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Non-Adherence to Anti-Epileptic Drugs and Associated Factors among Epileptic Patients in Dessie Town Public Hospitals, Northeast Ethiopia

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Background and Purpose: Patients who are non-adherent to their medication are frequently hospitalized with prolonged lengths of stay and make repeated emergency department visits. They are also more likely to miss work or school due to the seizure effects. In Ethiopia, although there is little evidence concerning anti-epileptic drug adherence, some studies were conducted with some controversy with studies done in another country. This study was therefore conducted to assess non-adherence to antiepileptic drugs and associated factors among adult epileptic patients attending in Dessie town public hospitals, northeast Ethiopia.

Methods: Hospital-based cross-sectional study design was employed on 368 patients from January 16, 2018 to March 16, 2018. A systematic random sampling technique was employed to recruit study participants. The collected data were entered into EpiData 3.1 and exported to SPSS version 22.0 for analysis. All covariates that were significant at *p*-value <0.25 in the bivariate logistic regression analysis were considered for further multivariable logistic regression analysis level of statistical significance at *p*-value <0.05.

Results: Among the respondents, 37.5% (95% confidence interval [CI], 32.1-42.9) of them were non-adhered to antiepileptic drugs. Patients who were unable to write and read (adjusted odds ratio [aOR], 22.30; 95% CI, 5.84-85.21), primary education level (aOR, 5.63; 95% CI, 1.90-16.69), being male (aOR, 2.37; 95% CI, 1.33-4.23), experience adverse effect (aOR, 13.68; 95% CI, 3.27-56.97), patients got medication by payment (aOR, 2.06; 95% CI, 1.04-4.11) were statistically associated with non-adherence.

Conclusions: This study revealed that over one-third of participants were non-adherent to antiepileptic drugs. Sex, educational level, adverse effect, and medication source were independent factors for non-adherence to antiepileptic drugs. Therefore, educations and instructions about the importance of recommended drug use can improve antiepileptic drug adherence in patients with epilepsy. **(2021;11:39-48)**

Key words: Eplipsy drug, Associeted factors, Dessie, Ethiopia

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Introduction

Epilepsy is a neurological disorder of the brain marked by sudden recurrent episodes of sensory disturbance.[1,2] It is characterized by recurrent seizures, which are brief episodes of involuntary movement of the partial or generalized body.[1,3] There are two types of epilepsy: idiopathic and symptomatic epilepsy. Idiopathic epilepsy is a group epileptic disorders epileptic disorders that are believed to have a strong underlying genetic basis and the most common type of epilepsy, which affects six out of 10 people, whereas symptomatic epilepsy is caused by severe head injury, congenital abnormalities associated with brain malformations, stroke, and infection of the brain.[1]

Phenobarbitone, phenytoin, sodium valproate and carbamazepine are the most common drug prescribed in Ethiopia, either independently or combined.[4] In many parts of the world, people with epilepsy and their families suffer from stigma and discrimination. People may fear even going outside their homes alone and concern what people might think of them if they were to have a seizure in public. The risk of epilepsy is high in developing countries due to the increased risk of endemic conditions such as malaria or neurocysticercosis.[5]

Drug adherence is defined as the extent to which a patient's behavior takes medications as prescribed by their health care provider. Across diseases, adherence is the single most important modifiable factor that compromises treatment outcome. The full benefit of the many effective medications that are available will be achieved only if patients follow prescribed treatment regimens reasonably.[6,7] Patients who are non-adherent to their medication are frequently hospitalized with prolonged lengths of stay, make repeated emergency department visits, and miss school or work frequently because of the seizure effects or out of fear of seizure occurrence.[8,9] To overcome the problems of epilepsy in the Ministry of Health of Ethiopia is implemented integrated treatment of mental disorders by improving the availability of drugs, training for trained professionals including primary health care providers with continuous supervision and support, but still the adherence issue is not well addressed.[4]

