ORIGINAL PAPER

Economic Burden of Seizure Disorders on Medication Adherence and Treatment Outcomes of People With Epilepsy in a Tertiary Hospital in Ibadan, Nigeria

A. E. IPINGBEMI*[A-F], J. A. ALADE[B-F]

Department of Clinical pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Ibadan Nigeria

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Introduction: The burden of seizure disorder in relation to adherence and outcome has not then explored in many developing countries.

Objective: The study aimed at estimating the economic burden of seizure disorder on the patient and their caregivers.

Methods: A Structured and pretested self-administered questionnaire was used to obtain information from the participants. Information was also retrieved from patients' case notes using a structured data form. Participants' self-report on medication adherence was assessed using Morisky's Medication Adherence Scale (MMAS-4). Cost of management (direct cost only) of the disorder was based on patients and families perspective. Data were analyzed with SPSS version 23. Relationship between duration of use of AntiEpileptic Drugs (AEDs) and adherence level was tested using Pearson moment product correlation and $p < 0.05$ considered significant.

Results: One third (19, 37.8%) of the patients were diagnosed with mixed seizure. Carbamazepine was the most commonly prescribed medication (60.8%). Only 18 (35.3%) had high adherence to prescribed medication(s) of which 3 (5.9%) had seizure remission for the past one year. Forgetfulness (31; 60.8%) and cost of medication(s) (24, 47.1%) were the most common reason(s) for non-adherence. Medical bill of 34 (66.7%) of the participants were paid by parents and relatives. Average monthly income of employed participants was ₦56,781.2 ($177.4). Average monthly cost of management per patient obtained was ₦11,723.9 ($36.6). The mean cost of AEDs (₦99,061.1±59,569.7) among adherent group was less than and non-adherent group (₦113,546.9±63,301.6). There is a significant negative correlation between years of use of AEDs and medication adherence score ($r = - 0.3$, $p = 0.04$).

Conclusion: Economy burden of seizure is huge among the participants. Medical bills of more than two-third of them was borne by caregivers while those employed spent one-fifth of their monthly income on the disorder. Treatment outcome was poor due to high level of non-adherence to medication(s) associated with financial constrain. Measure to improve adherence and ease of financial burden among seizure disorder patients is highly essential.

Keywords: Seizure disorders, Adherence, Cost, AED, Outcome.

INTRODUCTION

Epilepsy is a chronic non-communicable disorder which usually manifests as recurrent, unprovoked seizures. An individual is said to be epileptic when they experience one or more seizures of unknown cause (WHO, 2017).

About 80% of people affected with epilepsy globally are living in developing countries where 80-90% of affected people are believed to receive inadequate or no treatment at all (WHO, 2018). According to WHO, estimated proportion of the general population with active epilepsy (i.e. continuing seizures or with the need for treatment) at a given time is between 4 and 10 per 1000 people (WHO, 2017). However, this proportion may be doubled in low- and middle-income countries (WHO, 2018).

Epilepsy is a major health issue especially in developing African countries. It is the most common non-infectious neurologic condition in developing African countries including Nigeria (Ogunrin, 2006). People from lower socioeconomic status have been reported to be more vulnerable to develop epilepsy due to their limited to access good quality healthcare (Senthil, 2015).

The quality of life of people living with epilepsy is affected by the disorder (Viteva, 2013) and the condition is highly stigmatized because of the misconception among people that epilepsy is contagious and negative meanings are attached to its outward manifestations of seizures (Paul et al, 2012). Epilepsy has been shown to have a negative impact on social life (employment, driving, marriage, social isolation, and education opportunities) of the sufferers (Paul et al, 2012; Dau et al, 2006).

The goal of therapy in epilepsy treatment is the restoration of a normal life through complete control of seizure by minimizing amount of medication used while avoiding unacceptable side effects. In an attempt to achieve this, the disorder imposes economic burden on sufferers, families and society at large (Senthil, 2015). To achieve adequate control of seizure among the patients, medication(s) have to be taken for many years, possibly a life-time; which implies that the condition financial burden may often time be life time. Adherence to medication by patients with chronic diseases has been shown to be a major problem to their management. Discontinuation of the antiepileptic drug(s) (AEDs) by patient may result in recurrence of the seizures while sudden withdrawal of AED(s) may result in life-threatening status epilepticus (Ghaffarpour et al, 2014).

