Treatment outcome and associated factors among patients with epilepsy

Yirga Legesse Niriayo1, Abraham Mamo1, Tesfaye Dessale Kassa1, Solomon Weldegebreal Asgedom1, Tesfay Mahari Atey1, Kidu Gidey1, Gebre Teklemariam Demoz2 & Seid Ibrahim1

Epilepsy is a major public health problem worldwide. Despite multiple drug therapies, people with epilepsy continue to have frequent seizures. There is a dearth of data on epilepsy treatment outcome and associated factors in our setting. Therefore, the aim of this was to assess treatment outcome and associated factors among epileptic patients on follow up at the neurologic clinic of Ayder comprehensive specialized hospital, Ethiopia. A cross-sectional study was conducted on randomly selected epileptic patients. Data were collected through patient interview and review of medical records. Epilepsy treatment outcome was evaluated in terms of seizure control status in the last one year follow up period. Binary logistic regression analysis was performed to identify predictors of treatment outcome. A total of 270 patients were included. Of whom, 46.6% had controlled seizures. Whereas, 38.5%, 8.8%, and 5.9% had experienced seizure attacks 1–5 times, 6–10 times, and greater than 10 times, respectively. Alcohol consumption [adjusted odds ratio ([AOR]: 14.87, 95% confidence interval (CI): 3.25–68.11], negative medication belief [AOR: 3.0, 95%CI: 1.31–6.71], low medication adherence [AOR:11.52, 95%CI: 3.25–40.82], and presence of comorbidities [AOR: 10.35, 95%CI: 4.40–24.40] were predictors of uncontrolled seizure. Our finding revealed that more than half of the epileptic patients had uncontrolled seizure. Epileptic patients with a negative medication belief, comorbidities, low medication adherence, and those who consume alcohol were more likely to have uncontrolled seizure. Therefore, more emphasis should be given to these patients.

Epilepsy is a chronic neurologic disorder characterized by repeated epileptic seizures attacks which result from paroxysmal uncontrolled discharges of neurons within the central nervous system1–4. The definition of epilepsy requires the occurrence of at least one epileptic seizure3. Epilepsy is a major public health problem that affects more than 50 million people worldwide, of whom, 80% were living in developing countries5–8. African countries are among the highly affected regions and it is estimated that ten million people live with epilepsy in Africa7,8. Likewise, Ethiopia is affected by epilepsy with a reported prevalence of 5.2/1000 population and annual incidence of 64 per 100,000 population9,10.

Antiepileptic Drugs (AEDs) can be indicated for Patients who have had one or more epileptic seizures attacks. The choice of therapy for the management of epilepsy varies depending on the type, frequency, and severity of the seizures4,11. Making an accurate diagnosis of the type of epilepsy is crucial to select the best therapy4,11. Majority of epileptic seizures are controlled with the optimal use of the currently available AEDs. However, about one-third remained uncontrolled despite optimal therapy12,13. Although most of the people with epilepsy can become seizure-free with the optimal use of drug therapy, the treatment outcome in the majority of epileptic patients remains unsatisfactory in resources limited countries8. Studies have shown that majority [80–90%] of the patients with epilepsy are not receiving appropriate treatment in developing countries8,14.

A number of problems affect the provision of adequate treatment of epilepsy and these problems are more pronounced in developing countries. The major problems include; lack of qualified medical personnel, unavailability of medications, poor community knowledge and awareness, cultural beliefs, stigma, poor economy, lack

1Department of Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Tigray, Ethiopia. 2Clinical Pharmacy and Pharmacy Practice Unit, Departments of Pharmacy, College of Health Sciences, Axum University, Axum, Tigray, Ethiopia. Correspondence and requests for materials should be addressed to Y.L.N. (email: yirga.legesse@mu.edu.et)
of prioritization, and poor health system infrastructure. Many studies have shown that inappropriate drug therapy and non-adherence were the leading causes of poor seizure control.

Several factors have been found to be associated with treatment outcome in epilepsy. These include; gender, age of seizure onset, type of epilepsy, seizure frequency, etiology of epilepsy, duration of epilepsy, electroencephalography abnormality and presence of comorbidities. Poorly controlled seizure leads to impairment of quality of life, excessive bodily injury, neuropsychological impairment, social stigma, reduced marriage rates, poor education, reduced employment levels, and finally shortened lifespan.

Assessment of epileptic patient’s treatment outcome and its predictors is crucial to develop treatment optimization strategies and responsible care of patients as clinicians may have difficulty in identifying patients that are less likely to have controlled seizure. Although different studies have been conducted in different parts of the world, there is no adequate data on epilepsy treatment outcome and associated factors in Ethiopia. To our knowledge, there is no study in our particular setting. Hence, our study investigated the treatment outcome and associated factors among epileptic patients.