Globally, an estimated 2.4 million people are diagnosed with epilepsy each year. In high-income countries, the incidence of epilepsy ranges from 30 to 50 per 100,000 people, whereas in low- and middle-income countries, this figure can be up to two times higher than high-income countries.[5] And the prevalence of epilepsy in Ethiopia is also high, 5.2/1,000.[2] The mortality rate in non-adherent patients was more than three times higher than that of adherent patients.[10] A study reports a six-fold increase in mortality in people with epilepsy. This is higher than the two- to three-fold increase reported in developed countries.[11]

Non-adherence is one of many reasons for pharmacological treatment failure and recurrence of seizure, which consequently results in poor quality of life, substantial worsening of disease, death, decreased productivity, and seizure-related social and economic crisis.[1,3,12,13]

A study conducted in Yirgalem Referral Hospital showed that elder age is significantly associated with non-adherence (p=0.002). All ages over 60 years were non-adherent to their AEDs.[4] Another study conducted in Malaysia showed that poor adherence to anti-epliptic drug (AED) therapy was significantly associated with younger age (p=0.022).[14] All of the studies done in Ethiopia do not address the clinician-patient relationship factor. Therefore, this controversy and clinician-patient relationship factor needs to be cleared and studied.

In general, examining the extent of adherence and identifying the underlying causes for non-adherence are necessary to improve the overall quality of life in patients. In Ethiopia, there is little evidence concerning antiepileptic drug adherence, with some controversial issues. Therefore, this study intended to show non-adherence to antiepileptic drugs and associated factors among epileptic patients who follow in the study area.

Methods

Study area and period

The study was conducted from January 16, 2018 to March 16, 2018 in Dessie town public hospitals located in Amhara Region, Ethiopia, a road distance of 401 km from Addis Ababa, the capital city of Ethiopia.

Study design

Hospital based cross-sectional study design was conducted using quantitative data collection method.

Source population

The source population of the study is all epileptic patients attending at Dessie town public hospitals.

Study population

The study population constituted selected epileptic patients attending at Dessie town public hospitals, fulfilling the inclusion criteria during study period.

Inclusion/exclusion criteria

Inclusion criteria

The study comprised of all adult individuals (18 and above years of age) who are diagnosed with epilepsy and have been on AEDs treatment for at least 3 months, including patient's chart with complete records and willingness to participate in the study.

Exclusion criteria

Individuals who are unable to communicate due to serious illness/conditions were excluded.

Sample size determination

To determine the sample size, outcome variable and various factors significantly associated with the outcome variable are considered. Based on both the first and the second objectives, the sample size was calculated and the larger sample size has been used for the study. The required sample for the first specific objective of this study is calculated by using single population proportion formula through assumption of

95% confidence interval (CI) and 5% margin of error, and non-adherence to antiepileptic drug was 38.1% from the research in Dilla University Referral Hospital, Southern Ethiopia.[15]

We calculated the sample size relying on an established formula: $n = (z(\alpha/2))^2 p(1-p)/d^2$.

$$n = \frac{1.96^2 \times 0.38(1-0.38)}{0.05^2} = 363$$

where, n=the minimum sample size, z (α/2)=the desired level of 95% CI (1.96), d=margin of error 5% (0.05). By considering of 10% non-response rate, the total sample size for the first specific objective is (363+37)=400. Sample size become, n=400.

Sampling procedure and technique

There are two public hospitals in Dessie. Dessie Referral Hospital has 804 epileptic patients who follow monthly in three psychiatric Out Patient Departments (OPDs) and Boru Meda District Hospital has 170 epileptic patients who follow monthly in one psychiatric OPD. Study participants were proportionally allocated based on the number of patients in each hospital and systematic random sampling method was used to select the study units: K=N/n, K=974/400=2.43~2.

