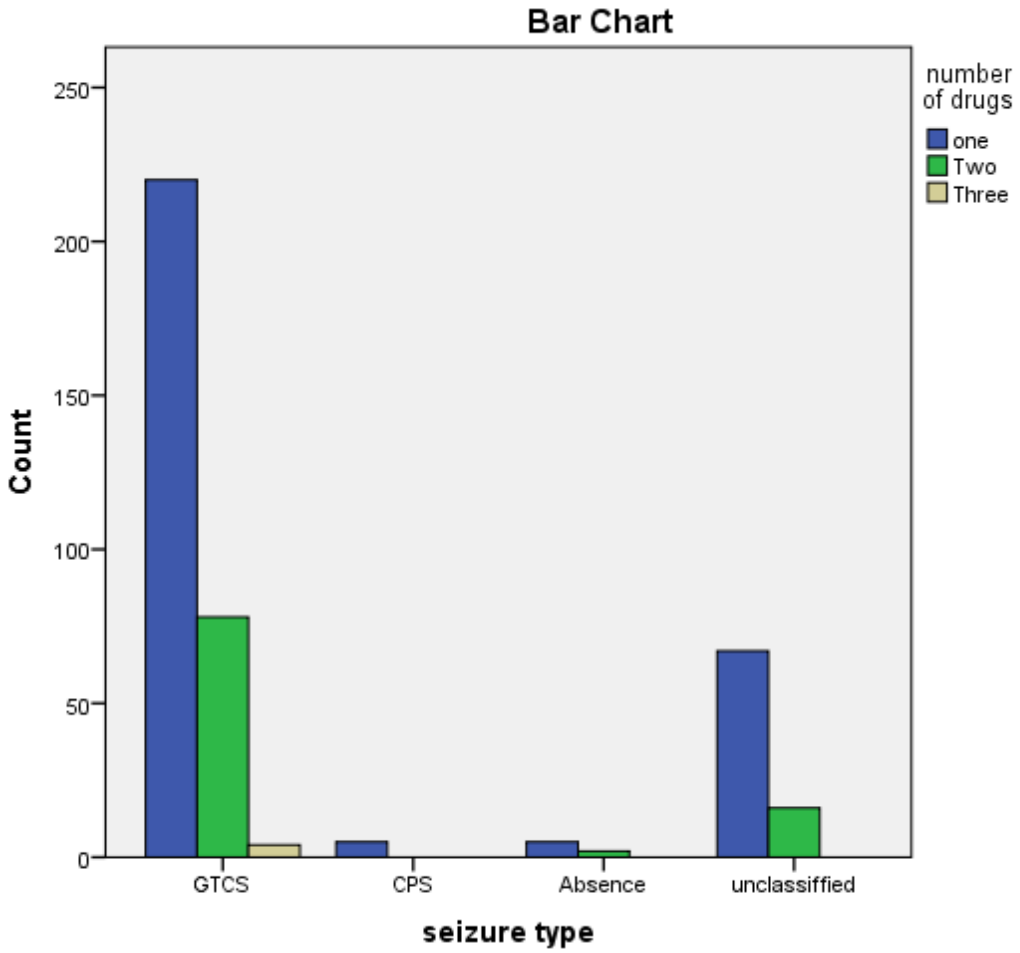

Figure 1: Distribution of mode of antiepileptic drugs therapy based on the type of seizure for epileptic patients at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

4.4. Seizure control status and Adherence

Determination of adherence using the Morsky scale revealed that majority (70%) of the participants were adherent to AEDs (Figure 2). By contrast, seizure control was achieved only in in about 39% of the participants (Figure 3). Out of those who had achieved seizure control, dose tapering was started for almost half of the patients, no plan had been made to taper for a sizable proportion of patients (Figure 4).

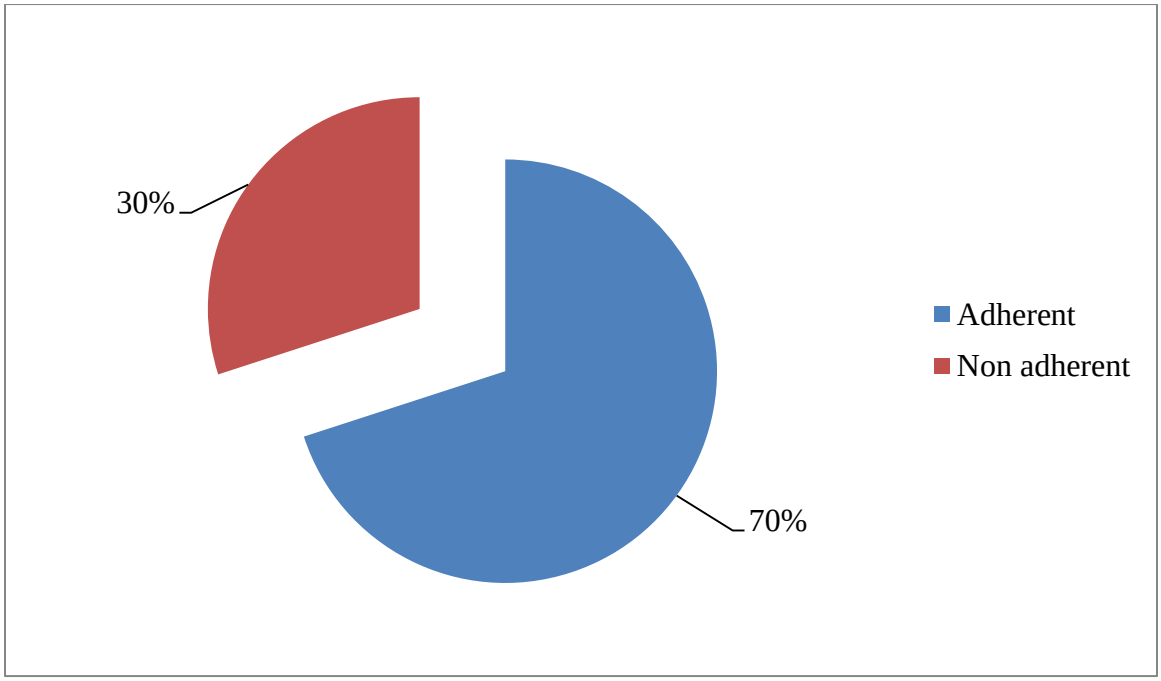

Figure 2: Adherence rate of epileptic patients at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