Methods

Study design, study setting and study period. A hospital-based cross-sectional study was conducted from March 2017 to May 2017 at the neurologic clinic of Ayder comprehensive specialized hospital (ACSH), which is the second largest public hospital in Ethiopia with a catchment population of about 10 million people. The study period was from March 2016 to May 2017.

Study participants. Adult patients (age ≥ 18 years) with the diagnosis of epilepsy who have been on regular follow-up for at least one year with at least one AED were included in the study. Patients were recruited into the study during their appointment for medication refilling. Patients were excluded if they had a follow-up period of less than one year, seriously ill to complete the interview, refused to give consent, and those with incomplete medical records. A total of 270 patients were included in the study using simple random sampling technique.

Data collection instrument and procedure. All consented epileptic patients who visited the hospital during the data collection period and fulfilled the inclusion criteria were included in the study. Data regarding sociodemographic, medication adherence, medication belief and experience were retrieved by interviewing patients using the standardized questionnaire. Respective medical and medication records were retrieved by reviewing patient’s medical record chart using data abstraction checklist. The clinical information of the patients during the last one year follow up period (starting from the date of interview during the data collection period until the last one year) were assessed. All patient were followed for one year to determine their clinical and treatment related characteristics. We trained the data collectors about the objective of the study, methods of data collection including data extraction from patient charts as well as techniques of interviewing patients.

Patients’ belief about their medication was assessed using the belief about medicines questionnaire (BMQ), which has been validated for use in deferent chronic illness group studies. It is a self-reported questionnaire that contains two five-item scales assessing patients’ belief about the necessity of the prescribed medications for controlling their illness and their concerns about the potential adverse consequences of taking it. Accordingly, participants were considered to have strong medication necessity belief if the average sum of the five-item medication necessity scale score (ranging from 5–25) is above the midpoint. Conversely, if the score is below this point they were considered to have low medication necessity belief. Similarly, participants were considered to have strong concern belief about their medication adverse effect if the average sum of the five-item medication concern scale score (ranges from 5–25) is above the midpoint, otherwise, they were considered to have low medication concern belief. The overall patients’ belief about their medication is obtained by subtracting the average 5-item medication concerns scale score from the average sum of 5-item patient’s medication necessity scale score. If the difference is positive, the patient is said to have positive medication belief. Conversely, if it is negative, the patient is said to have negative medication belief.

Medication adherence was assessed using Morisky’s medication adherence scale, which has been validated for use in chronic illness adherence assessment. It is a self-reported questionnaire which contains eight adherence related questions, in which the total score ranges from 0 to 8 points. The degree of adherence was determined according to the score resulting from the sum of all items. Accordingly, medication adherence was considered as low, medium, and high if the total score is <6, 6 to <8, and 8 points, respectively.

Epileptic patients were defined and identified according to the international league against Epilepsy (ILAE).

Accordingly, the definition of epilepsy requires the occurrence of at least one epileptic seizure. Participants who had any chronic disease other than epilepsy were considered to have comorbidity. Epileptic patients were said to have psychiatric disorder comorbidity if they had confirmed diagnosis of psychiatric disorders such as depression, schizophrenia, mood disorders, and anxiety by psychiatrist according to Diagnostic and Statistical Manual of Mental Disorder (DSM-5)35. Treatment outcome was measured in terms of seizure control status and seizure frequency. In order to evaluate epilepsy treatment outcome, seizure status of the patients in the last one-year follow-up period was considered. Every patient was followed for one year to determine the frequency of seizure in the one-year follow-up period. Operationally, the seizure status was considered to be controlled if the patient had not experienced any seizure attacks in the last one year, and not controlled if the patient experienced one or more seizure attacks in the last one year follow up period.

Data analysis. Data were recorded into an EPI data management (version 4.2.0) and analyzed using the Statistical Package for the Social Science (SPSS version 21.0). Descriptive analysis was computed using frequency and mean (standard deviation, SD) for categorical and continuous variables, respectively. The frequency of seizure
control status was determined. Multicollinearity was checked to test correlation among predictor variables using variance inflation factor (VIF) and none was collinear. A VIF < 8 was considered as a cut point for excluding collinearity. Independent variables with p < 0.2 in univariable binary logistic regression analysis were re-entered into a multivariable binary logistic regression model to identify predictors of treatment outcome in epilepsy. A p value of < 0.05 was considered statistically significant in all analyses.