Total epileptic patients who are follow in psychiatric OPD and their registration book was used as the sampling frame. During the interview and chart review, for the defaulter and incomplete patient medical records were replaced with the next patient and record until the calculated sample size 400 were achieved. The permission to collect the information including each psychiatric outpatient monthly follow up from registration book was obtained from the psychiatric head nurse.

Data collection methods

Data collection instruments

Pretested structured questionnaire by interview and data extraction format to extract clinical data from the medical records was used to collect data. The interview with structured questionnaires is prepared in English and translated in Amharic, which includes patient/socio-economic-related factors and health care team and system-related factors. Chart review and data extraction format which contain therapy-related factors and condition-related factors in English will be used.

Data collectors

Four diploma clinical nurses were trained about tools and data collection procedure and recruited for data collection in four psychiatric OPD. One B. Sc. nurse from other health institution was recruited for supervision in the both hospitals or four psychiatric OPDs. Training of data collectors and supervisors on objectives, questionnaires and ways of conducting interview was provided by the principal investigator for one day before the actual data collection time.

Procedure of data collection

Data were collected through pretested and structured questionnaire by interview and data extraction format was used to extract clinical data from the medical records for chart review in order to get quantitative data. First informed voluntary written consent was obtained from each study participant after explaining the purpose of study, then the data collectors interviewed the patient after they finished their follow up and allowed them to take time to think and respond to the interview questions. In addition, the chart review and data extraction format to identify therapy-related and condition-related factors were collected before interview.

Variables

Dependent variables

Non-adherence to anti-epileptic drugs.

Independent variables

Patient/socio-economic-related factors (sex, marital status, ethnicity, age, residence, educational level, monthly income, occupation, source of medication, social support, and felt/perceive stigma); therapy-related factors (number of AEDs prescribed, side effect and duration of treatment); patient-clinician therapeutic relationship; condition-related factors (seizure type, frequency of symptoms, and comorbid illness).

Operational definitions

For level of adherence, patients were classified as adherent if the-Morisky Medication Adherence Scale (MMAS)-8 score is 0 and non-adherent if the MMAS-8 score is 1-8.[4,16-18] Felt stigma was measured by using Kilifi stigma scale of epilepsy (KSSE) and patients were classified as indicated presence of perceived stigma if the score is above 20 out of 30 and not felt stigma if below 20.[19] For unclassified seizure, the diagnosis was documented as epilepsy.[1] Clinician patient relationship was determined as good if the sum of therapeutic alliance score is 22 to 33, moderate clinician patient rela-

tionship if the sum of therapeutic alliance score is 11 to 21 and weak if the sum of therapeutic alliance score below.[1,20]

Data quality control

For data collectors and a supervisor, 1 day training on the data collection tool were given. At the institutions, data collectors were supervised by the supervisors and reported to principal investigator in a daily basis. Prior to the actual data collection, pre-tested was done 5% of sample size which are 20 individuals and their records in pre-test in Akesta district hospital which was far from 15 km the study area. After pre-testing, difficult questions were revised and after adjustment of those questions, the actual data collection was conducted by using Amharic version questionnaire and English version chart review data extraction format. The anonymity of the patient was preserved.

Methods of data processing and analysis

All filled questionnaire were checked for completeness and consistency. Frequencies, proportion, and summary statistics were used to describe the study population in relation to relevant variables and presented in tables. To measure non-adherence of epileptic patients to their AEDs were measured by using a MMAS-8.[21] Bivariate analysis was carried out to identify variables that are significantly associated with non-adherence. Multicollinearity test was conducted to see correlation among the independent variables by using standard error >2 were dropped from the multi-variable analysis. The Hosmer-Lemeshow test was found to be insignificant (p=0.57) and the Omnibus test was significant (p=0.001) which indicate that the model was fitted. Those variables in bivariate analysis whose p value less than 0.25 were included in multiple logistic regression in order not to miss associated factors. Then multiple logistic regression analysis was performed for those factors that showed a statistically significant association in bivariate analysis and investigate independent predictors by controlling for possible confounders. Finally, variables whose p value less than 0.05 in logistic regression were declared as statistically significant association.