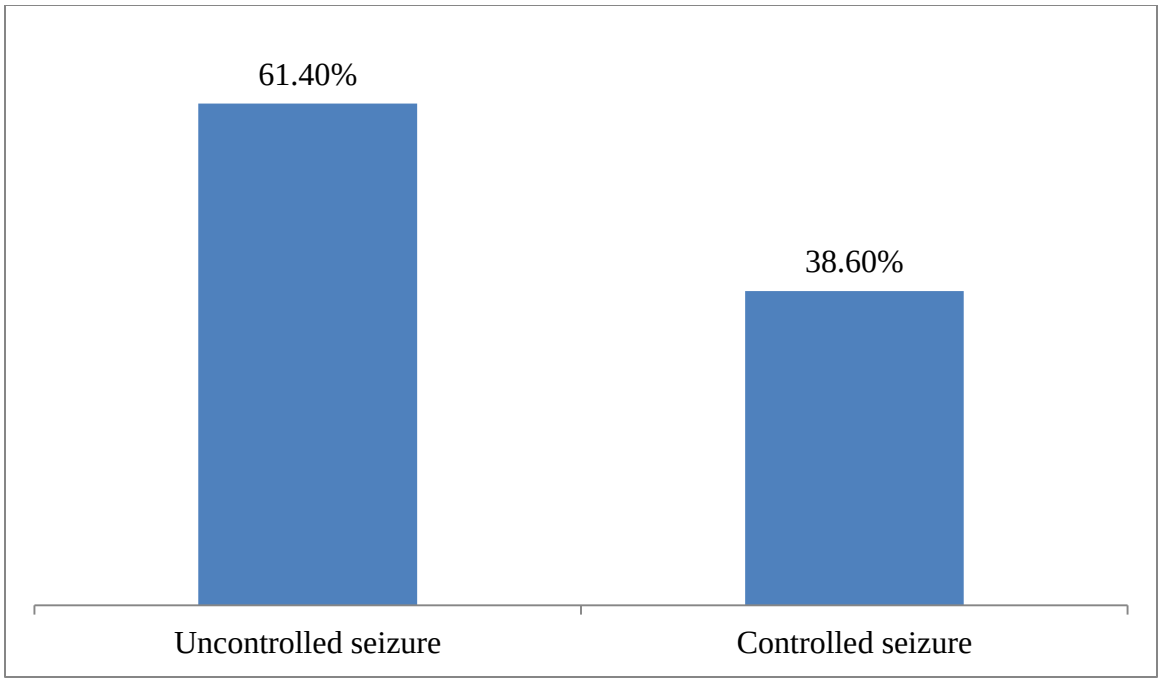

Figure 3: Seizure control status of epileptic patients at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

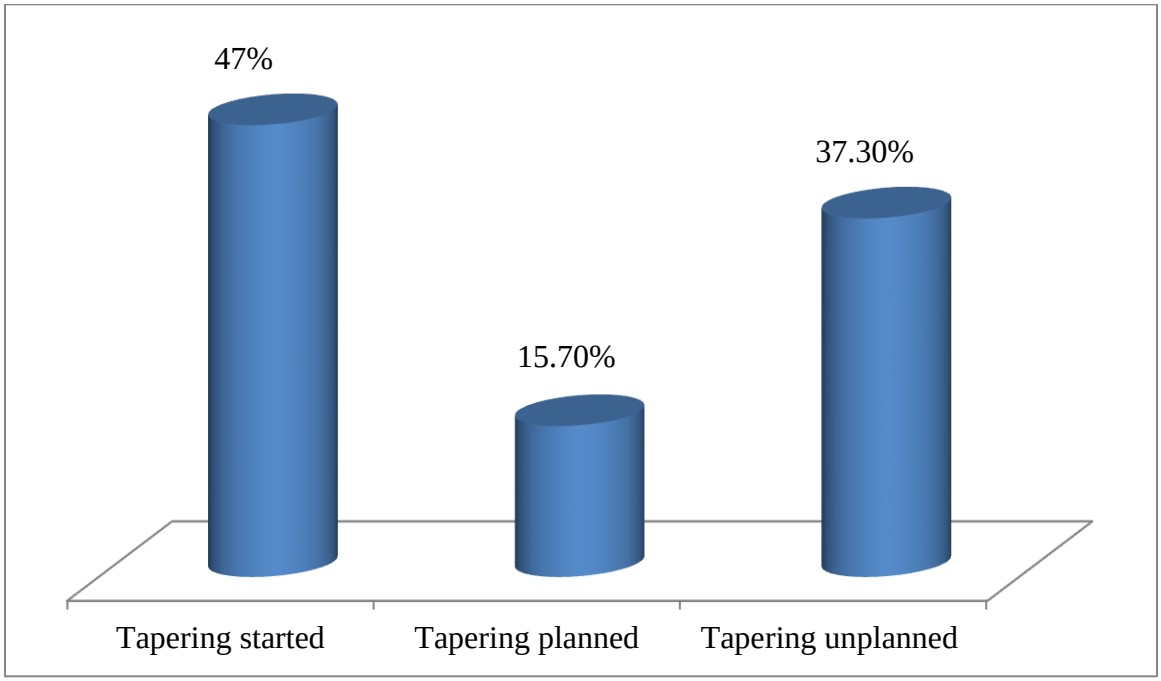

Figure 4: Planning of tapering to discontinue antiepileptic drugs for epileptic patients at Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

4.5. Determinant factors

In the present study, multivariable binary logistic regression analysis showed that there was no statistically significant association between place of residence and occupation of the patient with non-adherence to medication. However, follow up years and seizure free years had statistically significant association with adherence. The odds of being non adherent to medication for patients who had greater than ten years follow up period was decreased by 52.7% (AOR = 0.473, CI: 0.454, 0.719) as compared to those patients who had two to five years follow up, indicating year of follow up to have a statistically significant association with non-adherence. The odds of being non adherent to medications for those patients who had seizure free years greater than five was decreased by 59.7% as compared to those patients who had less than two years of seizure free period (AOR = 0.403, CI: 0.169, 0.959) (Table 6).