Economic impact of epilepsy to the patients and society is high. In the US, epilepsy was shown to have huge national impact of about $9.6 billion of medical expenditures and informal care (Yoon et al, 2009). Patient with epilepsy in Netherlands spent as much as €147 monthly as out-of-pocket expenditure on epilepsy care received from a university hospital (Kotsopoulo et al, 2003). In Nigeria, patients with epilepsy were found to incur substantial out of pocket burdens for caregivers. For example, Lagunju et al (2011) reported that caregiver of half of the cohort children attending a tertiary healthcare facility spent more than 20% annual family income on management of epilepsy. Accurate estimates of the burden of Non-Communicable Diseases are vital to the monitoring of diseases and policy planning, but currently this is lacking in many of developing countries (Dau et al, 2006). This study aimed to quantify economic burden of seizure disorder- a non-communicable disease from the patients and family's perspective and assessed it effects on adherence to therapy and treatment outcome among patients diagnosed of seizure disorder in a tertiary hospital in Ibadan, Nigeria. The outcome of the research knowledge on cost associated with management of seizure would inform the development of targeted interventions, enlightenment of the public on the National Health Insurance Scheme in order to benefit from co-payment mechanism that will reduce the economic burden on patients/caregivers.

METHODOLOGY

Study design

The study was a cross-sectional study among patients diagnosed and being managed for seizure disorder in a tertiary healthcare facility in South-west Nigeria. Clinical and administrative data were collected retrospectively from participants' case notes while data on cost were collected prospectively. Data were collected prospectively and retrospectively. The prospective study was carried out between September and November, 2017. While retrospective data covered September 2016 to October, 2017.

Study site

The study was carried out in the Medical Out Patient (MOP) unit of the University College Hospital (UCH), Ibadan, Oyo state, Nigeria. UCH is an 850 bedded hospital established in 1948 and it serves as a referral center for many secondary and even tertiary healthcare facilities across the country because of its ample and qualified personnel in different specialized fields of medicine.

Study population

All patients diagnosed with seizure disorder and attending the neurology clinic at MOP of the hospital.

Sample size determination

Verbal communication with the record department at the Medical Outpatient clinic of UCH, Ibadan indicated that neurology clinic held once a week. The record department also estimated an average of 7 patients with seizure disorder attends the neurology clinic every week. Pilot study carried out before the commencement of data collection, showed an average of 5 patients diagnosed and being managed for seizure disorder attends the neurology clinic per week.

Sample size was determined using the Yamane (1967) sample size formula below:

$$n = \frac{N}{1+N(e)^2}$$

n=sample, N= Population= 70 (7 patients per week multiplied by 10 weeks)

n (sample size) was calculated to be 59.5. Approximately 60

Adjusting the sample size for 10% non-response = 66

The researchers met with patients on clinic days and as many patients diagnosed of seizure disorders that consented to participate in the research were involved in the study. Data was collected weekly for 10 weeks.

Sampling technique

A purposeful sampling technique was used to select eligible participants. Only patients identified as seizure disorder patients after checking through all the case notes (pulled out from the record department) for all the patients for each clinic were approached for consent to participate in the study. Although 66 was calculated as sample size, a total of 63 patients being managed for seizure disorder came to the clinic within the eight weeks of study and were approached for participation but 51 gave their consent to participate in the study giving a response rate of 81%.

Data collection procedure

Using a structure data form, the following information was obtained retrospectively from the patients' medical records; number of clinic attended, medications, laboratory investigations, number of seizures experienced by patient before registering for care in the hospital, and number of seizures experienced by patient after the last clinic visit as noted by the physician in their case notes. Cost of management of patient within a year (September 2016 to October, 2017) was estimated.

The prevalence based approach of cost of illness studies was carried out based on patients and families perspective in which Out–of-Pocket (OOP) expenditure of patient and/or the caregiver was estimated for a period of one year (September 2016 to October, 2017). In this perspective, amount spent by patients/ caregiver in relation to the disorder was calculated for one year period. Only the direct cost of management of the disorder was estimated using the bottom-up approach. In this approach each cost items for each patient was calculated and summed up. Overall cost for study population was achieved by summing up the values for individuals. These cost items included medical and non-medical costs.

Medical costs included:

Cost of consultation: cost of each consultation multiply by the number of clinic attended as noted in patients' medical record during the year under studied.

Cost of laboratory investigations: summation of total cost of all laboratory investigations carried out during the year under study for each patient using the hospital laboratory department tariff.

Cost of medications: cost of all medications prescribed (that are related to management of seizure disorder) during the one year period. It was estimated using the cost of daily dose for patient using the hospital pharmacy tariff.

Non-medical costs included:

Transportation to and from hospital for both patient and caregiver bearing in mind patients' resident and number of clinic attended. This was estimated using the National Union of Road Transport Workers (NURTW) tariff of the year studied.

The total cost of all these cost items was calculated for each patient for the period of September 2016 to October 2017 to give the economic burden per patient per annum. Exchange rate of the Nigerian Naira (₦) to USD ($) was ₦320 to USD $ 1 at the time of data collection (2017/2018). *https://www1.oanda.com › currency › converter*.

The participation was voluntary and the identity of the participants was kept confidential and anonymous. The participants were informed on the objectives of the study and the need for utmost sincerity.

For the prospective study, a structured and pretested interviewer-administered questionnaire was used to obtained information from the patients. It consisted of the following sections;

Section A: It assessed the demographic variables of the respondents.