Ethical considerations

The study was approved by the Haramaya Cniversity, College of Health and Medical Sciences Institutional Health Research Ethics Review Committee. Research purpose was briefly explained to the participants and informed, voluntary, written and signed consent was obtained from the heads of each health institution and the participants. Individuals were told that they have a right to withdraw from the study at any time and this would not affect the service they get from the hospital. After non-adherent patient were seen linkage to the health care provider after interview were considered. Confidentiality was ensured during the process of chart review and thus name and address of the patient were not recorded in data abstraction formats.

Results

Socio-demographic characteristics

In this study, a total of 368 study participants were involved, making a response rate of 92%. From the total number of respondents, 208 (56.5%) were males and mean age of the respondents was 33.55+9.066. Almost half of the study participants (191 participants, or 51.9%) were married. One hundred twenty five of participants (34.0%) were Muslim by religion and 230 (62.5%) were Amhara by ethnicity. Regarding educational status, more than one third (145 participants, or 39.4%) had secondary education and more than half of participant residence (66.3%) was urban. Most of patient medication sources were by payment (70.9%) and more than half of the participant's monthly income (242 participants, or 65.8%) were average. Regarding social support, more than half of the study participants (222 participants, or 60.3%) had poor social support and more than two third of patients (322 patients, 87.5%) perceived felt stigma in Table 1.

Therapy and condition/illness-related variable

The majority of the respondents (335 respondents, or 91.0%) has recent seizure since their last visit and the majority of them (319 respondents, or 86.7%) has seizure episode ranging from 0 to 5 seizure. Generalized seizure was dominant seizure type (362 respondents, or 98.3%). Most of patients (328 patients, or 89.1%) were on monotherapy and phenobarbital was the most commonly prescribed AED (271 patients, or 73.6%). Comorbid illness (Gout arthritis, asthma, congestive heart failure, diabetes mellitus, human immunodeficiency virus/acquired immunodeficiency syndrome, hypertension, leprosy) was reported by 13 participants (3.6%) and more than one third of the participants (138 participants, or 37.5%) were treated for epilepsy for 25 to 60 months (2 to 5 year). Majority of the patients (355 patients, or 96.5%) did not take drug other than AEDs. Adverse effect is reported among 26 of participants (7.1%) and de-

Table 1. Frequency distribution of participant socio-demographic variables in government hospitals of Dessie town public hospitals, 2018

Variable	Value (n=368)
Sex	
Male	208 (56.5)
Female	160 (43.5)
Age (years)	
18-28	109 (29.6)
29-39	169 (45.9)
40-50	77 (20.9)
51-61	8 (2.2)
>61	5 (1.4)
Marital status	
Single	73 (19.8)
Married	191 (51.9)
Divorced	76 (20.7)
Widowed	28 (7.6)
Religion	
Orthodox	99 (26.9)
Muslim	125 (34.0)
Protestant	84 (22.8)
Catholic	50 (13.6)
Other	10 (2.7)
Ethnicity	
Oromo	29 (7.9)
Amhara	230 (62.5)
Tegrie	68 (18.5)
Other	41 (11.1)
Educational status	
Unable to write and read	45 (12.2)
Primary education	133 (36.1)
Secondary education	145 (39.4)
Above secondary education	45 (12.2)
Occupation	
Unemployed	20 (5.4)
Farmer	74 (20.1)
Merchant	98 (26.6)
Housewife	64 (17.4)
Daily labourer	30 (8.2)
Student	42 (11.4)
Employed	38 (10.3)
Other	2 (0.5)
Monthly income	
Very low	9 (2.4)
Low	33 (9.0)
Average	242 (65.8)
Above average	68 (18.5)
High	16 (4.3)
Medication source	
Free	107 (29.1)
Payment	261 (70.9)
Residence	
Rural	124 (33.7)
Urban	244 (66.3)
Social support	
Poor social support	222 (60.3)
Moderate social support	103 (28.0)
Strong social support	43 (11.7)
Stigma	
Felt/perceived stigma	322 (87.5)
Not felt/perceived stigma	46 (12.5)

Values are presented as frequency (%).