Ethical approval and informed consent. This study was approved by the institutional review board (IRB) of Mekelle University, College of Health Sciences. The aim and protocol of the study were fully explained to all patients included in the study and written informed consent was obtained from all participants. The privacy of individual information was strictly preserved. All the methods were performed in accordance with approved institutional guidelines.

Results
Sociodemographic characteristics of the study participants. A total of 270 epileptic patients were included in this study and analyzed. Of whom, 62% were males and the mean (±SD) age was 30.31 ± 10.95 years. Majorities of the participants were unemployed (73%) and urban dwellers (60%). A large proportion of the participants attended primary and secondary school (30.7% and 51.9%, respectively). With regard to social drug use, 6.3%, 4.1%, and 4.4% of the participants were using alcohol, khat, and cigarette, respectively (Table 1).

Medication belief and adherence status of the participants. Our study reported that majority (70%) of the participants had strong necessity belief towards the importance of their medication while 35% had strong concern belief. Overall, 70% had a positive belief about their medication. More than half (51.5%) of the patients had low adherence to their prescribed medications (Table 2).

| Characteristics          | Number (%)     |
|--------------------------|----------------|
| Gender, male             | 168 (62)       |
| Age in years             |                |
| 18–30                    | 163 (60.4)     |
| 31–60                    | 99 (36.6)      |
| >60                      | 8 (3)          |
| Residence, urban         | 162 (60)       |
| Educational level        |                |
| Illiterate               | 29 (10.7)      |
| Primary education        | 83 (30.7)      |
| Secondary education      | 140 (51.9)     |
| College and above        | 18 (6.7)       |
| Marital status           |                |
| Married                  | 70 (25.9)      |
| Single                   | 162 (60)       |
| Divorced                 | 24 (8.9)       |
| Widowed                  | 14 (5.2)       |
| Employment status        |                |
| Employed                 | 73 (27)        |
| Unemployed               | 197 (73)       |
| Social drug use          |                |
| Abstain                  | 230 (85.2)     |
| Alcohol                  | 17 (6.3)       |
| khat                     | 11 (4.1)       |
| Cigarette                | 12 (4.4)       |
| Monthly income (in Ethio) |              |
| Birr 1 <=1500             | 141 (52.2)     |
| Birr 1 >=1500             | 129 (47.8)     |
| Age at the time of first seizure |          |
| <=15                     | 77 (28.5)      |
| 16–30                    | 108 (40)       |
| 31–45                    | 61 (22.6)      |
| 46–60                    | 21 (7.8)       |
| >60                      | 3 (1.1)        |

Table 1. Socio–demographic characteristics of the participants (n = 270).
| Characteristics                        | Number (%) |
|---------------------------------------|------------|
| Medication necessity belief           |            |
| Strong necessity belief               | 189(70)    |
| Low necessity belief                  | 81(30)     |
| Medication concern belief             |            |
| Strong concern belief                 | 94(35)     |
| Low concern belief                    | 176(65)    |
| Overall medication belief             |            |
| Negative belief                       | 81(30)     |
| positive belief                       | 189(70)    |
| Level of medication adherence         |            |
| High adherence                        | 27(10)     |
| Medium adherence                      | 104(38.5)  |
| Low adherence                         | 139(51.5)  |

Table 2. Medication belief and adherence status of the participants (n = 270)

| Characteristics                        | Number (%) |
|---------------------------------------|------------|
| Presence of comorbidity               |            |
| No                                    | 102(37.8)  |
| Yes                                   | 168(62.2)  |
| Commonly identified co morbidities    |            |
| Psychiatric disorder                  | 55(20.37)  |
| Migraine headache                     | 20(7.4)    |
| Hypertension                          | 15(6)      |
| Human immune deficiency virus (HIV)   | 11(4)      |
| Others                                | 16(6)      |
| Duration of epilepsy in years         |            |
| Mean ± SD                             | 5.42 ± 3.08|
| Median (IQR)                          | 5(3–7)     |
| ≤ 5                                   | 109(40.4)  |
| ≥ 5                                   | 161(59.6)  |
| Type of seizure                       |            |
| GTCS                                  | 220(81.5)  |
| Focal seizure                         | 36(13.3)   |
| Absence seizure                       | 5(1.9)     |
| Unclassified seizure                  | 9(3.3)     |
| Number of AED(s)                      |            |
| One                                   | 131(48.5)  |
| Two                                   | 125(46.3)  |
| Three                                 | 14(5.2)    |
| ADE                                   |            |
| Yes                                   | 117(43.3)  |
| No                                    | 153(56.7)  |

Table 3. Clinical and treatment related characteristics of the participants (n = 270). GTCS, General tonic-clonic seizure, AED, Anti-epileptic drug, ADE, Adverse drug event, SD, standard deviation, IQR, interquartile range.