Section B: It assessed the medications, frequency of hospital visits, caregiver who accompany patients to clinic, and impact of seizure disorders on education, marriage and employment, and self-reported four item Morisky's medication Adherence Scale (MMAS 4) was used to collect data on adherence of the participants to their medications (Morisky et al, 2008). The items are summed and the scores was categorized as: 3-4-low adherence; 1-2- medium adherence and a score of zero as high adherence. Reason(s) for non-adherence was also obtained from the patients. Each consented patient was administered the pretested questionnaire while information that the patient could not make available were retrieved from the patient's case note using a structured data form. The data form contained information such as: date of first registration, year of first seizure, frequency of seizure before reporting in hospital, last frequency of seizure documented by physician, year since diagnosis, year since management, medication history and current medication(s), its frequencies and duration, number of clinic attended yearly, laboratory investigations and

other information that the patient could not make available.

Drug resistant epilepsy (DRE) cases were defined as a participant on two or more antiepileptic drugs who still had a seizure in last one year before data collection (Kwon et al, 2016).

Inclusion criteria
All consenting out-patients diagnosed with seizure disorder who has been attending the neurology clinic of MOP of the hospital for at least one year.

Exclusion criteria
Non consenting patients diagnosed with seizure disorder met during the period of the research. Patients who had been attending the clinic for a period of less than one year. Patients newly diagnosed of seizure disorder.

Data Analysis
Data obtained were coded and analysed using IBM-Statistical Package for the Social Sciences version 23. Descriptive statistics such as: frequency counts, percentages, mean, standard deviation were used to summarize and present the results. Relationship between duration of use (years) of AEDs, and adherence's score was tested using Pearson moment product correlation. Independent student t-test was used to test for differences in mean cost of AEDs among adherent and Non-adherent groups. Value of p <0.05 was considered statistically significant.

RESULTS
A total of 63 patients were approach for the study but 51 patients consented and were interviewed giving a response rate of 81% out of which 20 (39.2%) were males, and 31 (60.8%) females. Their age range was 14-70 years. The mean age was 35.45±15.87 years.

The average monthly income of the 32 employed patients was ₦56,781.2 ($177.4) (SD ± ₦33,785.6) with minimum of ₦15,000 ($46.9) and maximum of ₦200, 000 ($625.0). Details of Socio-demographic data of the patients are shown on Table 1.

Table 1: Socio demographic data of participants

Demographic factors	Option	Frequency	Percentages (%)
Sex	Male	20	39.2
	Female	31	60.8
	Total	51	100.0
Age	14-19	11	21.6
	20-29	11	21.6
	30-39	5	9.8
	40-49	14	27.5
	50-59	5	9.8
	>60	5	9.8
	Total	51	100.0
Marital status	Single	29	56.7
	Married	21	41.2
	Divorced	1	2.0
	Total	51	100.0
Educational level	No formal education	2	3.9
	Primary school	9	17.6
	Secondary school	18	35.3
	Tertiary	22	43.0
	Total	51	100.0
Occupation	Student	16	31.4
	Privately employed	18	35.3
	Civil servant	4	7.8
	Retiree	3	5.9
	Self employed	7	13.7
	Unemployed	3	5.9
	Total	51	100.0
	Yes	3	5.9
NHIS enrollee	No	48	94.1
	Total	51	100.0

Laboratory investigations carried out among the participants

Aside patients' clinical presentations and medical history (both from patients and an eyewitness of seizure attack), the most common laboratory investigations carried out on these patients included Electroencephalography (EEG) (29, 56.7%), cranial magnetic resonance index (MRI) scan (10, 19.6%), cranial Computerized tomography (CT) scan (6, 11.8%), urinalysis (2, 3.9%), glycosylated hemoglobin (HBA1C) test (1,1.9%), hormonal profile (FSH, LH, Estrogen) (1, 1.9%), Full blood count (3, 5.9%), skull x-ray (2, 3.9%), thyroid function tests (1, 1.9%), chest X-ray (2, 3.9%), and Electrocardiography (ECG) (1, 1.9%).

Diagnosis of Seizure disorders

The specific diagnosis and classes of seizure among the patients that participated in the study is shown in Table 2

Effect of seizure disorders on education, marriage and employment

Seizure disorder was shown to have a negative effect on the social life of the patients involved in this study. The effect of seizure disorder on social life which included education, marriage and employment are shown in Table 3

Out of the 51 patients involved in this study, 6 were below 18 years of age which was considered as marriageable age and are also not expected to be in labor market.