Table 2. Distribution of patients with epilepsy disorder by therapy and condition/illness-related factors

Variable	Value (n=368)
Time of first seizure occurs (months)	
1-6	21 (5.7)
7-12	56 (15.2)
13-24	55 (14.9)
25-72	161 (43.8)
≥73	75 (20.4)
Did you have recent seizure	
Yes	335 (91.0)
No	33 (9.0)
How many seizure happen since the last visit	
0-5	319 (86.7)
6-10	40 (10.9)
11-15	8 (2.2)
≥16	1 (0.3)
Seizure type	
Generalized	362 (98.3)
Partial	6 (1.7)
When did you start AEDs/duration (months)	
3-12	36 (9.8)
12-24	92 (25.0)
25-60	138 (37.5)
61-120	58 (15.8)
>121	44 (12.0)
Type of AEDs	
Carbamazepine	20 (5.4)
Phenytoin	17 (4.6)
Phenobarbital	271 (73.6)
Sodium valproate	20 (5.4)
Sodium valproate and carbamazepine	29 (7.9)
Carbamazepine and phenobarbital	3 (0.8)
Sodium valproate and phenobarbital	7 (1.9)
Sodium valproate and phenytoin	1 (0.3)
Number of AEDs	
Monotherapy	328 (89.1)
Polytherapy	40 (10.9)
Diagnosis other than epilepsy	
Gout arthritis	3 (0.9)
Asthma	1 (0.3)
CHF	1 (0.3)
DM	1 (0.3)
HIV/AIDS	2 (0.5)
Hypertension	4 (1.0)
Leprosy	1 (0.3)
No	355 (96.4)
Drug other than AEDs	
Yes	13 (3.6)
No	355 (96.5)
Adverse effect of AEDs	
Yes	26 (7.1)
No	342 (92.9)
Type of adverse effect	
Depressed mood	5 (1.4)
Epigastric pain	5 (1.4)
Confusion	4 (1.1)
Weakness	4 (1.1)
Blurring of vision	3 (0.8)
Headache	2 (0.5)
Nightmare and forgetfulness	1 (0.3)
Other	2 (0.5)
Total	26 (7.1)

Values are presented as frequency (%).
AED, anti-epileptic drug; CHF, congestive heart failure; DM, diabetes mellitus; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

Table 3. Client - provider relationship/ therapeutic relation of epileptic patient in Dessie town public hospitals

Client provider relation	Value (n=368)
Low therapeutic relation	5 (1.4)
Moderate therapeutic relation	66 (17.9)
Good therapeutic relation	297 (80.7)

Values are presented as frequency (%).

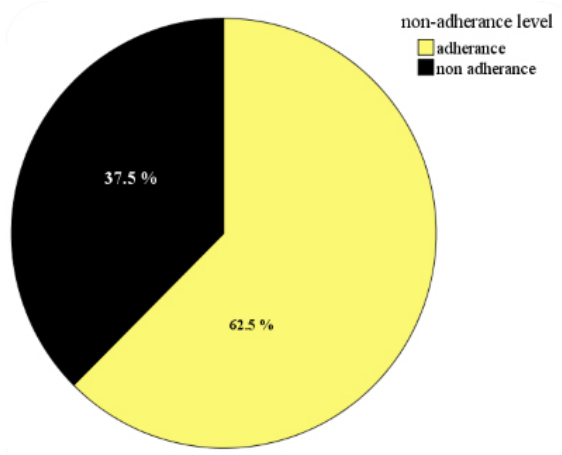

Figure 1. Frequency distribution of participant non-adherence level in hospitals of Dessie town public hospitals (n=368).

pressed mood, epigastric pain, confusion, weakness, blurring of vision, headache, nightmare and forgetfulness were type of adverse effect reported among the participants in Table 2.

