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ASSESMENT OF FACTORS ASSOCIATED TO POOR TREATMENT OUTCOMES AMONG EPILEPTIC PATIENTS TAKING ANTI EPILEPTIC MEDICATIONS AT SHAMBU GENERAL HOSPITAL, NORTH WEST ETHIOPIA

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ABSTRACT

Background: Epilepsy is one of the most prevalent neurological disorders that can be effectively prevented and treated at an affordable cost. Adherence to AED therapy is critical for effective disease management, yet adherence and persistence rates are low due to several barriers. No adherence to treatment is one factor, which affect treatment outcome. A significant association was seen among some of the commonly reported triggering factors for epileptic patients. **Objective**: To assess treatment outcomes and associated factors for poor treatment outcomes among patients taking AEDs at Shambu General Hospital, North West Ethiopia **Methods and patients**: A hospital based retrospective cross – sectional study was conducted from October 24 to December 9, 2016, through patient interview and patient chart review to assess the level of poor treatment outcome and influencing factors in epilepsy patients on AEDs attending at Shambu General Hospital. Samples of 132 patients were selected to gather a required data and convenient sampling technique was used. Structured standard interview questionnaires were prepared to collect data and data analysis was done using tally, pen, pencil and papers manually. Pre-testing of the questionnaire was done on 10 patients. Verbal consent from participants was taken before the interview. **Result**: One hundred fourteen (86.4%) were reported one or more triggering factors that can increase their seizure attacks. The most common triggering factors were emotional stress (97.4%), sleep deprivation (78.1%), missing meal (29.8%), missing medication (21.9%), and noise (15.5%) as reported by the patients. Fifty-nine patients (44.7%) had poor seizure control. Seventy one patients (53.8%) were classified as non-adherent to medication. The major reasons for non-adherence were as a result of forgetfulness (73.2%), Feeling sick/side effects (60.6%), being away from home (The schedule of their work makes it impossible) (26.8%), and Poly-pharmacy (Drugs are too many) (22.5%).Therefore there is significant association between level of adherence (P=0.001), number of seizure attacks before AEDs initiation (p=0.028), EEG (neurologic abnormality) (p=0.04) and age at onset of seizure (diagnosis) (p=0.026). There is no significant association between brain injury (p=0.61) and epilepsy treatment outcome. **Conclusion:** Assessment of adherence should be a routine part of management of epilepsy to identify modifiable factors that could be acted on to improve seizure treatment outcome. Poor adherence to prescribed medication is considered to be the main cause of unsuccessful drug treatment for epilepsy. The major reasons for non-adherence with their descending order were as a result of forgetfulness, Feeling sick/side effects, being away from home (The schedule of their work makes it impossible), Poly-pharmacy (Drugs are too many). The most common triggering factors were: emotional stress, sleep deprivation, missing meal, missing medication, and noise. There is significant association between level of adherence, number of seizure attacks before AEDs initiation, EEG (neurologic abnormality) and age at onset of seizure (diagnosis). There is no significant association between brain injury and epilepsy treatment outcome. **Recommendation**: The health professionals working at Shambu Hospital should prepare some interventions to improve adherence to anti-epilepsy medications. There should be assessment of seizure triggering factors and inform the patient so that they can avoid those triggering factors to increase their quality of life by reducing/eliminating seizure. Since there is no research done on this topic in the country specifically in Shambu Hospital, further studies are needed.

KEYWORDS: Epilepsy, Seizure, Shambu Hospital, Treatment Outcome, Adherence, Antiepileptic Drug.

1. INTRODUCTION

1.1 Back Ground

Epilepsy is a common neurological disease affecting almost 50 million people worldwide. 5million of who have seizures more than once per month.[1,2] Approximately 85% of people afflicted with epilepsy live in developing countries. Two million new cases occur in the world each year. The results of studies suggest that the annul incidence in developed countries is approximately 50 per 100 000 of the general population whereas in developing countries this figure is nearly doubled to 100 per 100 000.[1]

In developing countries, few patients with epilepsy receive adequate medical treatment, and an estimated 75 to 90% receive no treatment at all.[3] The treatment of epilepsy in developing countries remains far from satisfactory, mainly because of the general lack of medical personnel; non-availability of medications; and lack of information and/or education on epilepsy for both patients and medical staff.[1,3,4]

Epilepsy is characterized by a tendency to recurrent seizures and it is defined by two or more un provoked seizures [generally within 2 years]. Seizures may vary from the briefest lapses or muscle jerks to severe and prolonged convulsions. They may also vary infrequency, from less than one a year to several per day.[1] The risks of recurrent seizures include intractable epilepsy, cognitive impairment, physical injury, psychosocial problems and death.[5] Children suffer mainly from idiopathic generalized epilepsy and absence, myoclonus and generalized tonic– clonic seizures are the most common forms of seizure seen in children. In adults, symptomatic partial epilepsy is the most common form, and it may cause simple partial, complex partial, or secondarily generalized tonic–clonic seizures. Convulsive or tonic–clonic status epilepsy is of major concern, as it is associated with a mortality rate of 5–15%.[6]

Much of the treatment of epilepsy aimed at creating a balance between prevention of seizures and minimization of side effects to a level that the patient can tolerate. Although AED therapy does not offer a permanent cure, successful therapy can eliminate or reduce symptoms.

The most commonly used AEDs are [in alphabetical order]: carbamazepine, ethosuximide, phenobarbital, phenytoin and valproic acid. New AEDs such as gabapentin, lamotrigine, leviteracetam, felbamate, oxcarbazepine, tiagabine, topiramate, vigabatrin and zonisamide have a role in the management of the 20–30% of patients with epilepsy who remain refractory to conventional drug therapy.[5,7]

About 25% of patients with epilepsy have intractable seizure disorders; of those between 12 and 25% are candidates for surgery. The direct costs attributable to epilepsy include physician visits, laboratory tests, emergency department visits, antiepileptic drugs and hospitalizations. Indirect costs include working days lost, lost income, decreased quality of life, the cost of failed therapy and side-effects of drugs. Garnett et al. referring to the "Epilepsy Foundation of America data, reported that the annual direct and indirect costs of epilepsy exceeded $12.5 billion. The direct costs of epilepsy are significantly lower for patients whose epilepsy is controlled than for those whose disease is not controlled.[5]

Recent studies in both developed and developing countries have shown that up to 70% of children and Adults newly diagnosed with epilepsy can be successfully treated [i.e. their seizures can be completely controlled for several years] with antiepileptic drugs. After 2–5 years of successful treatment, drugs can be withdrawn in about 70% of children and about 60% of adults without relapse occurring.[1]

In the case of treatment failure, it is crucial to establish whether the failure is a result of inappropriate drugs election, inappropriate dosing, refractory disease or poor adherence to the therapeutic regimen.[5]

Poor adherence to prescribed medication is considered to be the main cause of unsuccessful drug treatment for epilepsy.[8] Non-adherent patients experience an increase in the number and severity of seizures, which leads to more ambulance rides, emergency department visits and hospitalizations. Non-adherence therefore results directly in an increase in health care costs, and reduced quality of life.[8,9]

As epidemiology of adherence to medication shows, adherence can vary from an occasional missed dose to chronic defaulting on medication regimens. Adherence to antiepileptic drugs in patients with epilepsy generally ranges from 20 to 80%.[10] Some studies reported different ranges of adherence for adult patients [40–60%] and children [25–75%].[8]

Some interventions have designed to improve adherence to anti-epilepsy medications. Some of them target specific factors. Those factors are:- the therapeutic relationship [increasing communication between patient and health professional],giving full instructions about the treatment and discussing the pros and cons of treatment with the patient, reducing the number of medications and the frequency of doses, suggesting memory aids, linking doses to events in the patient's daily schedule, and using alarmed watches or pill cases, motivating patients to incorporate drug adherence into their lifestyles and providing a regular, un interrupted supply of medicines in developing countries. In addition, Education in the diagnosis and management of epilepsy was found to be effective in improving recruitment of patients into treatment programmers' and in improving drug adherence.[9,11,12,13,14]

1.2 Statement of the Problems

Epilepsy is a common neurological disease affecting almost 50 million people worldwide.[1,2] 5 million of who have seizures more than once per month. Approximately 85% of people afflicted with epilepsy live in developing countries. Poor adherence to prescribed medication is considered to be the main cause of unsuccessful drug treatment for epilepsy.[2,8,11] Non-adherent patients experience an increase in the number and severity of seizures, which leads to more ambulance rides, emergency department visits and hospitalizations.[8,9] No adherence therefore results directly in an increase in health care costs, and reduced quality of life.[9]