Table 2: Specific diagnosis of seizure disorders among participants

Class of seizure	Specific diagnosis	Patients number	Percentage (%)
Generalized	Tonic clonic	16	31.4
	Myoclonic	1	2
Partial	Simple partial seizures	3	5.9
	Complex partial seizures	4	7.8
Mixed seizures	Mixed seizures	19	37.3
Status epilepticus	Status epilepticus	1	2
Temporal lobe epilepsy	Temporal lobe epilepsy	1	2
Lennox gastaut syndrome	Lennox gastaut syndrome	1	2
Juvenile onset seizures	Juvenile onset seizures	1	2
Post stroke seizures	Post stroke seizures	4	7.8
Total		51	100

Table 3: Effect of seizure disorder on academic, marital life and career development as stated by participants

Variable	Number of patients	Percentages (%)
Effect of seizure disorders on education		
Failing a course	13	25.5
Missing an exam	11	21.6
Repeating a class	9	17.6
Others (No effect on education)	18	35.3
Total	51	100
Effect of seizure disorders on marriage		
Inability to marry	5	12.5
Having relationship problems	8	20.0
No negative effect	27	67.5
Total	40	100
Effect of seizure disorders on carrier development		
Hindered chance of getting a good job	16	35.5
Hindered promotion	4	8.8
No negative effect	25	55.6
Total	45	100

Anti-epileptic drug prescription pattern

Anti-epileptic drug prescription pattern included both monotherapy and multidrug therapy using various drugs is depicted in Table 4. Carbamazepine was the most prescribed AED (60.8%). Carbamazepine was prescribed in combination (multidrug therapy) with other AEDs in about 23.5% of the participants.

Duration of disorder

Duration of seizure disorder among participants ranged between 1 and 35years with those of 1-3years duration being 26 (51.0%). More than half (29, 56.9%) of the patients had attended other hospitals before they were referred to UCH while 22 (43.1%) reported directly in UCH at first seizure episode. Majority of

the participants 35 (68.6%) had experienced seizure
more than a year as of the time they reported in UCH.

Table 4: Antiepileptic medications prescription pattern among the participants

Medication prescribed	Number of patients using medication	Percentage (%)
Carbamazepine	31	60.8
Levetiracetam	4	7.8
Lamotrigine	2	3.9
Gabapentin	1	2.0
Phenytoin	1	2.0
Carbamazepine/levetiracetam	8	15.7
Carbamazepine/phenytoin	1	2.0
Carbamazepine/sodium valproate	1	2.0
Carbamazepine/gabapentin	1	2.0
Carbamazepine/levetiracetam/sodium valproate	1	2.0
Total	51	100

Table 5: Treatment outcome (frequency of seizure) based self-reported adherence status among the studied participants

Seizure frequency	Non-adherent group (N=33)		Adherent group (N=18)	
	At first clinic presentation	As of time of study	At first clinic presentation	As of time of study
Remission (no seizures in ≥1 year)	0 (0.0)	3 (10.0)	0 (0.0)	0 (0.0)
At least one episode in 6 months to 1 year	0 (0.0)	5 (15.1)	0 (0.0)	1 (5.5)
At least one episode in 2-6months	2 (6.1)	14 (42.4)	0 (0.0)	8 (44.4)
1 seizure per month	3 (10.1)	5 (15.1)	4 (22.2)	2 (11.1)
2–3 seizure per month	6 (18.2)	2 (6.1)	5 (27.8)	4 (22.2)
1–5 seizures per week	2 (6.1)	0 (0.0)	2 (11.1)	1(5.6)
Daily	3 (10.1)	0 (0.0)	1 (5.6)	0 (0.0)
Not certain	16 (48.5)	4 (12.1)	7 (38.9)	2 (11.1)
Total	33	33	18	18

There is a significant negative correlation between years of use of AEDs and adherence to medication (r = -0.3, p = 0.04). Patients with higher score of MMAS-4 (non-adherence) have lower duration of use of AEDs.

Among those who had remission for 1 year and above, 5 of them are on AED monotherapy, while 1 is on more than one AEDs. Fourteen out of fifteen patients on more than one AEDs still experience seizure at least

once in a month while thirty-one patients on monotherapy still experience seizure in past one year on treatment.

Results obtained from the self-report MMAS-4 score showed that, 12 (23.5%), 21 (41.2%), and 18(35.3%) of the participants had low adherence (scored 3-4), medium adherence (scored 1-2) and high adherence (scored 0) scores respectively. Participants with low adherence and medium adherence were merged as non-adherent, indicating 33 (64.7%) non-adherent patient to their antiepileptic medication(s) (AEDs). Among adherent patients, 3 (16.7%) were on multidrug therapy while 15 (83.3%) were on monotherapy. Among the non-adherent patients, 21 (63.6%) were on monotherapy while 10 (30.3%) were on multitherapy. Barriers to non-adherence as reported by the participants included: Forgetfulness (31; 60.8%), cost of medication(s) (24, 47.1%), use of faith-based therapy by praying (9, 18%), denial of illness (patient does not belief he/she have seizure disorder) (2, 3%) and side effects of AEDs (3, 5.9%).