Client-provider relationship/therapeutic relationship characteristics

About four of fifth of the respondents (297 respondents, or 80.7%) have good therapeutic relationship with their health care providers and the client-provider relationship/therapeutic relationship questionnaire has a good internal consistency in Table 3 (Cornbrash's α=0.82).

Overall non adherence level of patients taking antiepileptic drugs

Out of 368 participants, 138 (37.5%; 95% CI, 32.1-42.9%) are non-adherence to antiepileptic drugs while the remaining (230 participants, or 62.5%) had adherence (Fig. 1).

Factors associated with non-adherence to anti-epileptic drugs

Bivariate analysis result showed that sex, marital status, age, educational level, residence, first seizure occurrence, source of medication, adverse effect, duration of AEDs, drug other than AEDs, social support and client provider relation were significantly associated with non-adherence. In multivariate analysis, sex, educational level and adverse effect medication source were identified to be significantly associated with non-adherence. Patients who were unable to write and read (adjusted odds ratio [aOR], 22.30; 95% CI, 5.84-85.21) and finished primary education (aOR, 5.63; 95% CI, 1.90-16.69) were 22.3 times more likely to be non-adherent to AED as compared to patients who had diploma and above educational status. Male epileptic patients were 2.37 times more likely to non-adherence as compared to female (aOR, 2.37; 95% CI, 1.33-4.23). Patients who experienced adverse effect were 13.68 times more likely to be non-adherent as compared to their counterpart (aOR, 13.68; 95% CI, 3.27-56.97). Patients who get medication by payment were 2.06 times more likely to be non-adherent as compared to those who get or take medication by free in Table 4 (aOR, 2.06; 95% CI, 1.04-4.11).

Discussion

Findings of non-adherence in the present study showed that more than two-third (37.5%; 95% CI, 32.1-42.9%) of the study participants were non-adherent to antiepileptic drugs. Among factors, sex, educational level, adverse effect and medication source were independent predictors for non-adherence to antiepileptic drugs. The prevalence of non-adherence to antiepileptic drugs in this study was in line with the result of the studies conducted in Dilla southern Ethiopia (38.1%) and northwest Ethiopia (37.8%), lower than the studies done in Yirgalem Southern Ethiopia (68%), Brazil (66.2%), Malaysia (64.1%), and Africa (65.1%), and higher than the studies done in India (27.7%) and USA (31.8%).[1,3,14,16,17,20,22,23] The probable explanation for this difference could be due to the difference in the study design and methods used to measure the non-adherence scale and socio-demographic characteristics of the study participant as well study area. Additionally, it also might be due to differences in availability of resources like the level of patient care and epilepsy management as some hospitals provide care by specialist physicians, medical residents and post-graduate clinical pharmacy students. In the current study area, general practitioners and psychiatric nurses

Table 4. Bivariate and multivariate analysis result for Factors associated with non-adherence among epileptic patient who follow in Dessie town public hospitals Northern Ethiopia, 2018 (n=368)