Poor treatment outcome is defined as increase in number of seizure episode or uncontrolled seizure in patients taking AEDs due to different reasons. Medication adherence has been defined in terms of agreement between the patients and behavior of taking medication and the clinician prescription.[15]

Reason for non-adherence is complex and multilayered.[16] There are various strategies suggested for managing patient's non-adherence but these are highly dependent on the reason why a patient has not followed clinician advice initially. Poor control of epilepsy is still a major problem with a prevalence of 40%. The poor drug adherence is a major factor, which was associated with poor control of epilepsy due to financial reasons.[17] Epilepsy is a common and world wide spread neurologic disorder, affecting people of all ages and socioeconomic classes worldwide.[18] Approximately one third of patients with epilepsy continue to have experience seizure despites the prescription of appropriate doses of AEDs.[19] The direct costs attributable to epilepsy include physician visits, laboratory tests, emergency department visits, antiepileptic drugs and hospitalizations. Indirect costs include working days lost, lost income, decreased quality of life, and the cost of failed therapy and side effects of drugs. The direct costs of epilepsy are significantly lower for patients whose epilepsy is controlled than for those whose disease is not controlled.[20]

As a research done Among 309 participants, by self-reporting questionnaires, shows experiencing one trigger that resulted in a seizure were reported by 89.8% of patient with epilepsy and 85.5% of caregivers. The most common triggers were tiredness, stress, and sleep deprivation.[21]

As the research conducted among 405 patients attending the Epilepsy Clinic at the All India Institute of Medical Sciences [AIIMS], shows 89% of the participants reported at least one triggering factors [TF]. Between one and ten TFs were endorsed. The most common TFs reported by the patients [in descending order] were found to be missing medication [40.9%], emotional stress [31.3%], sleep deprivation [19.7%], fatigue [15.3%], missing meals [9.1%], fever [6.4%], and smoking [6.4%]. A significant association was seen among some of the commonly reported TFs [missing medication, sleep deprivation, emotional stress, and fatigue].[22]

1.3. LITERATURE REVIEW

A number of rigorous reviews have found that, in developed countries, adherence among patients suffering chronic diseases averages only 50%. The magnitude and impact of poor adherence in developing countries is assumed to be even higher given the paucity of health resources and inequities in access to health care. This represents a tremendous challenge to population health efforts where success is determined primarily by adherence to AEDs.[23]

As indicated by different study Adherence can vary from an occasional missed dose to chronic defaulting on medication regimens.[16] Adherence to antiepileptic drugs in patients with epilepsy generally ranges from 20 to 80%.[9,15,16] Some studies reported different ranges of adherence for adult patients [40–60%] and children [25–75%].[9,10,24,25]

Non-adherence is a problem that has many detrimental effects and health professionals, the health care system, the community and the patients must share the responsibility for adherence. Many studies have identified factors affecting adherence, and these have been grouped into the five dimensionsdescribed.1, socioeconomic related factors 2, health care team/health system-related factors 3, condition related factors 4, treatment related factors, and 5, patient related factors. Many factors, such as, misunderstanding instructions about how to take the drugs, combined antiepileptic medication, complex medication regimens, forgetfulness, duration and previous treatment failures, fear of dependence, feeling stigmatized by the epilepsy, inadequate or nonexistent reimbursement by health insurance plans, and poverty are among many others, that have been shown to be significant barriers to adherence, and should be taken into account when developing interventions.[12,26,27,28]

Poor adherence to drug therapy is one of the primary causes of treatment failure. Forgetfulness of patients that may or may not be linked to memory difficulties, refusal to take medication and side effects are the factors most commonly associated with decreased adherence. The impact of epilepsy and the side effects of its treatment on cognition and of limited or compromised cognition on adherence deserve more attention. The use of memory aids, linking doses to events in the patient's daily schedule or watch alarms, calendar packs, pill cases or specialized dose dispensers may be helpful tools to increase adherence to treatment this were found in the literature search.

Communication with the patient about medication regimens and the value of treatment is extremely important. It can facilitate the identification of problems

and barriers to adequate adherence, and help with treatment planning. In addition, a real partnership between the physician and the patient is needed to set and achieve goals related to treatment outcomes and adherence.[29]

Almost one-third of people with epilepsy continue to have seizures despite appropriate antiepileptic drug treatment, placing them at considerable risk of cognitive and psychosocial dysfunction and death. Factors that have been associated with treatment-resistant epilepsy include: Early onset of seizures, Long history of poor seizure control, Having more than one type of seizure, Remote symptomatic etiology [eg, patients with a history of brain infection or head trauma], Certain structural abnormalities [eg, cortical dysplasia], Certain abnormalities on electroencephalography [EEG], Cognitive disability and History of status epilepticus. While Causes of apparent or "false" pharmacoresistant epilepsy are:-Misdiagnosis of epilepsy, inappropriate drug selection, Inappropriate assessment of response or lack of response, inappropriate dosage, poor compliance and detrimental lifestyle.[30]

As research done in UK shows Factors influencing compliance with antiepileptic drug regimens Out of 696 patients, 95% were taking AEDs[68% were on one type of drug only, i.e. mono-therapy, and 27% were on poly-therapy]. Of these 95%, almost three-quarters [72%] of patients said they never missed taking their AEDs, 15% missed less than once a month, 9% missed more than once a month but less than weekly and 4% missed at least once a week. Patients were asked how well they felt AEDs controlled their attacks: 61% said they were very well controlled, 32% said fairly well, 6% said not very well and 1% said not at all. Fifty per cent of patients taking AEDs reported experiencing AED side-effects, the most commonly reported being related to the central nervous system: tiredness [80% of those on AEDs], memory problems [71%] concentration [63%] sleepiness[63%] depression [60%] and headaches [58%].[31]

As a research done on Chinese epilepsy patients' shows, Of a total of 368 patients studied, 48.1% of patients were non-adherent with regards to AEDs. There were no demographic differences [based on gender, age, seizure type, and rural or urban location] between adherent and non-adherent patients. Adherence was positively and significantly correlated with duration of illness [p=0.007]. The primary reason for non-adherence was forgetfulness or not having medication on hand [69.6%], followed by a negative attitude [12.8%], a bad patient-prescriber relationship [9.5%], side effects [5.4%], inability to buy drugs [1.9%], and other reasons [0.8%]Medication adherence remains an important issue in epilepsy treatment. The non-adherence of epilepsy patients is common in China. Targeted management programs and communication strategies are necessary to improve adherence to antiepileptic drug treatment for patients with epilepsy and avoid the clinical consequences of poor adherence.[32]

Prospective cross-sectional study that was done in Brazilian 385 epilepsy outpatients in a tertiary referral center. Those patients' are 18 years or older, literate, without cognitive impairment or active psychiatric disorders, who were independent in daily living activities. Data were analyzed with correlation tests and conjoint analysis using multivariate logistic regression. Non-adherence rate, measured by the Morisky–Green Test, was 66.2%, a moderate-to-low adherence level. Non-adherence was higher in men, in younger patients and in patients with uncontrolled seizures. Increasing treatment complexity was also associated with decreased treatment adherence. Strategies designed to improve treatment adherence should address peculiarities associated with younger ages and male gender. Physicians should be made aware that prescription of less complex treatment regimens may result in better treatment adherence, and, therefore, better seizure control. The challenge in adjusting AED treatment in this population is to minimize treatment complexity, thus increasing chances for treatment adherence.[33]

An estimated 30–50% of persons with refractory epilepsy have major depression, and depression has a stronger correlation than seizure rate with quality of life. Suicide is one of the leading causes of death in epilepsy. Available data indicate that depression may result from underlying brain dysfunction rather than social and vocational disability.[34]

According to the International League against Epilepsy, juvenile myoclonic epilepsy is idiopathic generalized epilepsy characterized by a genetic predisposition, no evidence of neurological or intellectual deficit, and an average age at onset around puberty. Among 155 consecutive patients with newly diagnosed juvenile myoclonic, epilepsy retrospectively analyzed and followed up for at least 1year. There were 15 pseudo resistant patients [9.7%: lack of compliance [eight], insufficient treatment [three], abnormal lifestyle [four]] and 24 patients [15.5%] who had persisting seizures despite adequate therapy and lifestyle. Clinical features associated with drug resistance were[1] the presence of psychiatric problems [58.3% *v* 19%; p<0.001] and[2] independently, the combination of seizure types [Fischer's exact 2 by 4, p=0.0026]. Others [15.5% in this series] may be considered as truly resistant.[35]