Table 6: Multivariable logistic regression analysis of factors associated with medication adherence among epileptic patients attending Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Variables	Adherence, n (%)		COR (95%CI)	AOR (95%CI)
	Non adherent	Adherent		
Educational Level				
Illiterate	14(20)	56(80)	1.00	1.00
Primary	32(25.2)	95(74.8)	0.347(0.663,2.739)	0.294(0.603,2.780)
Secondary	39(30.7)	88(69.3)	0.773(0.883,3.557)	0.574(0.699,3.548)
Tertiary	34(46.6)	39(53.4)	0.487(1.656,7.343)	0.913(1.156,7.341)*
Residence				
Rural	18(22.8)	61(77.2)	1.00	1.00
Urban	101(31.8)	217(68.2)	1.577(0.886,2.807)	0.894(0.395,2.011)
Occupation				
Unemployed	33(28.4)	83(71.6)	1.00	1.00
Housewife	16(29.6)	38(70.4)	1.059(0.521,2.154)	1.325(0.625,2.806)
Farmer	7(18.4)	31(81.6)	0.568(0.228,1.417)	0.768(0.249,2.374)
Student	15(36.6)	26(63.4)	1.451(0.684,3.080)	1.178(0.524,2.650)
Daily laborer	1(7.7)	12(92.3)	0.210(0.026,1.677)	0.352(0.042,2.943)
Employed	37(39.4)	57(60.6)	1.633(0.916,2.910)	1.350(0.696,2.619)
Merchant	4(15.4)	22(84.6)	0.457(0.146,1.429)	0.435(0.130,1.456)
Others	6(40)	9(60)	1.677(0.553,5.083)	1.543(0.461,5.170)
Seizure free years				
<2	86(35.2)	158(64.8)	1.00	1.00
2-5	25(23)	84(78)	2.449(1.090,5.505)	0.504(0.288,0.882)*
>5	8(18.2)	36(81.8)	1.339(0.552,3.251)	0.403(0.169,0.959)*
Follow up years				
2-5	47(37.6)	78(62.4)	1.00	1.00
6-10	41(31)	91(69)	0.748(0.264,1.217)	0.505(0.289, 0.586)*
>10	31(22)	109(78)	0.472(0.275,7.463)	0.473(0.454, 0.719)*

* Statistically Significant at P<0.05

Regarding seizure control status, whether controlled or uncontrolled, multivariable binary logistic regression analysis did not show any significant association with occupation, monthly income and source of medication (Table 7). However, educational level, adverse effect of drugs, number of drugs and adherence status were found to have a significant association with seizure control status. The odds of developing controlled seizure among patients with tertiary education were increased by 1.234 times than illiterate patients (AOR = 1.234, CI: 0.526, 2.896). On the other hand, the odds of developing controlled seizure among patients taking combination drugs were decreased by 63.2% as compared to monotherapy (AOR = 0.368, CI: 0.210, 0.646). The odds of developing controlled seizure among patients who had experienced drug side effects were decreased by 41.2% as compared to those patients who didn't experience drug side effects (AOR = 0.467, CI: 0.280, 0.779). Similarly, the odds of developing controlled seizure among non-adherent patients were decreased by 53.3% as compared to adherent patients (AOR = 0.467, CI: 0.280, 0.779) (Table 7).

Table 7: Multivariable logistic regression analysis of factors associated with seizure control status among epileptic patients attending Amanuel Specialized Mental Hospital from 1 July to 31 August 2015

Variables	Seizure control status, n (%)		COR (95%CI)	AOR(95%CI)
	Uncontrolled	Controlled		
Educational level				
Illiterate	39(55.7)	31(44.3)	1.00	1.00
Primary	85(67)	42(33)	0.622(0.341,1.132)	0.461(0.236,0.902)*
Secondary	83(65.4)	44(34.6)	0.667(0.367,1.211)	0.495(0.244,1.004)
Tertiary	37(50.7)	36(49.3)	1.224(0.634,2.364)	1.234(0.526,2.896)
Occupation				
Unemployed	81(70)	35(30)	1.00	1.00
Housewife	37(68.5)	17(31.50)	1.063(.529,2.137)	0.116(0.004,3.393)
Farmer	21(55.3)	17(44.7)	1.873(0.883,3.976)	0.182(0.006,5.173)
Student	28(68.3)	13(31.7)	1.074(0.498,2.316)	0.982(0.424,2.275)
Daily labor	6(46.2)	7(53.8)	2.700(0.846,8.615)	0.415(0.038,4.560)
Employed	53(56.4)	41(43.6)	1.790(1.014,3.161)	0.245(0.024,2.469)
Merchant	11(42.3)	15(57.7)	3.156(1.318,7.557)	0.548(0.049,6.121)
Others	7(46.7)	8(53.3)	2.645(0.890,7.860)	0.304(0.024,3.850)
Monthly income				
Very low	115(70.1)	49(29.9)	1.00	1.00
Low	33(50)	33(50)	2.347(1.305,4.221)	8.285(0.851,80.690)
Average	23(53.5)	20(46.5)	2.041(1.028,4.053)	5.059(0.500,51.152)
Above average	10(45.5)	12(54.5)	2.816(1.141,6.950)	5.913(0.525,66.621)
High	7(53.8)	6(46.2)	2.012(0.643,6.293)	3.010(0.237,38.235)
Missing	56(63)	33(37)	1.383(0.802,2.385)	7.200(0.257,201.642)
Number of drugs				
Monotherapy	167(56.2)	130(43.8)	1.00	1.00
Combination therapy	77(77)	23(23)	0.384(0.228,0.645)	0.368(0.210,0.646)*
Adherence status				
Adherent	158(56.8)	120(43.2)	1.00	1.00
Non adherent	86(72.3)	33(27.7)	0.505(0.317,0.805)	0.467(0.280,0.779)*
Adverse effect				
No	48(51.6)	45(48.4)	1.00	1.00
Yes	196(63.6)	108(36.4)	0.588(0.367,0.940)	0.588(0.349,0.989)*
Source of medication				
Free	168(64.6)	92(35.4)	1.00	1.00
Payment	76(55.5)	61(44.5)	1.466(0.961,2.235)	1.111(0.654,1.887)