Variable	Adherence level		COR (95% CI)	aOR (95% CI)
	Non adherence	Adherence		
Sex				
Male	92	116	1.97 (1.27, 3.05)*	2.37 (1.33, 4.23)*
Female	46	114	1.00	1.00
Age (years)				
>41-61	28	62	0.42 (0.29, 0.81)	0.42 (0.31, 0.93)
29-40	54	115	0.44 (0.24, 0.80)	0.47 (0.18, 1.20)
18-28	56	53	1.00	1.00
Marital status				
Single	40	33	2.18 (0.89, 5.37)	1.37 (0.36, 5.20)
Married	61	130	0.85 (0.37, 1.94)	0.70 (0.23, 2.18)
Divorced	27	49	0.99 (0.40, 2.45)	1.93 (0.55, 6.70)
Widowed	10	18	1.00	1.00
Educational level				
Unable to read/write	24	21	7.43 (2.63, 21.02)†	22.30 (5.84, 85.21)†
Primary education	63	70	5.85 (2.32, 14.75)†	5.63 (1.90, 16.69)†
Secondary	45	100	2.93 (1.16, 7.40)*	2.62 (0.88, 7.75)
Diploma & above	6	39	1.00	1.00
Residence				
Rural	48	167	0.20 (0.13, 0.32)*	0.15 (0.08, 0.27)
Urban	90	63	1.00	1.00
Source of medication				
Payment	110	151	2.05 (1.25, 3.38)*	2.06 (1.04, 4.11)*
Free	28	79	1.00	1.00
Time of first seizure occurrence (months)				
1-6	3	18	0.21 (0.06, 0.78)	0.61 (0.03, 12.96)
7-12	25	31	1.03 (0.51, 2.06)	2.30 (0.23, 23.11)
13-24	19	36	0.67 (0.33, 1.38)	1.66 (0.18, 15.72)
25-72	58	103	0.72 (0.41, 1.25)	1.23 (0.36, 4.24)
≥73	33	42	1.00	1.00
Duration of AEDs taken (months)				
3-11	11	25	0.48 (0.19, 1.21)	0.81 (0.05, 13.62)
12-24	34	58	0.64 (0.31, 1.33)	0.58 (0.06, 6.02)
25-60	50	88	0.62 (0.31, 1.24)	0.56 (0.13, 2.44)
61-120	22	36	0.67 (0.30, 1.48)	0.75 (0.24, 2.37)
>121	21	23	1.00	1.00
Drug other than AEDs				
Yes	8	5	2.77 (0.89, 8.64)	1.62 (0.32, 8.14)
No	130	225	1.00	1.00
Adverse effect				
Yes	23	3	15.07 (4.43, 51.23)†	13.68 (3.27, 56.97)†
No	115	226	1.00	1.00
Social support				
Strong	6	8	0.45 (0.16, 1.23)	0.38 (0.10, 1.40)
Moderate	5	18	1.21 (0.41, 3.55)	0.71 (0.18, 2.86)
Poor	127	204	1.00	1.00

Table 4. Continued

Variable	Adherence level		COR (95% CI)	aOR (95% CI)
	Non adherence	Adherence		
Client provider relation				
Good	118	206	0.68 (0.11, 5.45)	0.34 (0.04, 3.17)
Moderate to week	20	24	1.00	1.00

COR, crude odds ratio; CI, confidence interval; aOR, adjusted odds ratio; AED, anti-epileptic drug.
*p-value <0.05.
†p-value <0.001.

provide the service.[4,16]

In this study, patients who were unable to read and write were nearly 22 times more likely to be non-adherent (aOR, 22.30; 95% CI, 5.84-85.21) and patients who had primary education were more than five times non-adherent to the antiepileptic drug (aOR, 5.63; 95% CI, 1.90-16.69) as compared to those who had diploma and above educational level. This finding was supported by other studies done in Yirgalem southern Ethiopia, Nigeria, and Pakistan.[4,24,25] This might be that the different educational level influence the understanding of patients as it is clearly known that illiteracy make patients difficult to understand the disease process and effect of non-adherence, which cause for pharmacological and non-pharmacological treatment failure. They may lack an understanding of the role of therapy, be fearful of dependency on long-term medication, and assume that the need for medication is intermittent and thus stop taking the drug in order to see whether medication is still required.