Cost (Burden) of seizure disorders

Direct medical costs (medications, cost of laboratory investigations, and consultancy fee) and non-medical costs (transportation fee) for one-year management were calculated for all the patients. More than one-third of the participants were unemployed (students, children, housewives or job applicants) and they depend either on their parents, spouse or relatives for their medical bills. This indirectly implies that the cost of management of their illness is the sole responsibility of their caregivers (Table 6).

Table 6: Individuals responsible for the healthcare bills of participants

Variable	Frequency	Percentage
Self	9	17.6
Parents	27	52.9
Relatives (other than parents)	7	13.7
Self and spouse	5	9.8
Self and parents	1	2
Self and relatives	2	3.9
Total	51	100

Among the 38 on monotherapy, 16 (88.9%) out of the 18 Adherent patients and 22 (66.7%) out of 33 non-adherent patients were on monotherapy. Multidrug therapy was used by 2 (11.1%) adherent patients and 11 (33.3%) non-adherent patients.

The direct cost of treating patients with seizure disorders in fifty-one patients involved in the study was estimated to be ₦7,175,050 ($22,422.0) per annual and ₦11,723.9 ($36.6) per month.

Table 7: Mean costs of monotherapy and multi drug therapy among participants

Drug therapy	Number of patients (%)	Total cost (₦)	Mean cost per patient (₦)	% of total AEDs cost
Monotherapy	38 (74.5)	3,742,050 ($11,693.9)	98,475.0 ($307.7)	64.6
Multidrug therapy	13 (25.5)	2,049,700 ($6,405.3)	157,669.2 ($492.7)	35.4
Total	51	5,791,750 ($18,099.2)		35.4

Exchange rate of the Nigerian Naira (₦) to USD ($) was ₦320 to USD $ 1 at the time of data collection (2017/2018).

Table 8: Cost of treatment of seizure disorder among the studied population

Cost items	Amount ₦ ($)	Mean ($)	Standard deviation	Cost percentage (%)
Antiepileptic drugs (AEDs)	5,530,150 (17,281.7)	108,434 (338.9)	61805	77
Laboratory investigations	896,000 (2,800)	17,568 (54.9)	27086	12.5
Consultation fee	555,000 (1,734.4)	5,142 (16.1)	5142	7.7
Transportation fee	193,900 (605.9)	3,801 (11.9)	2662	2.7
Total	7,175,050 (22,422.0)	134, 945 (421.7)		100

Table 9: Cost of management and adherence status

Cost items	Amount ₦ ($)	
	Adherent	Non-adherent
Antiepileptic drugs (AEDs)	1,783,100 (5,572.2)	3,747,050 (11,709.5)
Laboratory investigations	474,800 (1,483.8)	421,200 (1,316.3)
Consultation fee	249,900 (781.0)	306,000 (956.3)
Transportation fee	94,500 (295.3)	99,400 (310.6)
Total	2,602,300 (8,132,.2)	4,572,750 (14,290.0)

The mean cost of AEDs among adherent and non-adherent groups were ₦99,061.1±59,569.7 and 113,546.9±63,301.6 respectively (p=0.429, t= -0.77).

DISCUSSION
The economic impact of seizure disorder among the studied participants is of great importance (Table 8). Majority of the studied participants paid for their treatment out of their pocket and this could impose a significant economic burden on the patients as well as their caregivers since their medication(s) are usually taken for a long period of time. Among those employed, the amount spent on the disorder per month was 20.6% of their average monthly income. In addition, half of them are unemployed as shown in table 1 (students, children, unemployed and retirees). This group of patients depends on their parents, relatives, spouse or children for financial support and medical bills (Table 6). The United Nations Development Program in 2015 estimated that more than 80% of people in the sub-Sahara Africa live on less than $1.9 per day ($57 per month) (UNDP, 2015), hence the added burden of the cost of seizure disorders

on the merge family budget cannot be overemphasized. Past studies have also reported high rates of unemployment (66.7% and 80%) among patients living with epilepsy (Ezeala-Adikaibe et al, 2009; Ipingbemi, 2014). Unfortunately, less than ten percent of the participants in this study are National Health Insurance Scheme (NHIS)'s enrollee. The scheme was established by the Federal Government of Nigeria to improve the health of its citizens through various co-payment systems. Under this program, the patient and the government are involved in co-payment of some of the patients' healthcare bills (NHIS, 2017).
One of the factors that contributed to increase in cost of management is the prescription of more than one Antiepileptic drugs (AEDs) for about one-quarter of the participants. Monotherapy has been reported by previous studies (Kwan and Brodie, 2000; Krishnan et al, 2004) to satisfactorily controlled seizures in around