* Statistically Significant at P<0.05

5. DISCUSSION

A series of conceptual reconsiderations and therapeutic advances in recent years has resulted in meaningful changes in the classification, diagnosis, and treatment of epilepsy. However, the practice of managing epilepsy appears to differ in different countries depending on the available expertise and resource. The present study attempted to assess treatment outcome among epileptic patients at ASMH. The overall treatment outcome revealed that 38.6 % of the patients had controlled seizure. 70 % of the patients were adherent and 76.6 % of the patients experienced at least one side effect from AEDs.

GTCS was the most common type of epileptic seizure encountered which accounted for about 76% followed by unclassified seizure 20.9%. The present result is in line with a study conducted in Jimma University, Ethiopia (80%) (Gurshaw *et al*., 2014) and Bangladish (74%) (Habib *et al*., 2013). This similarity might be due to classifying the seizure type is a problem for resource limited countries. However, the present study result is higher than from a study done in India (55.22%) (Li *et al*., 2007), Pakistan teaching hospital (47%) (Faizan & Sumbul, 2014) and Saudi Arabia (65%) (Gabr & Shams, 2015). This could be due to the difference in qualification of expertises and the diagnostic tools used which can facilitate the clasification of seizure type. The 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.

Most patients with epilepsy respond to one of the first- line AEDS; second-line agents may be useful in patients who do not respond to one or a combination of the first- line agents. In the present study, phenobarbitone (60.5%) was found to be the most frequently prescribed drug as monotherapy. This is in line with a study in Jimma University Hospital, Ethiopia (54.5 %)

(Gurshaw *et al*., 2014) and Gondar University Hospital, Ethiopia (61.89%) (Hailu *et al*., 2012). The reason for this could be due to its availabilty, affordability and all hospitals might use the same treatment guidline and they might follow WHO recommendation. WHO recommends phenobarbitone as the first line drug almost for all types of seizure except for absence seizure in resource limited countries. However, the present study finding is different from studies done elswhere, where phenytoin in India (Li *et al*., 2007), valproate in Pakistan (Faizan & Sumbul, 2014) and Saudi Arabia (Gabr & Shams, 2015), and carbamazepine in UK (Morgan *et al*., 2004) and Bangladish (Habib *et al*., 2013) were mostly prescribed. The reason for this difference could be due to the difference in treatment guidelines and WHO recommendation.

The present study also revealed that monotherapy (74.8%) was used as the prefered tereatment modality. This finding is in line with the findings in Jimma, Ethiopia (54.5%) (Gurshaw *et al*., 2014), ASMH (61.9 %) (Tegegne *et al*., 2015), UK (95.7%) (Morgan *et al.*, 2004), India (62.4%) (Li *et al*., 2007), Cambodia (60%) (Bhalla *et al*., 2013), Bangladish (67%) (Habib *et al*., 2013), Pakistan (77.5%) (Faizan & Sumbul, 2014) and Saudi Arabia (76.6%) (Gabr & Shams, 2015). All this findings showed that about 50% to 70% of patients can be maintained on one antiepileptic drug. Treatment should be started with a single conventional AED (monotherapy) and the dose should be slowly built up until seizure control is achieved or side effects occur.

Adherence to AEDs can be measured in several ways including self-report, pharmacy refill reports, electronic monitoring, and direct observation and by serum level drug concentration measuring. A gold standard measure of adherence remains elusive, but the experience of using MMAS-8 suggests that it is useful as an objective measure because the older techniques of interviewing patients in order to gain an estimate of their adherence is liable to the error of under

reporting. The findings showed that seizure free years and follow up years of the patients were found to have statistically significant association with adherence of patients. Adherence was 64.8% for those patients who had less than two seizure free years. This rate increased to 78 % and 81.8 % for those patients who had 2-5 and > 5 seizure free years, respectively. Likewise, improved adherence was observed with years of follow up, as it was increased from 62.4 % for 2-5 years to 78% for >10 years of follow up. These findings strongly suggest that longer duration of follow up and seizure free years would make patients to be more adherent to their medications and is in line with other studies (Liu *et al*., 2013). By contrast, adherence of the patients to their medication didn't show significant association with place of residence and occupation. This result is in line with the findings in Nigeria (Johnbul *et al*., 2011), UK (Jones *et al*., 2006) and China (Liu *et al*., 2013).

The rate of adherence to AEDs observed in the present study is in line with the study found in Gondar, Ethiopia (70.8%) (Abula *et al*., 2001) and USA (71%) (Hovinga *et al*., 2008). However, it was less than that of Palestine (85.3%) (Sweileh *et al*., 2011) and India (98.6%) (Sebastian *et al*., 2013). But, higher than that of Jimma, Ethiopia (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 & Shams, 2015). The probable reason for these discrepancies could be due to the differences in the methodology and sample size used for assessing adherence rate.