The National General Practice Study of Epilepsy [NGPSE] conducted in the United Kingdom shows, Patients with newly diagnosed confirmed or suspected epilepsy were identified. Cumulative remission rates that is, actuarial estimates of percentage seizure-free at any time during follow up. At a median follow up of 7.1 years, among the 564 patients with ''definite'' epilepsy, the chance of ever achieving five year remission after nine years from diagnosis was 68%, and 54% of patients

were in five year terminal remission. Thity seven analysis of prognostic factors showed that only the number of seizures occurring in the first six months after presentation predicted the chance of remission. The higher the ‘‘seizure density’’ within this initial phase of the seizure disorder, the less likely was it for the patients to enter remission. Other modern large scale studies that include only newly diagnosed patients followed up for long periods also tend to suggest a remission rate of 60–80%. Poor prognostic factors include a high initial seizure density, symptomatic etiology, and presence of structural cerebral abnormalities, all of which can be identified early on.[36]

As a research conducted on Patients with Epilepsy in Rural Communities of Kaduna State, Nigeria shows, Epilepsy, one of the most important non-communicable neurological illnesses, is particularly under-resourced and under-treated in the developing world. Epidemiological studies have made it clear that the magnitude of the problem makes it a public health priority. Adherence to AED was low despite high level of knowledge due to forgetfulness, fatigue and being away from home, therefore a need for mounting adherence counseling in the clinic and health educational interventions to improve adherence in our rural communities. Large numbers of people are at risk of morbidity and mortality, mainly because of difficulties with treatment infrastructure and the availability of suitable drugs. However, people with epilepsy need more than drug treatment because their local cultural context adds social and economic burdens to the physical burden of their seizures. The education of health workers, patients, and the wider community is therefore essential and further exploration of the relationship between clinical outcomes and other nondrug self-management strategies is needed. Adherence to AED was low despite high level of knowledge due to forgetfulness, non-availability, being expensive, fatigue and being away from home, therefore a need for mounting adherence counseling in the clinic and health educational interventions to improve adherence in our rural communities where the disease cannot be managed. Further exploration of the relationship between clinical outcomes and other non-drug self-management [traditional] strategies is needed.[37]

A cross-sectional comparative study undertaken at Kenyatta National Hospital, Adult neurology clinic shows, Three hundred and sixty patients had seizures for more than 2 years and out of whom 180 were selected. The prevalence of poorly controlled epilepsy was found to be 40%. The mean age of the subjects was 28.73+/-11.96 years with a peak age group of 21-30 years and age range of 13 to 70 years. Poorly controlled patients were younger compared to well-controlled patients [27.53 years versus 29.93 years, P=0.028], and had longer duration of epilepsy [11.12 years versus 8.63 years, P=0.015]. Although not statistically significant, the poorly controlled group had more focal spikes and waves EEG pattern [40 versus 30, P=0.772], had more patients using alternative therapy [25 versus 15, P=0.0729], had poor drug adherence which was statistically significant [48 versus 24, P<0.00l], had missed drugs for longer duration in the last 3 months which was significant [12.81 versus 5.12 days, P=0.005].The number of AEDs, drug side effect profile, occupation, and education level were similar among the groups. Poor control of epilepsy is still a major problem with a prevalence of 40%. The poor drug adherence is a major factor, which was associated with poor control of epilepsy due to financial reasons.[38]

Epidemiological data indicate that 20-40% of the patients with newly diagnosed epilepsy will become refractory to treatment. Factors that may be used to predict whether a patient will respond favorably to AED therapy include the type of epilepsy, underlying syndrome, etiology, and the patient's history of seizure frequency, density, and clustering. Environmental factors such as: trauma and prior drug exposure, and genetic factors. Treatment resistance is, therefore, a multifaceted phenomenon. Since individuals with refractory epilepsy do not share a common reason for their treatment resistance, the use of targeted drug therapies may be our best option for improving treatment outcomes in this patient population.[39]

The estimated lifetime prevalence of epilepsy in the adult [≥ 16 years old] population of England was 1.2% [95% confidence interval [CI] 1.0-1.5]. Almost one-third of the people with epilepsy had an International Classification of Diseases, Tenth Revision [ICD-10] anxiety or depressive disorder [compared with one in six people without epilepsy]. Among these, social phobia and agoraphobia, generalized anxiety disorder, depression, and measures of suicidality had strong associations with epilepsy, which remained robust after accounting for potential confounders. These associations were consistently stronger than those in people with asthma or diabetes were, similar to those in people reporting migraine or chronic headaches.[40]

As a Report prepared for the World Health Organization, November 2006, on Sodium valproate in childhood epilepsy shows, Phenobarbitone is the WHO’s first line anti-epileptic drug in developing countries where it is the most commonly prescribed anti-epileptic drug. Indeed, a number of studies claiming phenobarbitone to be both effective and tolerated in patients with epilepsy treated in developing countries. However, whilst it is cheaper than other agents used frequently in developed countries [e.g. phenytoin, sodium valproate and carbamazepine], questions have been raised about its suitability with respect to its efficacy and profile of adverse effects. Certainly, in Europe and the USA, phenobarbitone is no longer considered afirst line drug due to concerns over its efficacy and short and long-term tolerability. There is a paucity of studies on the comparative efficacy of anti-epileptic drugs in specific epilepsy syndromes. In newly diagnosed epilepsies, across age groups and all seizure types, several randomised controlled trials of

carbamazepine, sodium valproate, clobazam, phenytoin and phenobarbitone show they are effective but fail to identify significant differences in efficacy between these medications. The potential adverse effects of anti-epileptic drugs should be a major determinant of the choice of drug in the individual child.[41]

1.4 Significance of the study

This research is useful for identifying and avoiding seizure triggers can help patients to avoid seizures and live better life. In addition to this, it is useful for creating awareness about status of epilepsy treatment outcome, adherence and associated factors as well as impact of non-adherence on health and promoting appropriate medicine usage habit to earn desirable outcome [seizure free life] through well utilization of AEDs.

There are various strategies suggested for managing patient's non-adherence but these are highly dependent on the reason why a patient has not followed clinician advice initially. Therefore, strategies for improvement of poor treatment outcome depend on underling factors affecting treatment out come and so the research is aimed to identify the common factors associated with poor treatment out come to AEDs and to give recommendation for health professional and concerned bodies, those giving care for patients in Ethiopia, specifically in Shambu General Hospital.

Finally yet importantly, since there is no research done on this topic in the country specifically in Shambu Hospital, it can be used as initial point or reference for who those are interested to perform similar studies on this area.

2. OBJECTIVES

2.1 General Objective

To assess factors associated for poor treatment outcomes among patients taking AEDs at Shambu General Hospital Psychiatric Clinic.

2.2 Specific Objectives

- To assess the status of treatment outcomes of epileptic patients to AEDs.
- To assess the status of adherence to AEDs.
- To identify seizure triggering factors among epileptic patients.
- To identify factors contributing to poor treatment outcome among epileptic patients.

3. METHOD AND PARTICIPANTS

3.1 The Study Area and Period

The study was carried out from 24 to 9, 2016 at Shambu General Hospital, Shambu, which is located 315 km west of Addis Ababa. Located in the Horro Guduru Wollega Zone of the Oromia Region, this town has a latitude and longitude of 8°59′N 37°51′E and an elevation of 2101 meters.

3.2 Study Design

A hospital based cross sectional study was conducted to assess the poor treatment out come and associated factors among epileptic patients' at Shambu General Hospital. Patient chart review and Self-report based cross-sectional study was conducted using structured questioners.

3.3 Populations

3.3.1 Source Population

All Epilepsy patients who were on follow up in Shambu Hospital and on AED during the study period.

3.3.2 Study Population

All 132 epilepsy patients who were on follow up in, Shambu Hospital at the time of study.

3.4 Sample Size and Sampling Technique

Convenient sampling technique was used to collect data from 132 epileptic patients.

3.5 Selection Criteria

3.5.1 Inclusion Criteria

- Patients presented with a history of Epilepsy at chronic clinic of this hospital for at least six months duration and on medication during the study period.
- Patients with chronic disease as comorbid and epileptic patients were a part of the study proved that they are on AED medication during the study period.
- Epileptic patients whose age is equal and greater than 15 years. Patients who have no active mental problems and who can communicate [conscious].

3.5.2 Exclusion Criteria

Epileptic patients on admission [in ward].

3.6 Study Variables

The variables to be included in the study categorized as dependent and independent variables.

3.6.1 Dependent

Status of treatment outcome.