161

75% of seizure disorder patients. Multidrug therapy increased cost of management in this study (Table 7) as also reported in a previous study in eastern part of Nigeria (Ezeala-Adikaibe et al, 2009). Though, it is expected that physicians should prescribe cheap and affordable AEDs, however, factors which may influence the physicians' choice may include, seizure frequency, side effects of the drugs as well as the physicians' choice by virtue of their experience (Ezeala-Adikaibe et al, 2009). Another factor that could increase cost of management of the disorder is poor adherence to antiepileptic drugs which usually leads to higher rates of seizure recurrence which in turn results in increase in medical resource utilization and costs as reported in previous study (Davis et al, 2008). The average cost of AEDs in this study was found to be higher among non-adherent groups as compared to the adherent group. The increase in cost among the non-adherent group (Table 9) is related to increase in numbers of AEDs use among these patients as compared to the adherent patients. Patient usually required additional AED when the seizure is uncontrolled. In this study, two-third of the patients had poor adherence (<100.0%). Non-adherence has been reported to be common among seizure disorder patients. Past studies have shown 36% to 70.8% adherent rate among people living with epilepsy (Liu et al, 2013; Gabr and Shams, 2015; Hasiso and Desse, 2010). However, more than 95% adherence has been reported to be necessary to adequately suppress epileptic seizures. This implies that missing one or more doses of an AED per week may be enough to cause treatment failure and trigger seizures (Johnbull et al, 2011). Patients that failed to adhere to therapy experienced an increase in number and severity of seizures (WHO, 2004). The treatment outcome in this study (table 5) showed that there was an improvement in the frequency of seizure but very few numbers of the patients had been seizure free for up to one year since commencement of AEDs especially among the non-adherent group. Using a pragmatic definition of medication-resistant epilepsy to be a patient who is currently taking more than one AEDs (Kwan et al, 2010), and still experiences at least one seizure per year (Bruno et al, 2017), it is difficult to conclude that the participants who were adherent to their AED and are still experiencing seizure in last 1 year of management (Table 5) may be experiencing resistance seizure until they have been on more than one AEDs (as seen in two adherent patients in this study). These patients might need additional AED to their regimen in order to achieve good seizure control.

Adherence was found to correlate negatively with years of use of AEDs in this study. This implies that patients who had been on AEDs for a longer period tends to adhere to their medications. Good adherence among those who had been on AEDs for some years could be attributed to the fact that they have been able to overcome some of the barriers to adherence reported among the studied participants. Such barriers/reasons included forgetfulness, cost of medication(s) and their belief that they can be healed by praying without the use of medication(s), a common practice in the country as shown by previous studies in other part of Nigeria (Eseigbe et al, 2014). Previous studies among PWE showed that forgetfulness is most common reason for non-adherence to medications (Lui et al, 2013; Gabr and Shams, 2015).

The effect of seizure disorder on the social life of the patient cannot be overemphasized. About two-third of the patients involved in this study at one time or the other have had to miss an examination, failed a course and even repeated a class because of the disorder (table 3). This is consistent with previous studies in Western Nigeria which reported cognitive impairment due to recurrent seizures affected the patient's attendance as well as performance at school Ogunrin et al., (2003). Adewuya et al., (2006) also noted that school children with seizure disorders had lower performance at school compared to other pupils. Furthermore, the employment status of the patients this study was affected by the disorder (table 3) as reported in previous studies (Chaplin et al 1998; Heaney et al, 2008). This further worsen the burden of the disorder on family/relation who have to pay for medical bills of the patients because of their financial constrain related to inability to get good job/ desired promotion. More importantly, patients with seizure disorders have been shown to have marital problems particularly in getting spouses as well as sustaining their marriages as seen among this study population. Ogunrin et al., (2006) reported that seizure disorder patients may find it difficult to marry or even lose their spouse due to the disorder. Paul et al., (2012) also reported that frequent seizure had a determining effect not only on education but also on marital life.

In this study, diagnosis of seizure disorder was based on patients' clinical presentations, history (both from patients and an eyewitness of seizure attack) as well as laboratory investigations as reported in previous study (Heaney et al, 2008;). Majority of the patients presented with mixed seizure disorder (Table 2) in contrary to some previous studies in Nigeria and other parts of the world where generalized seizure was found to be most common (Al–Zakwan et al, 2013; Ipingbemi, 2014; Hasiso et al, 2016). However, Pato-pato et al, (2013) in their study in Spain reported highest prevalence of partial seizure among the studied population. The low or lesser frequency of partial seizures in this study could be because manifestations of partial seizures may not be noticed or as frightening

as seen in generalized seizures, hence patients/or caregivers may therefore not seek for immediate medical attention.

The most frequently prescribed AED among the studied participants was carbamazepine (Table 4), which was reported in previous studies (A–Zakwan et al, 2013; Ipingbemi, 2014; Sanya et al, 2015). Carbamazepine is a drug of choice for both generalized and partial seizures except in myoclonic seizures and this could account for its frequent use among the studied population. However, in a study in northern part of Africa, a combination of phenobarbitone and carbamazepine was the most frequently prescribed (Gabr and Shams, 2015).