In this study, adherence status, adverse effect, educational level and number of drugs were found to have statistically significant association with treatment outcome of the patients. Those patients who were secondary and tertiary school, 34.6 % and 49.6 % respectively, of the patients had controlled seizure. Of those patients who took combination therapy only 23 % of them had

controlled seizure. But, of those patients who took monotherapy, 43.8 % of them developed controlled seizure. Of those patients who were adherent, 43.2 % of them developed a controlled seizure and only 27.7 % of non- adherent patients had a controlled seizure. Of those patients who had experienced side effect of the drugs, only 36.4 % of the patients had controlled seizure whereas 48.4 % of the patients had controlled seizure among those patients who didn't experienced side effect of the drugs.

The present study showed that 38.6 % of the participants were found to have a seizure free period of greater or equal to two years. Educational level, adverse effect of drugs, number of drugs and adherence status were found to have significant association with seizure control status. The multivariable logistic regression analysis showed the odds of developing seizure control among tertiary level educational level was increased by 1.234 times as compared to the illiterate patients. This might be due to patients who are more literate might question their health care providers about their disease and its medications and might be more aware of the disease progression. Patients taking combination drugs were less likely to control their seizure. Similar studies found a negative association between complexity of medication with seizure control (Jones *et al*., 2006; Ahmad *et al*., 2013). This might be due to the fact that when the number of drugs prescribed to patients increase, the adherence of patients to take medication will be decreased. Since adherence was shown to positively associate with seizure control in the present and others study (Hovinga *et al*., 2008; Nakhutina *et al*., 2011), combination drugs obviously would have negative effect on seizure control.

The present study also found that patients experienced drug side effect become less likely to develop seizure control. Similar study was found in South Africa that showed a negative association between side effect of drugs and seizure control (Egenasi *et al*., 2015). This might be

because of those patients who experienced drug side effect became non-adherent to their medication. This lead to negative association of side effect with seizure control status.

6. LIMITATIONS OF THE STUDY

- The cross-sectional nature of the study did not allow a follow up, which would have provided a better design for identifying the factors associated with adherence and seizure control status.
- Self-reported measure of adherence was used to measure adherence which could have caused overestimation of adherence.
- Patients might not remember or recognized their seizure activity after their attack.
- The type of drugs collected were drugs prescribed at the time of recent follow up; it didn't include drugs that were switched or withdrawn.
- Finally, the questionnaire was only administered to patients of a single center, which might not represent the general population of epileptic patients and have a limit in broader applications of these findings.

7. CONCLUSION

The findings from the present study indicated that the rate of adherence to AEDs was found to be 70 %. Duration of follow up and seizure free years were found to have a significant association with adherence status of the patients.

Seizure control was achieved in 38.6 % of the patients. Adherence to medication and educational level were found to have a positive and significant association with seizure control status. However, combination therapy and side effect burden were found to have a negative association. A fifth of the patients the patients were diagnosed as unclassified seizure. The most widely used treatment modality was monotherapy and phenobarbitone was the most commonly prescribed drug.

In general, those patients who were adherent, without apparent drug side effects and monotherapy had better treatment outcome.

8. RECOMMENDATIONS

- Prescribers should classify the type of seizure for proper selection of treatment.
- All health care providers should give tailored educations and instructions about the importance of adherence to AEDs treatment to the patients as well as care givers.
- For those patients who had seizure free period of greater or equals to two years, there must be a consideration of clinical assessment to withdraw AED treatment.

References

Abula T, Worku A (2001). Patient non-compliance with drug regimens for chronic diseases in northwest Ethiopia. *EJHD* **15**(3): 185-192.

Ahmad N, Othaman NI, Islahudin F (2013). Medication adherence and quality of life in epilepsy patients. *IJPP* **5**(2): 3–6.

ILAE (2005). Conceptual definition of seizure and epilepsy.

ILAE (2014). A practical clinical definition of epilepsy.

Ahmed N, Spencer S (2004). An approach to the evaluation of a patient for seizures and epilepsy. *WMJ* **103**(1): 49–55.

Banerjee PN, Filippi D, Hauser WA (2009). The descriptive epidemiology of epilepsy - a review. *E R* **85**(1): 31–45.

Bhalla D, Chea K, Hun C, Chan V, Huc P, Chan S et al (2013). Epilepsy in Cambodia-treatment aspects and policy implications: a population-based representative survey. *PS* **8**(9): 1-9.

Egenasi C, Steinberg WJ, Raubenheimer JE (2015). Beliefs about medication, medication adherence and seizure control among adult epilepsy patients in Kimberley, South Africa. *SAFP* **57**(5): 326–332.

Elson L (2011). Predictors of outcome in newly diagnosed epilepsy. *NA* **16**(1): 27-9.

Epilepsy Implementation Task Force (2015). Provincial Guidelines for the Management of Epilepsy in Adults and Children.

Faizan M, Sumbul S (2014). Drug Utilization Evaluation of Antiepileptics in Three Selected Multidisciplinary Teaching Hospitals of Pakistan. *IJPPS* **6**(5): 59–66.

Fanta T, Azale T, Assefa D, Getachew M (2015). Prevalence and Factors Associated with Perceived Stigma among Patients with Epilepsy in Ethiopia. *PJ* **20**(15): 1–7.

Faught RE, Weiner JR, Guérin A, Cunnington MC, Duh MS (2009). Impact of nonadherence to antiepileptic drugs on health care utilization and costs: findings from the RANSOM study. *EJ* **50**: 501-502.

Ferrari CM, Sousa RM, Castro LH (2013). Factors associated with treatment non-adherence in patients with epilepsy in Brazil. *Seizure* **22**(5):384.

Gabr WM, Shams ME (2015). Adherence to medication among outpatient adolescents with epilepsy. *SPJ* **23** (1): 33–40.