3.6.2 Independent

- Educational level Age
- Sex
- Ethnicity Religion
- Marital status Occupation
- Monthly income Drug side effect Duration of illness Triggering factors
- Prognostic determinant [EEG abnormality, brain injury, number of seizure attacks, age at diagnosis and medication adherence]
- Medication related factors Patient related factors and
- Health system facility and health professional related factors.

3.7. Data Collection Instrument

The Questionnaires was structured based on the study objective and was designed as simple as possible to meet

the knowledge of both respondent and interviewers to collect the necessary data. Questionnaires were interpreted as much as possible to the language the respondent know.

3.8 Data collection technique

Data collectors were principal investigators with Shambu psychiatry clinic staffs and were trained for two days on data collection and quality before the day of data collection. Data collection method was by using patient chart review and patient interview method by structured and pre-tested questioner which was translated to local language afan Oromo and Amharic.

3.9 Data Handling Technique

The collected data was edited, cleared and cross checked. Finally data was presented in tables, chart and graphs.

3.10. Quality Control Methods

The pre-test was done to check the feasibility of the study. Pre-testing of the questionnaire was done on 10 patients. The results of the pilot study were used to modify the contents and wordings of the questionnaire. Data collectors had brief orientation on the study and its objective. Data collectors were supervised and data was checked for completeness. The questions were translated to the language the patient knows as much as possible.

3.11 Data Processing and Analysis

Data collected from the study area was compiled manually and the Chi-squared test was calculated using scientific calculator which was analyzed to draw association between different factors. The finding was presented using frequency distribution and percentages. The association of poor treatment out come and associated factors in epilepsy treatment was analyzed. Adherence to AEDs- has been defined in terms of agreement between the patients and behavior of taking medication and the clinician prescription. High adherence is considered if the patient score 0/8, medium adherence if score is 1-2 and low adherence if score is >2, according to the morisky 8 item medication adherence questionnaires'. Poor treatment outcome– is defined as increase in number of seizure episode or uncontrolled seizure in patients taking AEDs due to different reasons. If the patient is not seizure free for at least one year it is considered as uncontrolled seizure per this study paper. A p-value of 0.05 or less was considered statistical significant.

3.12 Ethical Consideration

Permission letter was written to the authorized body in order to obtain the desired cooperation and participation of the community. The study subjects were requested for their consents to provide the required information. Verbal consent from participants was taken before the interview. Respondents were assured about confidentiality of the information. The right of the respondents for being interviewed was respected. Confidentiality was ensured in the handling of data. The official letters was obtained from Medical Director of Shambu General Hospital. The objective of study was made clear to the concerned bodies including, Shambu Hospital.

3.13 Definition of Terms

3.13.1 Standard Definition

- **Epilepsy**–Epilepsy is characterized by a tendency to recurrent seizures and it is defined by two or more un-provoked seizures [generally within 2 years].[1]
- **Seizures-**is a neurologic event in which there is a temporary change in behavior resulting from a sudden, abnormal burst of electrical activity in the brain. May vary from the briefest lapses or muscle jerks to severe and prolonged convulsions.[1]
- **Adherence to AEDs-** has been defined in terms of agreement between the patients and behavior of taking medication and the clinician prescription. High adherence is considered if the patient score 0/8, medium adherence if score is 1-2 and low adherence if score is >2, according to the morisky 8 item medication adherence questionnaires'.[15]
- **Poor treatment outcome–** is defined as increase in number of seizure episode or uncontrolled seizure in patients taking AEDs due to different reasons.[15]

3.13.2 Operational Terms

- **Uncontrolled seizure**-If the patient is not seizure free for at least one year provided that the patient is on AEDs.
- **Triggering factors-** factors which increase the number of seizure attacks in individual person.
- **Illiterate**-One who can't read and write.
- **Morbidity -**An illness due to various causes and characterized by certain signs.
- **Mortality-** Death as a result of certain diseases.

3.14 Dissemination of the Result

The final finding of the study will be disseminated for concerned bodies.

- International Pharmaceutical Research Federal Ministry of Health
- Oromia Regional Health Beraue. Shambu General Hospital.
- And other bodies as needed.

3.15 Limitation of the study

This study will be carried out in Shambu General Hospital, which will not represent the Ethiopian population. Even though a self-reported cross-sectional study is cost effective method of data collection, there may be same over or under report of their triggering factors, and adherence level. Local works on epilepsy treatment outcome and adherence to AEDs are limited; therefore, no locally conducted studies were reviewed for comparison.

4. RESULTS

4.1 Socio-Demographic Characteristics of the Study Subjects

One hundred thirty two epileptic patients were interviewed and their medical record data was revised. There were 69[52.3%] female and 63[47.7%] male. Most patients [84.1%] were below 45 years of age and the majority of patients age fall between 15 & 30, which accounts 56.8% among the total patients. Majority of them were single [57.6%], Christians [85.6%], Oromo ethnicity [82.6%], students [42.4%], rural residence [62.1%], had some formal education [81.8%], and earn less than 500 ETB monthly [51.5%][Refer table 4.1].

Table 4.1: Distribution of Socio Demographic Characters of Epilepsy Patients on AEDs at Shambu General Hospital, December 2016.

Socio demographic characteristic		Frequency	Percent
Age	15- 30	75	56.8
	31–45	36	27.3
	46-60	21	15.9
Sex	Female	69	52.3
	Male	63	47.7
Ethnicity	Oromo	109	82.6
	Amhara	12	9.1
	Gurage	7	5.3
	Tigre	4	3.0
Religion	Orthodox	68	51.5
	Protestant	45	34.1
	Muslim	12	9.1
	Others [wakefata, Hawariat]	7	5.3
Marital status	Single	76	57.6
	Married	47	35.6
	Divorced	6	4.6
	Widow	3	2.3
Occupation	Student	56	42.4
	Farmer	30	22.7
	Government employee	20	15.2
	Merchant[business man/woman]	12	9.1
	Unemployed	9	6.8
	Other[NGO, daily labour, house wife]	5	3.79
Residence	Rural	82	62.1
	Urban	50	37.9
Education	Illiterate[not educated]	24	18.2
	Primary	55	41.7
	Secondary	30	22.7
	University/college	23	17.4
Monthly in come	< 500	68	51.5
	500-1000	18	13.6
	1001-2000	21	16.7
	>2000	24	18.2

4.2. Clinical Information and Determinants of Prognostic Factors of Seizure Treatment Outcome of the Study Subjects

The duration of patients on AEDs were greater than 1 year for most [108 patients/ 81.8%] and follow up in the clinic [Shambu Hospital] was greater than 1years 100 [75.7%].

As indicated on table 4.2, among total of study patients [132] epileptic patients, 31[23.5%] had other chronic disease in addition to epilepsy. One hundred forty patients [86.4%] were reported one or more triggering factors that can increase their seizure attacks.

According to this study's definition of poor seizure control, 59 patients [44.7%] had poor seizure control while 73 [55.3%] patients seizure was controlled [seizure free for at least one year] irrespective of number of antiepileptic drugs prescribed.

Among 123 patients on phenobarbitone alone, only 12 [9.8%] patients are seizure free with the initial dose while 111 [90.2%] have no response to the initial. Among those, there was dose titration for 61 [55%] epileptic patients before adding 2nd drug while not for 50 [45%]. As indicated on table 4.5 and table 4.2, among patients

who used carbamazepine as 2nd drug with phenobarbitone,[33] nine of them controlled with initial dose of 200mg/day as 2nd drug and 2 patients titrated to 400mg/day, while 22 [66.7%] still continued to have seizure.

Table 4.2: Clinical information and determinants of prognostic factors of seizure treatment outcome of Epilepsy patients on AEDs at Shambu General Hospital, December 2016.

Clinical information and determinants of prognostic factors		frequency	Percent
Time since on AEDs	6mon-1yr	24	18.2
	1-5yrs	62	47.0
	>5yrs	46	34.8
Follow up in the clinic	< 6 months	3	2.3
	6months-1yr	29	22.0
	>1yr	100	75.7
Co morbid condition	Yes	31	23.5
	No	101	76.5
Triggering factors	Yes	114	86.4
	No	18	13.6
Status of seizure treatment outcome	Controlled	73	55.3
	Not controlled	59	44.7
Dose titration if no Res.[1] for phenobarbitone [n=111]	Yes	61	55
	No	50	45
Dose titration if no Res.[1]for carbamazepine [n=24]	Yes	2	8.3
	No	22	91.7

NB: Res.[1] = response.

As indicated on fig 4.1, among those patients with co morbid conditions,[31] psychiatric is the leading co morbid condition which accounts for 18 [58.1%].