Limitations to the study
This study excludes new patients who may have a higher cost of management. The period of study was also short which resulted to low sample size. In addition, 19% non-response among patients seen affected the sample size. The sample size may limit the generalization of the findings of this study, therefore caution should be exercise in interpretation of the results.

CONCLUSION
The clinical outcome of the participants is poor which could be associated with non-adherence to medication(s) which was basically due to forgetfulness and cost of medication(s). The burden of seizure disorder on patients /caregiver was estimated to be an average of $36.6 monthly. This is huge because more than one-third of the patients were unemployed and depends on their family and relatives for medical bill while those employed spent one-fifth of their monthly income on the disorder. Efforts should be directed towards resolving non-adherence associated with behavioural factors and also reducing the direct cost of treating seizure disorders possibly through co-payment mechanism using appropriate policy interventions.

REFERENCES
Adewuya, A.O., Oseni, S.B and Okeniyi, J.A. (2006). School performance of Nigerian adolescents with epilepsy. Epilepsia. 47:415-420.

Al-Zakwani, I., Hanssensy, D.D., Cohen, A and Mcghan, W. (2003). Annual direct medical cost and contributing factors to total cost of epilepsy in Oman. Seizure. 12:555-560.

Bruno V., Klein J.P., Nidup, D.,Nirola D.K., Tshering L., Deki,S., Clark, S.J., Linn, K.A., Shinohara, R.T., Dorji,C., Ram, D., Dema,U., Mateen F.J., Bhutan Epilepsy Project. (2017). Yield of brain MRI in clinically diagnosed epilepsy in the Kingdom of Bhutan: a prospective study. Ann. Global Health. 83: 415–422.

Chaplin, J.E., Wester, A and Tomson, T. (1998). Factors associated with the employment problems of people with established epilepsy. Seizure. 7: 299-303.

Dua, T., deboer, H.M, Prilipko, L.L and Saxena, S. (2006). Epilepsy care in the world: results of an ILAE/IBE/WHO Global campaign against epilepsy survey. Epilepsia. 47(7):1225-1231.

Davis, K.L., Candrilli, S.D and Edin, H.M. (2008). Prevalence and cost impact of non-adherence with antiepilepsy drugs among adults in a managed care population. Epilepsia. 49:446-454.

Eseigbe, E.E., Nuhu, F.T., Sheikh, T.L., Adama, S.J., Eseigbe, P., Aderinoye, A.A., Adebayo, O and Gazali KY. (2014). Factors associated with treatment gap in children and adolescents with epilepsy in a rural Nigerian community. Nig. J. Paedia. 41 (1):22-27

Ezeala-Adikaibe, B, Onwueke, I., Ekenze, S and Achor, J. (2009). Estimated direct cost of treating epilepsy per month in Southeast Nigeria. Int. J. Neurol. 13.1:1-6

Gabr, W.M. and Shams, M.E.E. (2015). Adherence to medication among outpatient adolescents with epilepsy. Saudi Pharm. J; 23(1):33±40. doi: 10.1016/j.jsps.2014.05.003 PMID: 25685041

Ghaffarpour, M., Ghelichnia, H.A., Harrichian, M.H., Ghabaee, M., Tehrani S.M.M. and Bahrami P. (2014). Strategies of Starting and Stopping Antiepileptic Drugs in Patients with Seizure or Epilepsy; A Comprehensive Review. Arch. Neurosci.1 (3):e14182. doi: 10.5812/archneurosci.14182

Hasiso, T.Y and Desse, T.A. (2016). Adherence to Treatment and Factors Affecting Adherence of Epileptic Patients at Yirgalem General Hospital, Southern Ethiopia: A Prospective Cross-Sectional Study. PLoS ONE; 11(9): e0163040. doi:10.1371/journal.pone.0163040

Heaney, D.C., Bell, G.S and Sander, J.W. (2008). The socioeconomic, cultural, and emotional implications of starting or withholding treatment in a patient with a first seizure. Epilepsia. 49 Suppl 1: 35-39.

Ipingbemi, A.E. (2014). Management, treatment outcome and cost of epilepsy in a tertiary health care facility in northern Nigeria. Int. J. Med. Update. 10(2):25-36.

Johnbull, O., Farounbi, B., Adeleye, A and Uche, A. (2011). Evaluation of factors influencing medication adherence in patients with epilepsy in rural communities of Kaduna state, Nig. Neurosci. Med 2 (4): 299-305.

Kotsopoulos, I.A., Evers, S.M., Ament, A.J., Kessels, F.G., de Krom, M.C., Twellaar, M, Metsemakers, J.F and Knottnerus A.J. (2003). The costs of epilepsy in three different populations of patients with epilepsy. Epilepsy Res. 54(2):131–40.