Garnett WR (2000). Antiepileptic drug treatment: outcomes and adherence. *PJ* **20**(8): 1915–1995.

Getachew H, Dekema HN, Awol SS, Abdi AA, Mohammed MA (2014). Medication adherence in epilepsy and potential risk factors associated with non-adherence in tertiary care teaching hospital in southwest Ethiopia. *GMJ* **20**(1): 59–65.

Gurshaw M , Agalu A , Chanie T (2014). Anti-epileptic drug utilization and treatment outcome among epileptic patients on follow-up in a resource poor setting. *JYP* **6**(3): 47–52.

Habib M, Khan SU, Hoque, MA, Mondal MB, Hasan AH, Chowdhury RN, Haque B, Rahman KM et al (2013). Antiepileptic drug utilization in Bangladesh: experience from Dhaka Medical College Hospital. *BMCR* **6**: 473.

Hailu W, Tamiru W, Berhane A, Tsega B (2012). Prescription pattern of psychotropic , narcotic and anticonvulsant drugs in Gondar University. *IJPIR* **2**(4): 411–415.

Harold G (2000). Medication Non adherence: Finding solutions to a costly medical problem. *DBT* **12**(6): 57-62.

Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD et al (2008). Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. *E & B* **13**(2): 316–322.

Hsieh LP, Huang CY (2009). Antiepileptic drug utilization in Taiwan: Analysis of prescription using National Health Insurance database. *ER* **84**(1): 21–27.

Ipingbemi AE (2015). Management, treatment outcome and cost of epilepsy in a tertiary health care facility in northern Nigeria. *IJMU* **10**(2): 25-36.

Johnbull OS, Farounbi B, Adeleye AO, Ogunrin O (2011). Evaluation of Factors Influencing Medication Adherence in Patients with Epilepsy in Rural Communities of Kaduna State, Nigeria. *N& M* **2**: 2 99–305.

Jones RM, Butler JA, Thomas VA, Peveler RC, Prevett M (2006). Adherence to treatment in patients with epilepsy: Associations with seizure control and illness beliefs. *SJ* **15**(7): 504–508.

Li LM, Cendes F, Boer H, Miranda CT, Prilipko L, Sander JW et al (2007). Demonstration project on epilepsy in Brazil Situation assessment. *AN* **65**(1): 5–13.

Liu J, Liu Z, Ding H, Yang X (2013). Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. *ED* **15**(3): 289–294.

Louis EK, Rosenfeld WE, Bramley T (2009). Antiepileptic Drug Monotherapy: The Initial Approach in Epilepsy Management. *CNP* **7**: 77-82.

Manjunath R, Davis KL, Candrilli SD, Ettinger AB (2009). Association of antiepileptic drug nonadherence with risk of seizures in adults with epilepsy. *E & B* **14**(2): 372–378.

Morgan CL, Buchan S, Kerr MP (2004). The outcome of initiation of antiepileptic drug monotherapy in primary care: a UK database survey. *BJGP* **54**(507): 781–783.

Morisky D (2008). Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. *JCH* **10**(5):384-354.

Munger MA, Van TBW, La FJ (2007). Medication nonadherence: An unrecognized cardiovascular Risk factor. *MGM* **9**(3): 58.

Nakhutina L, Gonzalez JS, Margolis SA, Spada A, Grant A (2011). Adherence to antiepileptic drugs and beliefs about medication among predominantly ethnic minority patients with epilepsy. *E & B* **22**(3): 584–586.

Overweg J (1995). Withdrawal of antiepileptic drugs (AEDs) in seizure- free patients , risk factors for relapse with special attention for the EEG. *BEA* **4**: 19–36.

Privitera M (2011). Current Challenges in the Management of Epilepsy. *AJMC* **7**: 195-203.

Purcell B, Gaitatzis A, Sander J, Majeed A (2002). Epilepsy prevalence and prescribing patterns in England and Wales. *HSQ* **15**: 23–30.

Radhakrishnan K (2009). Challenges in the management of epilepsy in resource-poor countries. *NRN* **5**(6):323-30.

Riccardo P, Vietri J (2014). Comparison of the 4-item and 8-item Morisky Medication Adherence Scale in patients with type 2 diabetes. Montreal, Canada: Kantar Health.

Rout K, Kar M (2010). A review on antiepileptic agents, current research and future prospectus on conventional and traditional drugs. *IJPSRR* **3**(2): 19–23.

Scottish Intercollegiate Guidelines Network (2003). Diagnosis and management of epilepsy in adults: key to evidence statements and grades of recommendation.

Sebastian J, Adepu R, Keshava BS Harsha S (2013). Assessment of antiepileptic drugs usage in a South Indian tertiary care teaching hospital. *NA* **18**(2): 159–165.

Shih-Hui M, Eng-King N (1997). Pattern of anti-epileptic drug uasage in a refferal hospital in Singapore. *NJSA* **2**: 77–85.

Suurmeijer TP, Reuvekamp MF, Aldenkamp BP (2001). Social functioning, psychological functioning, and quality of life in epilepsy. *EJ* **42**(9): 1160-1168.

Sweileh WM, Ihbesheh MS, Jarar IS, Abu AS, Sawalha AF, Zyoud H, Jamous RM, Morisky DE (2011). Self-reported medication adherence and treatment satisfaction in patients with epilepsy. *E & B* **21**(3): 301–305.

Tefera GM, Woldehaimanot TE, Angamo MT (2015). Poor treatment outcomes and associated factors among epileptic patients at Ambo Hospital, Ethiopia. *GMJ* **21**(1): 9-16.

Tegegne MT, Mossie TB, Awoke AA, Assaye AM, Gebrie BT, Eshetu DA (2015). Depression and anxiety disorder among epileptic people at Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia. *BMCP* **15**(1): 210.

Tekle-Haimanot R Forsgren L, Ekstedt J (1997). Incidence of epilepsy in rural central Ethiopia. *EJ* **38**(5): 541–546.