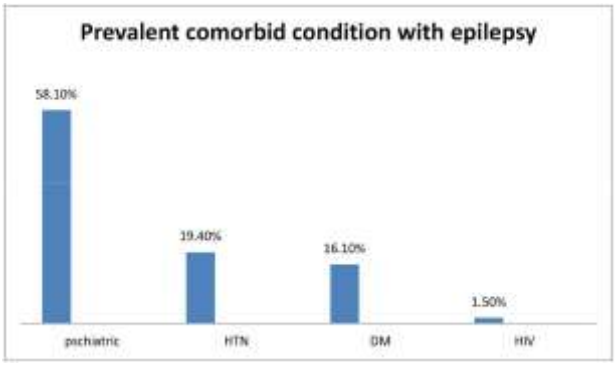

Figure 4.1: Chronic Co morbid condition of Epilepsy patients on AEDs at Shambu Hospital, December 2016.

NB. Percentage for each co morbid condition was calculated from a total of 31 epileptic patients who have co morbid condition.

As indicated on figure 4.2, the most common triggering factors were: emotional stress [97.4%], sleep deprivation [78.1%], missing meal [29.8%], missing medication [21.9%] and noise [15.5%] as reported by the patients.

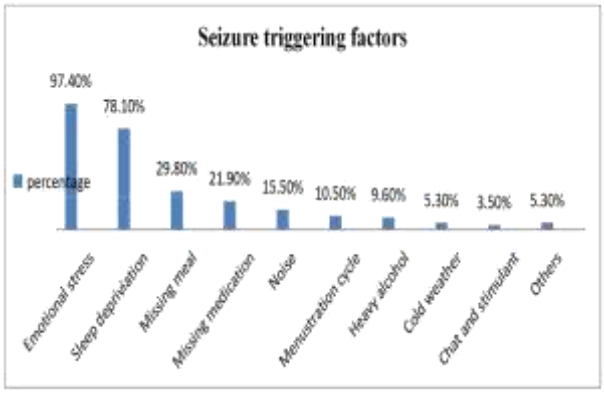

Figure 4.2: The most common Seizure triggering factors reported by Epilepsy patients on AEDs at Shambu General Hospital, December 2016.

NB. There was a multiple response for data on fig 4.2 and the percentage for each triggering factors were calculated from 114 patients who reported one or more triggering factors. **Others include** excessive sleep, long time TV visit, and mobile & TV game.

4.3 Types and Number of Seizure Diagnosed

There were no patients diagnosed with more than one type of seizure. All 132 patients have only one seizure. Among those patients 3 [2.3%] have Absence seizure and 129 [97.7%] have generalized tonic colonic seizure [GTC].

4.4 Medication History of Study Population

Since the major type of epilepsy diagnosed was GTC seizure, the initial AED prescribed was phenobarbitone

123 [93.2%] the remaining percentage accounts for phenytoin and Na valproate.

Among AEDs the most common drug use as add on [2nd drug] for patients whose seizure is not controlled was carbamazepine 33 [75%] while phenytoin and valproic acid accounts for 9 [20.5%] & 2 [4.5%] respectively. Majority of the patients are on mono therapy for AEDs 88.

[66.7%] and on poly therapy 75 [56.8%] for overall level of poly pharmacy [AEDs plus other medication for chronic co morbid conditions] [Refer Table 4.3].

Table 4.3: Common AEDs prescribed as initial drug, common AEDs prescribed as add on and level of poly-pharmacy of Epilepsy patients on AEDs at Shambu General Hospital, December 2016.

Medication history	Characteristics	Frequency	Per cents
AEDs prescribed as initial Rx	Phenobarbitone	123	93.2
	Phenytoin	6	4.5
	Valproic acid	3	2.3
AEDs prescribed as add on [2nd drug]	Carbamazepine	33	75.0
	Phenytoin	9	20.5
	Valproic acid	2	4.5
Status of poly-pharmacy with AEDs	Mono-therapy	88	66.7
	Poly-therapy	44	33.3
Status of poly-pharmacy irrespective of AEDs	Mono-therapy	57	43.2
	Poly-therapy	75	56.8

NB. Percentage of drugs as add on was calculated from 44 patients who used 2 AEDs, the 2nd as add on. Rx = treatment.

Majority of the patients 50 [68.5%] had been greater than or equal to two years since they were seizure free and duration to enter in to 12 months remission phase was greater than or equal to 1year 55 [75.3%] [Refer Table.4.4].

Table 4.4: Time since seizure free and time to enter remission phase for patients free of seizure for at least one year.

Variable	Time length	Frequency	%
Time since seizure free	1-2yrs	23	31.5
	2-5yrs	44	60.3
	>5yrs	6	8.2
Time to enter remission phase	<6 months	7	9.6
	6months-11months	11	15.1
	1yr-5yrs	33	45.2
	>5yrs	22	30.1

NB. This percentage is calculated from seizure free patients.[73]

As indicated on the Table 4.5, among a total of patients on mono-therapy for AEDs [88], 57 patients [64.8%] are seizure free with a single antiepileptic drugs [AEDs]. Among patients on poly-pharmacy or 2 AEDs [44 patients], 16 patients [36.4%] of them were seizure free, while 28 [63.6%] of patients on 2 drugs continue to have seizure. The maximum AEDs prescribed for the patients were 2 drugs. Among patients only on phenobarbitone [n=123], 54 [43.9%] patients were seizure free. There is no significant difference in terms of efficacy between AEDs use.

Table 4.5: Response [treatment outcome] with phenobarbitone alone Vs. add on drugs among Epilepsy patients on AEDs at Shambu General Hospital, December 2016.

AEDs	Seizure treatment outcome		P value
	Controlled [%]	Not controlled [%]	
Phenobarbitone alone[n=123]	54 [43.9]	69 [56.1]	0.449
Phenytoin alone [n=6]	2 [33.3]	4 [66.7]	
Valproic acid alone [n=3]	1 [33.3]	3 [66.7]	
Phenobarbitone plus carbamazepine [n=33]	11 [33.3]	22 [66.7]	0.16
Phenobarbitone plus phenytoin [n=9]	3 [33.3]	6 [66.7]	
Phenobarbitone plus valproic acid [n=2]	2 [100]	0	

Time length for dose titration for phenobarbitone after no response to initial dose, among patients for whom dose titration was done[61] table 4.2, for majority of the patient [40 (65%)] titration was done after 6 months [Refer Figure 4.3.]

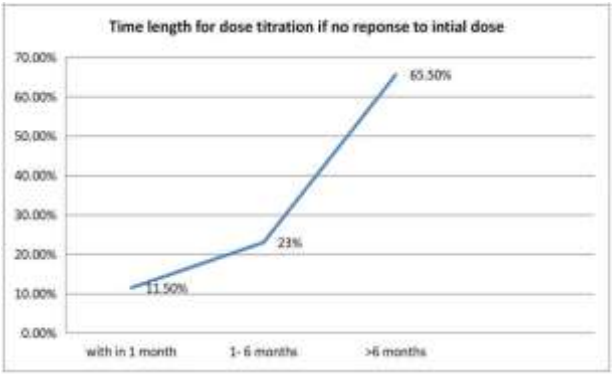

Figure 4.3: Time length for dose titration for phenobarbitone after no response to initial dose.

NB. This percentage is calculated among patients for whom dose titration was done[61] [Refer table 4.2].

Among 132 patients on AEDs, 55 [41.7] complain one or more adverse effects from AEDs. Among 123 patients on phenobarbital, 33 patients on carbamazepine, 15 patients on phenytoin, and 5 patients on valproate, respectively 52 [42.3%], 23 [69.7%], 4 [26.7%] and 2 [40%] reported one or more adverse effects to the respective drugs. The most common ADR reported for phenobarbital were sedation [42.3%], confusion or in concentration [37.4%], behavioral change or irritability [25.2%], for carbamazepine sedation [60.6%], GI irritation [54.6%], for phenytoin sedation [20%] and facial coarsening [20%] and for valproic acid GI irritation [40%] as calculated among patients who used the drugs. However, data was collected by patient self-report, which may lead to over or under report of the side effect and or bias of side effects of other medication they used during on AEDs [Refer Table 4.7].

Table 4.6: Antiepileptic drugs and associated adverse effects the patient complaining or suspected among Epilepsy patients on AEDs at Shambu General Hospital, December 2016.