Epileptic patients who paid for AEDs were nearly two times more likely to be non-adherent as compared to those who were getting their AEDs free of charge (aOR, 2.06; 95% CI, 1.04-4.11). This finding was supported by another study done in Kenya, Southern and Northwest Ethiopia.[15,16,19] The long-term nature of epilepsy treatment and the cost of medications might contribute to this association; buying medications for a long period of time makes the individual feel exhausted about his condition and consequently end up in non-adherence. In this study, male epileptic patients were 2.37 times more likely to be non-adherent to anti-epileptic medication as compared to female patients (aOR, 2.37; 95% CI, 1.33-4.23). This is in line with studies conducted in Brazil.[17] This might be that the variation related to sex could be a reflection of variation in societal role between male and females in northern Ethiopia, typically in the study area as males spend most of their time outside homes doing jobs that need more time and energy, which ultimately cause tiredness and exhausting situations, compared to women, but it also needs further investigations.

The presence of adverse effect was 13.68 times more likely to be non-adherent as compared to their counterpart (aOR, 13.68; 95% CI, 3.27-56.97). The finding of this study was supported by the study done in Malaysia, Debremarkos and Fenote selam.[16,14,26] This may be due to the fact that inadequate counseling and health education about its side effect was given by health care providers. Those patients who had insufficient information about its side effect may tend to stop taking AEDs immediately after the adverse effect occurred.

Research done in St John's Medical College and Hospital, India showed that user of phenytoin was (n=34, 14.1%), followed by valproic acid (n=30, 12.4%). The new AEDs used in AED monotherapy included oxcarbazepine (n=66, 27.4%), levetiracetam (n=53, 22.0%), and topiramate (n=6, 2.5%).[22] The current study showed that carbamazepine (n=20, 5.4%), phenytoin (n=17, 4.6%), phenobarbital (n=271, 73.6%), sodium valproate (n=20, 5.4%), sodium valproate and carbamazepine (n=29, 7.9%), and carbamazepine and phenobarbital (n=3, 0.8%) were the most common prescribed drugs. The difference was due to expensive drug cost and its availability in the study area.

As indicated by this study, age, social support, stigma, duration of epilepsy, number of AEDs, comorbid illness, and patient-provider therapeutic relation were not significantly associated with non-adherence. This is in contrast with studies conducted in Brazil, Malaysia, USA, UK, and Ethiopia.[4,13-17,27] The possible reason for this difference may be due to the differences in methodological approaches and place-to-place differences. Moreover, it could be due to the differences of the study subjects in the current and previous study. Therapeutic advances in recent years have resulted in meaningful changes in the classification, diagnosis and practice of managing epilepsy and non-adherence appears to differ in different countries depending on the available expertise with their level of knowledge, attitude, practice, and health facility resource.

Generally, the prevalence of antiepileptic drug non-adherence among patients with epilepsy was 37.5%. AEDs non-adherence was

significantly associated with variables like sex, educational level, adverse effect, and medication source. All health care providers should give tailored educations and instructions that the importance of sticking with the recommended drug use can improve AEDs adherence to the patients as well as caregivers. Effective interventions for behavioral approaches such as reminders, memory aids, and synchronizing therapeutic activities with routine life events (e.g., taking pills before you shower or after your prayers) used to prevent the complication of epilepsy. Information dissemination to people with epilepsy and the public is important to prevent AEDs no adherence and promote healthy living for those individuals. It needs to provide patient-centered care and show commitment to prevention methods to improve the quality of patient care, and also provide supportive supervision for health facilities that give AEDs to strengthen the service.

Strength of the study

This study has reliable questionnaires. It needs to provide the current base line data for some variable which was not done in Ethiopia before (e.g., client provider therapeutic relation with epileptic patients taking AEDs).

Limitation of the study

Self-reported measure of adherence was used to measure adherence, which could have caused overestimation of adherence. The other limitation of this finding was determining what type of drugs collected or prescribed at the time of recent follow up; it did not include drugs that were switched or withdrawn.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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