Tekle-Haimanot R, Forsgren L, Abebe M, Gebre-Mariam A, Heijbel J, Holmgren G, Ekstedt J (1999). Clinical and electroencephalographic characteristics of epilepsy in rural Ethiopia: a community-based study. *ER* **7**(3): 230–239.

Wells BG, DiPiro JT, Schwinghammer TL, DiPiro CV (2008). Pharmacotherapy: A Pathophysiologic Approach. 7th Edition (pp.927-953). United States of America: The McGraw-Hill Companies, Inc.

WHO (2004). Epilepsy in the WHO African region: Bridging the gap. The Global Campaign against Epilepsy.

ANNEXES

Annex I: English Version of Information Sheet

Dear participant, Good Morning/Afternoon

Introduction

My name is _____. I am a member of the study that is carried out at Amanuel Specialized Mental Hospital; Addis Ababa, Ethiopia entitled "Adherence and Treatment Outcome among Epileptic Patients on Follow up".

Objective

The main purpose of this study is to assess adherence and treatment outcome among epileptic patients at ASMH, Addis Ababa, Ethiopia. Your input will be extremely valuable as the information will be used to assess the medication use and adherence to identify gaps in treatment outcome.

Expected Outcomes and/or Benefits

At the end of the study, the adherence and treatment outcome will be evaluated. Therefore, the study will identify and investigate the main gaps and challenges associated with adherence and treatment outcome and will propose the feasible recommendations and may benefit you directly or indirectly by improving the epilepsy treatment in the hospital.

Thank you for your help.

Annex II: English Version of Informed Consent Form

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. None of this would affect the care you receive from ASMH, but will help in future planning for the hospital. No identifying names or characteristics will go into my report, so you may share your thoughts openly. 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 be grateful if you could sign the attached form to say you have no objections to our accessing any records and interviewing you. Would you be willing to assist me by having a 30-45 minutes' interview with me? Interview accepted: Yes □ No □

If the interviewee responds "Yes" please proceed and let him/her to sign or replies "No" gratitude him/her and quit the interview. If you have any questions concerning the study, please call Melak Gedamu (+251) 913-81 81 22.

_____ _____

Signature of respondent Signature of interviewer

Date: _____ (Day/month/year)

Principal Investigator: Melak Gedamu

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

Email: gedamumelak@gmail.com

Annex III: Data Abstraction Format from patient interview

Part I: Socio-demographic Characteristics

Scio Demographic Information			
Age: _____(Write in number)			
Sex			
❑ Male	❑ Female		
Marital Status			
❑ Single	❑ Married	❑ Divorced	❑ Widowed
Educational Level: _____(Write in number/word)			
❑ Illiterate		❑ Secondary school	
❑ Primary school		❑ Tertiary institution	
Place of Residence			
❑ Rural	❑ Urban		
Occupation			
❑ Unemployed	❑ Farmer	❑ Merchant	
❑ House wife	❑ Daily laborer	❑ Other(s) [Specify]:_____	
❑ Student	❑ Employed		
Monthly Income (ETB): _____(Write in number)			
❑ Very Low (< 445 Birr)	❑ Low (446-1200 Birr	❑ Above average (2501-3500 Birr)	
	❑ Average (1201-2500 Birr)	❑ High (>3501 Birr)	

Part II: Assessment of adherence

1.	**Morisky Medication Adherence Scale (MMAS-8)**		
	Questions	**Yes**	**No**
1.1.	Do you sometimes forget to take your pills?		
1.2.	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?		
1.3.	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?		
1.4.	When you travel or leave home, do you sometimes forget to bring along your medicine?		
1.5.	Did you take all your medicine yesterday?		
1.6.	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?		
1.7.	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
1.8.	How often do you have difficulty remembering to take all your medicine? ❑ Never/rarely ❑ Once in awhile ❑ Sometimes ❑ Usually ❑ All the time		

Annex IV: Data abstraction format from patient medical records

1. Date of registration_____
2. When did the first seizure episode occur? _____
3. How old were the patient when he/she encountered the first seizure episode? _____
4. When did he/she encounter the recent seizure episode? _____
5. Was there any seizure since the last visit? Yes _____ No _____
6. If yes, how many times? _____
7. Source of medication: free_____ payment_____
8. Diagnosis (seizure type)_____
9. When did you start antiepileptic drug(s) treatment? _____
10. Type(s) of antiepileptic drug(s) prescribed_____
11. Was tapering of the dose started? Yes_____ No _____
12. Was tapering of the dose planned? Yes_____ No_____
13. Diagnosis other than epilepsy _____
14. Drugs prescribed other than antiepileptic drug (s)? Yes_____ No_____
15. Was there any experienced adverse effect of the drugs? Yes_____ No_____
16. If yes, what type of adverse effect occurred?

Depressed mood___ epigastric pain___ confusion___ weakness___ blurring of vision___ headache___ nightmare___ forgetfulness___ skin rash___ Irritability____ gingival hyperplasia__ bone pain and fracture____ others_____

Thank you very much for your time

_____ _____

Name and Signature of Data Collector Name and Signature of Principal Investigator

Annex V: Questionnaire, Amharic Version (የአማርኛ መጠይቅ ቅፅ)

ቅጽ 1: የጥናቱ መረጃ ቅጽ

ቀን፡-_____

ውድ የቃለ መጠይቅ ተሳታፊ፤ እንደምን አደሩ/ዋሉ?