Antiepileptic drug	Adverse effects	Frequency	%
	Sedation	52	42.3
	Confusion/in concentration	46	37.4
	Behavioural change/irritability	31	25.2
	Weakness/lethargy	23	18.7
Phenobarbitone [n=52]	Others[headache, dizziness,rash, ataxia]	8	6.5
	Sedation	20	60.6
	GI irritation	18	54.6
Carbamazepine [n=23]	Confusion/in concentration	7	21.2
	Dizziness	6	18.2
	Others[headache, blurred vision]	3	9.1
	Facial coarsening	2	20
Phenytoin [n=4]	Sedation	3	20
	Gingival hyper-plasia	1	6.7
Valproic acid [n=2]	GI irritation	2	40
	Sedation	1	20

NB. There is a multiple response**. n** indicates number of patients who reported adverse effect for specific drugs.

4.5 Reasons for Non-Adherence

Using the accepted criterion of a score of one or more on the Morisky 8 item medication adherence questionnaire indicating non-adherence, 71 patients [53.8%] were classified as non-adherent to medication[medium adherent and poor adherent]. The most common reasons for non-adherence were as a result of forgetfulness [73.2%], Feeling sick, side effects [60.6%], being away from home [The schedule of your work makes it impossible] [26.8%], Poly-pharmacy [Drugs are too many][22.5%], Duration, and previous treatment failures [18.3%] and others less common factors were reported by the patients [Refer Table 4.7]. NB. There may be under or over estimation of adherence level by the patients, because data is collected by direct patient interview.

Table 4.7: Reasons of non-adherence among the study participant of patients on AEDs, Shambu General Hospital Feb 2016.

Reasons for non-adherence-general	Reasons for non-adherence-Specific	Frequency	Percent
Patient related factors	Forget to take medication	52	73.2
	The schedule of your work makes it impossible	19	26.8
	Cannot afford to buy the medications always.	7	9.9
	Don't believe in the medication	2	2.8
Health professional/health care system related	Poor relationship between patient and physician	7	9.9
	Irregular or poor drug supply	6	8.5
Medication related	Feeling sick, side effects	43	60,6
	Poly-pharmacy [Drugs are too many]	16	22.5

Socio economic related	local beliefs or beliefs about the origin of illness	9	12.7
	Long distance from treatment setting	4	5.6
Condition related factors	Duration, and previous treatment failures	13	18.3

NB. There is a multiple response. The percentage for each reason was calculated from patients who were not adherent [medium adherence and low adherence] or 71 patients [Refer Table 4.8].

4.6 Treatment Outcome and Associated Factors

As indicated on table 4.8, among patients with high adherent to AEDs 61 patients, 75% were seizure free, p=0.001 while among non-adherent [medium adherent plus poor adherent to AEDs] 71 patients, only 38% were seizure free, p=0.001. Therefore, there is significant association between level of adherence and seizure treatment outcome.

The majority of patients' age at diagnosis of epilepsy was less than 45 years [92.4%]. Patients whose their seizure was diagnosed at early age has poor treatment prognosis. Which indicate a significant association b/n age at diagnosis of epilepsy and treatment outcome [p=0.026]. Among patients diagnosed at age of </= 15years has poor treatment outcome [63.4% of them were not controlled]. Among patients, seizure diagnosed at age of greater than 15 years has good treatment outcome [34.8% of them were not controlled].

Among 132 epileptic patients 30[22.7%] reported that they have brain injury due to different insults. From those 30 patients, 21[70%] reported that the brain injury was before the occurrence of seizure, while the remaining 9[30%] reported that their brain injury is after the occurrence of seizure.There is no significant association between brain injury and epilepsy treatment outcome [p=0.61]. In addition there is no significant association between seizure treatment out come and weather brain injury is before seizure occurrence or after seizure occurrence [p=0.2].

Among study participant, 105 [79.5%] had no neurologic examination [EEG], among those who had EEG examination, 11 [8.3%] had confirmed EEG abnormality. Even though the majority of the patients had no EEG examination 79.6%, those who had EEG abnormality among examined one have poor seizure treatment prognosis [72.3% have poor seizure control, p=0.04] while among patients who had no EEG abnormality [75% were seizure free, p=0.04] which indicate significant association between EEG abnormality and treatment outcome.

The numbers of patients who reported seizure greater than 3 attacks per week before AEDs initiation accounts for, 71 [53.8%] while the remaining reported less than or equal to 3 attacks. Among patients with seizure attack of </= 3 per week before AEDs initiation had 63.9% seizure free while those who had more than 3 attacks pre week had 47.9% seizure free [p=0.028]. There is strong [significant] association between frequency of seizure attacks and treatment outcome, those patients who had few seizure attacks before initiation of AED has good seizure treatment outcome than with high attacks.

Table 4.8: Treatment outcome and associated factors among Epilepsy patients on AEDs at Shambu General Hospital, December 2016.

Variables [factors affecting treatment outcome		**Seizure treatment outcome**		**P value**
		Controlled [%]	**Not controlled [%]**	
Adherence	High adherence	46[75%]	15[24.6%]	P=0.001
	Medium adherence	16[59.3%]	11[40.7%]	
	Low adherence	11[25%]	33[75%]	
Age at time of diagnosis in year	</=5	1[20%]	4[80%]	P=0.026
	6-15	15[42.1%]	23[57.9%]	
	16-45	50[63.3%]	29[36.7%]	
	>45	7[60%]	3[40%]	
Status of brain injury	Yes[n=30]	15[50%]	15[50%]	P=0.61
	No [n=102]	58[56.9%]	44[43.1%]	
Time of brain injury	Before seizure occurrence	9[42.9%]	12[57.1%]	P=0.2
	After seizure occurrence	6[66.7%]	3[33.3%]	
EEG abnormality	Yes [n=11]	3[27.3%]	8[72.7%]	P=0.04
	No [n=16]	12[75%]	4[25%]	
	Not known[n=105]	58[55.3%]	47[44.7%]	
Frequency of seizure attack	</= 3 attacks	40[63.9%]	21[36.1%]	P=0.028
per week before AEDs initiation	>/= 4 attacks	33[47.9%]	38[52.1%]	

NB. Percentage of brain injury before and after seizure was calculated from the patients with brain injury[30] patients.

5. DISCUSSION

There was no published study to investigate the level of adherence to treatment, level of treatment outcome and related factors in epilepsy patients in Ethiopia. As this study indicates, the majority of patients' age at diagnosis of epilepsy was less than 45 years [92.4%] and the duration of patients on AEDs were greater than 1 year 108 [81.8%]. According to the International League against Epilepsy, juvenile myoclonic epilepsy is idiopathic generalized epilepsy characterized by a genetic predisposition, no evidence of neurological or intellectual deficit, and an average age at onset around puberty.[35]

As my result shows, among total of study patients [132] epileptic patients, 31 [23.5%] have other chronic disease in addition to epilepsy. Among those co morbid conditions,[31] psychiatric is the leading co morbid condition which accounts for 18 [58.1%]or around 14% from total study population, followed by HTN 6 [19.4%], DM 5 [16.1%] and the least co morbid condition is HIV which accounts for 2 [1.5%].When this result is compared with the study done in England on >/=16 years old patients almost one-third of the people with epilepsy had an International Classification of Diseases, Tenth Revision [ICD-10] anxiety or depressive disorder [compared with one in six people without epilepsy]. Among these, social phobia and agoraphobia, generalized anxiety disorder, depression, and measures of suicidality had strong associations with epilepsy. These associations were consistently stronger than those in people with asthma or diabetes were, similar to those in people reporting migraine or chronic headaches.[40]

As indicated on my results, among 132-study population, 114 [86.4%] were reported one or more triggering factors that can increase their seizure attacks. The most common triggering factors were emotional stress [97.4%], sleep deprivation [78.1%], missing meal [29.8%], missing medication [21.9%], noise [15.5%] and menstruation cycle, heavy alcohol, cold weather, chat and stimulant and other least common factors, which account for 34.2% as reported by the patients. This result is almost similar with a research done by [Pinikahana J, Dono J.,2009], Among 309 participants, by self-reporting questionnaires, shows experiencing one trigger that resulted in a seizure were reported by 89.8% of patient with epilepsy and 85.5% of caregivers. The most common triggers were tiredness, stress, and sleep deprivation.[21] As the research conducted among 405 patients attending the Epilepsy Clinic at the All India Institute of Medical Sciences [AIIMS] shows 89% of the participants reported at least one triggering factors[TF]. The most common TFs reported by the patients [in descending order] were found to be: Missing medication [40.9%], emotional stress [31.3%], sleep deprivation [19.7%], fatigue [15.3%], missing meals [9.1%], fever [6.4%], and smoking [6.4%].[22]

Types and Number of Seizure Diagnosed

Seizures may vary from the briefest lapses or muscle jerks to severe and prolonged convulsions. They may also vary infrequency; from less than one a year to several per day.[1] The risks of recurrent seizures include intractable epilepsy, cognitive impairment, physical injury, psychosocial problems and death.[5] Children suffer mainly from idiopathic generalized epilepsy and absence, myoclonus and generalized tonic–clonic seizures are the most common forms of seizure seen in children. In adults, symptomatic partial epilepsy is the most common form, and it may cause simple partial, complex partial, or secondarily generalized tonic–clonic seizures. Convulsive or tonic–clonic status epilepsy is of major concern, as it is associated with a mortality rate of 5–15%.[6] However, per this study, there were no patients diagnosed with more than one type of seizure. All 132 patients have only one seizure. Among those patients 3 [2.3%] have Absence seizure and 129 [97.7%] have generalized tonic colonic seizure [GTC]. This may be due to problems of diagnosis.