Krishnan, A., Sahariah, S.U. and Kapoor, S.K. (2004). Cost of epilepsy in patients attending a secondary-level hospital in India. Epilepsia. 45.3: 289-291

Kwan, P. and Brodie, M.J. (2000). Early identification of refractory epilepsy. New Eng. J. Med; 342: 314-319.

Kwan, P., Arzimangolou, A., Berg, A.T., Brodie, M.J., Hauser, W.A., Mathern, G., Moshé, S.L., Perucca, E., Wiebe, S and French J. (2010). Definition of drug resistant epilepsy: consensus proposal by the ad hoc task force of the ILAE commission on therapeutic strategies. Epilepsia. 51 (9):1069-1077.

Kwon, C.S., Neal, J., Telléz-Zenteno, J., Metcalfe, A., Fitzgerald, K., Hernandez-Ronquillo, L., Hader, W., Wiebe, S and Jetté N. (2016). CASES Investigator Resective focal epilepsy surgery – Has selection of candidates changed? A systematic review. Epilepsy Res.122:37–43.

Lagunju, I, Imam, Z. and Adedokun, B. (2011). Cost of epilepsy in children attending a tertiary centre in Nigeria. International Health. 3(3): 213-218.

Liu, J., Liu, Z., Ding, H., Yang, X. (2013). Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. Epileptic Disorder. 15 (3): 289-94. doi: 10.1684/epd.2013.0588 PMID: 23906632

Morisky, D.E., Ang, A., Krousel-Wood, M and Ward H.J. (2008). Predictive validity of a medication adherence measure in an outpatient setting. J. Clin. Hypertens (Greenwich).10(5):348-54

National Health Insurance Scheme https://www.nhis.gov.ng/ Assessed 18/12/2017

https://www1.oanda.com › currency › converter Assessed on 22nd October, 2018

Ogunniyi, A., Oluwole, O.S and Osuntokun, B.O. (1998). Two-year remission in Nigerian epileptics. East Afri. Med J. 75 (7): 392-395.

Ogunrin, O.A. (2006). Epilepsy in Nigeria- A review of Etiology, Epidemiology and Management. Benin J Postgraduate Med; 8.1: 27-28

Ogunrin, A.O., Adamolekun, B., Ogunniyi, A. (2003). Seizure frequency and cognitive performances of Nigerian epileptic patients. J. Med. and Biomed Res. 2: 53-60

Paul, A., Adeloye, D, George-carey, R. and Kolcic, I. (2012). An estimate of the prevalence of epilepsy in Sub-saharan Africa: A systematic analysis. J. Global Health. 2(2): 020405.

PatoPato, A., Cebrian, P.E., Cimas, H.I., Lorenzo, G.J., Rodriguez, C.I and Gude, S.F. (2011). Analysis of direct, indirect, and intangible costs of epilepsy. Neurologia. 26(1): 32-38.

Sanya, E.O., Wahab, K.W., Desalu, O.O., Bello, H.A., Ademiluyi, B.A., Alaofin, W.A and Busari K. (2015). A 3 year audit of adult epilepsy care in a Nigerian tertiary hospital (2011-2013). Ann. Afr. Med. 14:97-102

Senthil, A., Gopalkrishna, G. and Parthasarathy, S. (2015). Epilepsy in India II: Impact, burden and need for a multisectoral public health response. Seizure. 18(4): 369-381.

United Nations Development Programme. (UNDP). (2015). Sustainable development goals. http://www.undp.org/content/undp/en/home/sustainable-development-goals/goal-1-no-poverty.html .Assessed 30thJanuary, 2019.

Viteva, E. (2013). Impact of stigma on the quality of life of patients with refractory epilepsy. Seizure. 12 (1): 64-69.

WHO. (2004). Epilepsy in the WHO African region: Bridging the gap. The Global campaign against epilepsy "Out of the shadow". 1-24. https://www.who.int/mental_health/management/epilepsy_in_African-region.pdf. Assessed 8th March, 2018.

WHO. (2017). WHO updates fact sheet on Epilepsy (10 February 2017). Community Medicine for All Seeking Simple Explanations https://communitymedicine4asses.com/2017/02/11/who-updates-fact-sheet-on-epilepsy-10-february-2017/. Assessed 30th June, 2018.

WHO. (2018). Epilepsy. Key facts. 8th, February, 2018. http://www.who.int/news-room/fact-sheets/detail/epilepsy. Assessed 30th June, 2018.

Yamane, Taro. (1967): Statistics: An Introductory Analysis, 2nd Ed., New York: Harper and Row.

Yoon D., Frick K.D., Carr D.A., Austin J.K. (2009). Economic impact of epilepsy in the United States. Epilepsia. 50(10):2186-91. DOI: 10.1111/j.1528-1167.2009.02159

*Address for correspondence: Aduke E. Ipingbemi
Department of Clinical Pharmacy and Pharmacy Administration,
University of Ibadan,
Ibadan, Nigeria.
Telephone: +2348023635696
E-mails: pharmaduke@yahoo.com