የጥናቱ መግቢያ

ስሜ_____ ይባላል። ‘‘በአማኑኤል ስፔሻላይዝድ የአእምሮ ሆስፒታል በሚጥል በሽታ ታካሚዎች ዙርያ የሚጥል መድሃኒቶች በታዘዘው መሰረት በአግባቡ የአወሳሰድና የአጠቃቀም ሁኔታ’’ የተሰኘ የድህረ ምረቃ ጥናት አባል ነኝ።

በተለይ የእርስዎ የመድሓኒት አጠቃቀም በጥናቱ ላይ በደንብ ከሚጠኑ ነጥቦች አንዱ ነዉ።

የጥናቱ አላማ

የዚህ ጥናት ዋና አላማው የሚጥል መድኃኒቶች እንዴት እንደሚጠቀሙት፣ በታዘዘው መሰረት በአግባቡ እንዴት መድኃኒትዎን እንደሚወሰዱት እና መድኃኒትዎን ሁል ጊዜ እንዳይወሰዱ የሚያደርጉ ዋና ዋና ክፍተቶችን በመለየት፤ የመፍትሄ ሀሳቦችን ማቅረብ ነው።

ከጥናቱ የሚጠበቁ ውጤቶች/ጥቅሞች

በዚህ ጥናት ላይ የእርስዎ የሚጥል መድኃኒቶች በታዘዘው መሰረት በአግባቡ የአወሳሰድና የአጠቃቀም ክህሎት በድንብ ይጠናሉ። መድኃኒትዎን ሁል ጊዜ እንዳይወሰዱ የሚያደርጉ ዋና ዋና ክፍተቶችን በመለየት፤ የመፍትሄ ሀሳቦችን ማቅረብ ነው።በተጨማሪም ከጥናቱ በሚገኙ ግኝቶች የሚጥል ህክምና ዉጤትን በተወሰነ መልኩ ለማሻሻል እንደሚቻል በመገመት፤ እርስዎ የጥቅሙ ተቋዳሽ ይሆናሉ ብለን እናምናለን። 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 የሚዉል ነው። በተጨማሪም የእርስዎ ተሳታፊነት በፈቃደኝነት የተመሠረተ ነው። የጥናቱ አላምውን ተረድተውና ጊዜዎን ሰውተው፤ ከ 30-45 ደቂቃዎች ለሚፈጅ ቃለ-መጠይቅ እውተኛው መረጃ ለመስጠት ፍቃደኛ በመሆንዎ በቅድሚያ አመሰግናለሁ።

በየትኛው ጊዜ ጥያቄ ካለዎት መላክ ገዳሙ ብለው በ ስ.ቁ. (+251) -913-81 - 81- 22 ወይም

በ ኢ-ሜይል gedamumelak@gmail.com 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

ኢ-ሜይል: gedamumelak@gmail.com

ስ/ቁ: +251-913 81 81 22

ቅፅ 3: ቃለ-መጠይቅ ከታካሚው

ክፍል 1. ስለ ታካሚው አጠቃላይ መገለጫዎች

1.1. ዕድሜ:- _____ (በቁጥር ይፃፍ)

1.2. ፆታ

□ ወንድ □ ሴት

1.3. የጋብቻ ሁኔታ

□ ያላገባ □ ያገባ □ 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

1.6. መኖሪያ ቦታ

□ ገጠር □ ከተማ

1.7. የስራ ሁኔታ

□ ስራ የሌለው □ የቤት-እመቤት □ የግል ስራ/ነጋዴ □ ተማሪ □ የቀን ሰራተኛ □ ግብርና □ ሌላ/ሌሎች (ይገለፅ):_____

1.9. ወርሓዊ የቤሰተብ ገቢ (በብር)_____ (በቁጥር ይፃፍ)

□ በጣም ዝቅተኛ(< 445 ብር) □ ዝቅተኛ (446-1200 ብር) □ አማካይ (1201-2500 ብር)

□ከአማካይ በላይ (2501-3500 ብር) □ ከፍተኛ (≥3501 ብር)

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

ሞሪስኪ" መድኃኒትን በታዘዘው መሰረት በአግባቡ ስለመውሰድ" መለኪያ- 8		
ጥያቄዎች	አዎ	አይደለም
አንዳንድ ጊዜ መድኃኒትዎን ረስተው ሳይወስዱ ቀርተው ያውቃሉ?		
ሰዎች አንዳንድ ጊዜ ከመርሳት ውጪ ባሉት የተለያዩ ምክንያቶች መድኃኒታቸውን ሳይወስዱ ይቀራሉ፡፡ ባለፉት ሁለት ሳምንታት፣ መድኃኒትዎን ሳይወስዱ የቀሩበት ቀናቶች ነበሩ'?		
ሐኪምዎን ሳይነግሩ፣ መድኃኒትዎን እየወሰዱ ህመምዎ ሲባባስ፣ መድኃኒትዎን አቋርጠው ያውቃሉ?		
በጉዞ ምክንያት ወይም ከቤትዎ አርቀው ሲጓዙ፣ አንዳንድ ጊዜ መድኃኒትዎን (ወደጉዞው) ረስተውት ሳይወስዱት ያውቃሉ?		
በትላንትናው ዕለት ሁሉንም መድኃኒትዎን ወስደውታል?		
ህመምዎ ሲሻልዎት (የህመምዎ ስሜቶች ሲጠፉ) አንዳንድ ጊዜ መድኃኒትዎን አቋርጠው ያውቃሉ?		
በየቀኑ መድኃኒት መውሰድ፣ ለአንድ አንድሰዎች ምቾት አይሰጣቸውም፡፡ እርስዎ በየቀኑ፣ እንድሁም አንድም ሰዓት ሳያዛንፉ መድኃኒትዎን መውሰድዎ፣ የመሰላቸት ስሜት ተሰምቶት ያውቃል?		
መድኃኒትዎን አስታውሰው ለመውሰድ ምንያክል ይቸገራሉ?		
❑ ጭራሽ አይቸግረኝም ❑ ከዕለታት አንድ ጊዜ ይቸግረኛል ❑ አንዳንድ ጊዜ ይቸግረኛል ❑ አብዛኛው ጊዜ ይቸግረኛል ❑ ሁል ጊዜ ይቸግረኛል		