Medication History of Study Population

As the result of my study indicates, since the major type of epilepsy diagnosed was GTC seizure, the initial AED prescribed was phenobarbitone 123 [93.2%] the remaining percentage accounts for phenytoin and Na valproate. Among AEDs the most common drug used as add on [2nd drug] for patients whose seizure is not controlled was carbamazepine 33 [75%] while phenytoin and valproic acid accounts for 9 [20.5%], & 2 [4.5%] respectively.

My result is in line with WHO recommendation that suggests Phenobarbitone is the WHO's first line anti-epileptic drug in developing countries where it is the most commonly prescribed anti-epileptic drug. Indeed, in their review [Scott RA et al] include a number of studies claiming phenobarbitone to be both effective and tolerated in patients with epilepsy treated in developing countries. However, whilst it is cheaper than other agents used frequently in developed countries [e.g. phenytoin, sodium valproate and carbamazepine]; questions have been raised about its suitability with respect to its efficacy and profile of adverse effects. Certainly, in Europe and the USA, phenobarbitone is no longer considered a first line drug due to concerns over its efficacy and short and long-term tolerability. Despite a lack of hard evidence from individual randomized controlled trials, there is a strong recommendation in Europe and the USA that sodium valproate should be considered as a first line treatment in generalized, partial and other epilepsies.[41]

Majority of the patients are on mono therapy for AEDs 88[66.7%] and on poly therapy 75[56.8%] for overall level of poly pharmacy [AEDs plus other medication for chronic co morbid conditions]. This result is almost similar with the research done in UK shows Factors influencing compliance with antiepileptic drug regimens

Out of 696 patients, 95% were taking AEDs [68% were on one type of drug only, i.e. mono-therapy, and 27% were on poly-therapy].[31]

Generally, poor treatment outcome is defined as increase in number of seizure episode or uncontrolled seizure in patients taking AEDs due to different reasons. According to this study's definition of poor seizure control, 59 patients [44.7%] had poor seizure control while 73[55.3%] patients seizure was controlled [seizure free for at least one year] irrespective of number of antiepileptic drugs prescribed. When this result is compared with other studies: According to study done on 54 patients definition of poor seizure control [Epilepsy was arbitrarily defined as ''well controlled'' if the patient reported less than one seizure per month], 31 patients [57%] had poor control. Recent studies in both developed and developing countries have shown that up to 70% of children and Adults newly diagnosed with epilepsy can be successfully treated [i.e. their seizures can be completely controlled for several years] with antiepileptic drugs.

After 2–5 years of successful treatment, drugs can be withdrawn in about 70% of children and about 60% of adults without relapse occurring.[1]

Poor control of epilepsy is still a major problem with a prevalence of 40%. The poor drug adherence is a major factor, which was associated with poor control of epilepsy due to financial reasons.[17] In the case of treatment failure, it is crucial to establish whether the failure is a result of inappropriate drugs election, inappropriate dosing, refractory disease or poor adherence to the therapeutic regimen.[5]

My study indicate that majority of the patients 50 [68.5%] had been greater than or equal to two years since they were seizure free and duration to enter in to 12 months remission phase was greater than or equal to 1year 55 [75.3%]. The National General Practice Study of Epilepsy [NGPSE] conducted in the United Kingdom shows, Cumulative remission rates that is at a median follow up of 7.1 years, among the 564 patients with ''definite'' epilepsy, the chance of ever achieving five year remission after nine years from diagnosis was 68%. Other modern large scale studies that include only newly diagnosed patients followed up for long periods also tend to suggest a remission rate of 60–80%.[35]

As my result shows, among a total of patients on mono-therapy for AEDs,[88] 57 patients [64.8%] are seizure free with a single antiepileptic drugs [AEDs]. Among patients on poly-pharmacy or 2 AEDs [44 patients], 16 patients [36.4%] of them were seizure free, while 28 [63.6%] of patients on 2 drugs still continue to have seizure. This is may be due to negligence in dose titration to the maximum tolerable dose that can stop seizure. For example the major drug used as add on [second AED] is carbamazepine 200mg/day, this is not the maximum dose. As much as the patient tolerate we can titrate up to 1800mg/day. The maximum AEDs prescribed for the patients were 2 drugs.

Among patients only on phenobarbitone [n=123], 54 [43.9%] patients were seizure free. Among 123 patients on phenobarbitone alone, 12[9.8%] patients are seizure free with the initial dose while 111[90.2%] have no response to the initial. Among those, there was dose titration for 61[55%] epileptic patients before adding 2nd drug while not for 50 [45%]. Among patients who used carbamazepine as 2nd drug with phenobarbitone,[33] nine of them controlled with initial dose of 200mg/day as 2nd drug and 2 patients titrated to 400mg/day, while 22 [66.7%] still continued to have seizure. Time length for dose titration for phenobarbitone after no response to initial dose, among patients for whom dose titration was done [61], for 40 [65%] of patients titration was done after 6 months. This indicates poor duration in dose adjustment, which should be adjusted within 2 to 4 weeks of no response to the initial dose while assessing medication adherence. Delay in dose titration and refusal to titrate AEDs dose may cause delay in time to inter into remission phase.

As my result indicate among 132 patients on AEDs, 55 [41.7%] complain one or more adverse effects from AEDs. This percentage is almost similar with research done in UK, which shows 50% of patients taking AEDs reported experiencing AED side effects.[31]

My study shows, Among 123 patients on phenobarbital, 33 patients on carbamazepine, 15 patients on phenytoin, and 5 patients on valproate, respectively 52 [42.3%], 23 [69.7%], 4 [26.7%] and 2 [40%] reported one or more adverse effects to the respective drugs. The most common ADR reported for phenobarbital were sedation [42.3%], confusion or in concentration [37.4%], behavioral change or irritability [25.2%], for carbamazepine sedation [60.6%], GI irritation [54.6%], for phenytoin sedation [20%] and facial coarsening [20%] and for valproic acid GI irritation [40%] as calculated among patients who used the drugs. Because of this data was collected by patient self-report, there may be over or under report of the side effect and or bias of side effects of other medication they used during on AEDs. As research done in UK shows, the most commonly reported AEDs side effects were related to the central nervous system: tiredness [80% of those on AEDs], memory problems [71%] concentration [63%] sleepiness [63%] depression [60%] and headaches [58%].[31]

Most of the patients reported side effect for carbamazepine [69.7%], this is may be not due to carbamazepine alone but due to poly-pharmacy [carbamazepine plus phenobarbitone].

The patients reported the side effect as it is from carbamazepine because the side effect starts while carbamazepine was added on phenobarbitone as 2nd drug.

As indicated by different study Adherence can vary from an occasional missed dose to chronic defaulting on medication regimens.[16] Adherence to antiepileptic drugs in patients with epilepsy generally ranges from 20 to 80%.[9,15,16] Some studies reported different ranges of adherence for adult patients [40–60%] and children [25–75%].[9,10,24,25]

Adherence is difficult to measure accurately. For epilepsy, adherence to medication has previously been measured by self-reporting, drug blood level monitoring, and prescription refill monitoring. Each method has disadvantages. Adherence measured by self-reporting may be overestimated, but is considered to be the simplest and least expensive method.[32]

In this study, adherence was measured by self-reporting. As this study indicate, using the accepted criterion of a score of one or more on the Morisky 8 item medication adherence questionnaire indicating non-adherence, 71 patients [53.8%] were classified as non-adherent to medication [medium adherent [1-2 score] and poor adherent [>2 score]]. This percentage is almost the same as that reported in other countries, at around 50%: in china [48.1%], Arab countries [64%], the United States [29-58%], and the United Kingdom [59%] of patients were non-adherent to AED treatment.[32] Adherence to antiepileptic drugs in patients with epilepsy generally ranges from 20 to 80%.[10] Some studies reported different ranges of adherence for adult patients [40–60%] and children [25–75%].[8]

As a research conducted on Patients with Epilepsy in Rural Communities of Kaduna State, Nigeria shows, 32.6% of the patients were adherent to treatment, reason for non-adherence to AED was due to forgetfulness, fatigue and being away from home.[37] Prospective cross-sectional study that was done in Brazil on 385 epilepsy patients' non-adherence rate, measured by the Morisky–Green Test, was 66.2%, a moderate-to-low adherence level.[33]

According to Chinese epilepsy [2012-2013] data, there was no significant difference in rates of non-adherence between the different age groups as well as education and economic status were not factors that affected adherence. Similarly, in the USA, no demographic differences [*i.e.* gender, age] were reported between adherent and non-adherent patients. There was also no significant correlation between adherence rates and geographical location [rural or urban settlement].[32] Because of this, I did not consider those factors as study variables [association was not done for socio demographics characteristics of study participants].

Adherence to treatment depends on many factors, and there is no simple explanation to account for non-adherence. In my study, the primary reason for non-adherence was forgetfulness [73.2%]. Forgetfulness is a widely reported factor that causes non-adherence to medication or clinic appointments. In Chinese study, forgetfulness [69.6%] was the primary reason for non-adherence in different age groups, with varying degrees followed by a negative attitude [12.8%], a bad patient-prescriber relationship [9.5%], side effects [5.4%], inability to buy drugs [1.9%].[32] Written instructions are better than oral advice for reminding patients to take medication. Physicians should consider prescribing the simplest regimen with the fewest daily doses and tablets.

In my study, the 2nd leading cause of non-adherence was a feeling sick/side effect [60.6%]. The others reason were, away from home [The schedule of your work makes it impossible] [26.8%], Poly-pharmacy [drugs are too many] [22.5%], duration, and previous treatment failures [18.3%], and local beliefs or beliefs about the origin of illness [12.7%]. This data is almost similar with study done in different countries like: Forgetfulness of patients that may or may not be linked to memory difficulties, refusal to take medication and side effects are the factors most commonly associated with decreased adherence. The impact of epilepsy and the side effects of its treatment on cognition and of limited or compromised cognition on adherence deserve more attention.[29]

Treatment Outcome and Associated Factors

Almost one-third of people with epilepsy continue to have seizures despite appropriate antiepileptic drug treatment, placing them at considerable risk of cognitive and psychosocial dysfunction and death. Factors that have been associated with treatment-resistant epilepsy include: Early onset of seizures, Long history of poor seizure control, Having more than one type of seizure, Remote symptomatic etiology [eg, patients with a history of brain infection or head trauma], Certain structural abnormalities [eg, cortical dysplasia], Certain abnormalities on electroencephalography [EEG], Cognitive disability and History of status epilepticus. While Causes of apparent or "false" pharmacoresistant epilepsy are:-Misdiagnosis of epilepsy, inappropriate drug selection, Inappropriate assessment of response or lack of response, Inappropriate dosage, and Inappropriate patient behavior Examples: poor compliance, detrimental lifestyle.[30]

Among 155 consecutive patients with newly diagnosed juvenile myoclonic epilepsy retrospectively analyzed between 1981 and 1998 and followed up for at least 1 year shows, Clinical features associated with drug resistance were [1] the presence of psychiatric problems [58.3% *v* 19%; $p<0.001$] and [2] independently, the combination of seizure types [Fischer's exact 2 by 4, $p=0.0026$]. None of the resistant patients had myoclonic jerks as the only seizure type or a combination of absences and myoclonic jerks. Family history of epilepsy,

age at onset of seizures, sex, presence of photo paroxysmal response, results of conventional neuroimaging's [CT and MRI], and delayed diagnosis were not significantly associated with drug resistance.[35]

As my study indicates, among patients with high adherent to AEDs 61 patients, 75% were seizure free, p=0.001 while among non-adherent [medium adherent plus poor adherent to AEDs] 71 patients, only 38% were seizure free, p=0.001. Therefore, there is significant association between level of adherence and seizure treatment outcome.

Patients whose their seizure was diagnosed at early age has poor treatment prognosis as indicated on my study which indicate a significant association b/n age at diagnosis of epilepsy and treatment outcome [p=0.026]. Among patients diagnosed at age of </= 15years has poor treatment outcome [63.4% of them were not controlled]. Among patients, seizure diagnosed at age of greater than 15 years has good treatment outcome [34.8% 0f them were not controlled].

As indicated on this study results there is no significant association between brain injury and epilepsy treatment outcome [p=0.61]. In addition there is no significant association between seizure treatment out come and weather brain injury is before seizure occurrence or after seizure occurrence [p=0.2].However, when this result is compared with other research it is in opposite direction. This may be because of the data that is collected, as brain injury is not that have much effect on seizure treatment outcome. For example, the patient may report superficial/minimum injury as traumatized/penetrating brain injury, which has no effect on seizure treatment. Therefore, as a limitation I did not considered this data as different for those patients. As a conclusion, this may lead to weak association between brain injury and seizure treatment outcome.

Even though the majority of the patients had no EEG examination 79.6%, those who had EEG abnormality among examined one have poor seizure treatment prognosis [72.3% have poor seizure control, p=0.04] while among patients who had no EEG abnormality [75% were seizure free, p=0.04].

As this study indicates, among patients with seizure attack of </= 3 attacks per week before AEDs initiation had 63.9% seizure free while those who had more than 3 attacks pre week had 47.9% seizure free [p=0.028].There is strong [significant] association between frequency of seizure attacks and treatment outcome, those patients who had few seizure attacks before initiation of AED has good seizure treatment outcome than with high attacks. Thirty-seven Analysis of prognostic factors showed that only the number of seizures occurring in the first six months after presentation predicted the chance of remission. The higher the ''seizure density'' within this initial phase of the seizure disorder, the less likely was it for the patients to enter remission.[35]

6. CONCLUSION

Most patients were below 45 years of age and the majority of patients age fall between 15 & 30 Majority of them were Christians, Oromo ethnicity and students. The majority of patients' age at diagnosis of epilepsy was less than 45 years. The most common triggering factors as descending order were emotional stress, sleep deprivation, missing meal, missing medication, and noise as reported by the patients.

Since the major type of epilepsy diagnosed was GTC seizure, the initial AED prescribed was phenobarbitone. Psychiatric conditions were overrepresented in people with epilepsy as comorbid condition. These associations were stronger than with other non-neurologic chronic conditions.

According to this study's definition of seizure control, there was a problem of seizure control [seizure free for at least one year] irrespective of number of antiepileptic drugs prescribed. Majority of the patients had been greater than or equal to two years since they were seizure free and duration to enter in to 12 months remission phase was greater than or equal to 1year.

There was a problem of dose titration and time for dose titration in study area [Ambo Hospital]. Delay in dose titration and refusal to titrate AEDs dose may cause delay in time to inter into remission phase.

The patients complain one or more adverse effects from AEDs. Most patients' complain ADR from carbamazepine with GI irritation as the major ADR while phenobarbitone was the second drug to cause ADR with sedation and behavioral change/ irritable as a major side effects.

There was a problem of non-adherence to AEDs [medium adherent and poor adherent] in Ambo Hospital epilepsy patients. Good adherence to treatment and proper health education are fundamental to the successful management of epilepsy. Poor adherence to prescribed medication is considered the main cause of unsuccessful drug treatment for epilepsy. The major reasons for non-adherence with their descending order were as a result of forgetfulness, Feeling sick/side effects, being away from home [The schedule of their work makes it impossible], Poly-pharmacy [Drugs are too many]. Therefore, there is significant association between levels of adherence; number of seizure attacks before AEDs initiation, EEG [neurologic abnormality] and age at onset of seizure [diagnosis].There is no significant association between brain injury and epilepsy treatment outcome.

7. RECOMMENDATION

The health professionals working at Shambu General Hospital should prepare some interventions to improve adherence to anti-epilepsy medications. Some of those interventions are:- the therapeutic relationship [increasing communication between patient and health professional],giving full instructions about the treatment and discussing the pros and cons of treatment with the patient, motivating patients to incorporate drug adherence into their lifestyles and providing a regular, un interrupted supply of medicines.

The health professional should assess seizure-triggering factors and inform the patient so that they can avoid those triggering factors to increase their quality of life by reducing/eliminating seizure.

Since there is no research done on this topic in the country specifically in Shambu Hospital, Further studies are needed to evaluate the effect of adherence on seizure control, to evaluate the effect of other associated factors that contribute for poor treatment outcome in epilepsy, and to assess its impact on adherence, seizure control.

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