| Frequency of seizure during the last one year | Number (%) |
|-----------------------------------------------|------------|
| 0                                             | 126(46.6)  |
| 1–5 times                                     | 104(38.5)  |
| 6–10 times                                    | 24(8.8)    |
| >10 times                                     | 16(5.9)    |

Table 4. Distribution of seizure frequency and seizure status of the participants (n = 270).
| Variables                | Treatment outcome | p-value |
|--------------------------|-------------------|---------|
|                         | Controlled seizure, n (%) | Uncontrolled seizure, n (%) | COR (95% CI) |
| Gender, female           | 42(15.5)          | 60(22.2) | 1.43(0.87–2.35) |
| Age category             |                   |         | 0.160 |
| 18–30                    | 70(26)            | 93(34)  | 1 | 1 |
| 31–60                    | 51(19)            | 48(18)  | 0.71(0.43–1.17) |
| >60                      | 5(2)              | 3(1)    | 0.45(0.10–1.95) |
| Age at seizure onset     |                   |         | 0.287 |
| <=15                     | 33(12.2)          | 44(16.3) | 1 | 1 |
| 16–30                    | 50(18.5)          | 58(21.5) | 0.87(0.48–1.57) |
| 31–45                    | 30(11.1)          | 31(11.5) | 0.78(0.40–1.52) |
| >45                      | 13(4.8)           | 11(4.1) | 0.64(0.25–1.59) |
| Residence, urban         | 75(27.8)          | 87(32.2) | 1.04(0.637–1.69) |
| Marital status           |                   |         | 0.881 |
| Married                  | 70(26)            | 92(34)  | 1 | 1 |
| Single                   | 37(13.7)          | 33(12.2) | 1.47(0.84–2.59) |
| Divorce                  | 10(3.7)           | 14(5.2) | 1.57(0.62–4.01) |
| Widowed                  | 9(3.3)            | 5(2)    | 0.62(0.19–2.05) |
| Education                |                   |         | 0.435 |
| Illiterate               | 13(4.8)           | 16(5.9) | 1.54(0.47–5.02) |
| Primary                  | 38(14.1)          | 45(16.7) | 1.48(0.53–4.13) |
| Secondary                | 65(24.1)          | 75(27.8) | 1.44(0.54–3.87) |
| Tertiary                 | 10(3.7%)          | 8(3)    | 1 | 1 |
| Employment status        |                   |         | 1 |
| Unemployed               | 92(34.1)          | 105(38.9) | 0.99(0.58–1.70) |
| Employed                 | 34(12.6)          | 39(14.4) | 1 | 1 |
| Income (in Ethiopian birr)|                   |         | 0.985 |
| <=1500                   | 62(23.0)          | 79(29.3) | 1.26(0.78–2.03) |
| >1500                    | 64(23.7)          | 65(24.1) | 1 | 1 |
| Duration of epilepsy     |                   |         | 0.354 |
| <5 year                  | 48(17.8)          | 61(22.6) | 1.19(0.73–1.95) |
| >=5 year                 | 78(28.9)          | 83(30.7) | 1 | 1 |
| Alcohol use              |                   |         | 0.476 |
| No                       | 123(45.6)         | 130(48.1) | 1 | 1 |
| Yes                      | 3(1)              | 14(5.2) | 4.51(1.26–16.11) |
| Smoking                  |                   |         | 0.020 |
| No                       | 120(44.4)         | 139(51.5) | 1 | 1 |
| Yes                      | 6(2.2)            | 5(2)    | 0.81(0.24–2.71) |
| Khat chewing             |                   |         | 0.726 |
| No                       | 122(45.2)         | 136(50.4) | 1 | 1 |
| Yes                      | 4(1.5)            | 8(3)    | 1.93(0.57–6.59) |
| Medication belief        |                   |         | 0.293 |
| Positive belief          | 104(38.5)         | 85(31.5) | 1 | 1 |
| Negative belief          | 22(8.2)           | 59(21.9) | 3.28(1.86–5.79) |
| Medication adherence     |                   |         | <0.001 |
| High adherence           | 22(8.2)           | 5(2)    | 1 | 1 |
| Medium adherence         | 75(27.8)          | 29(10.7) | 1.70(0.59–4.92) |
| Low adherence            | 29(10.7)          | 110(40.7) | 16.69(5.82–47.87) |
| Co-morbidity             |                   |         | <0.001 |
| No                       | 115(42.6)         | 53(19.6) | 1 | 1 |
| Yes                      | 11(4.1)           | 91(33.7) | 17.950(8.87–36.34) |
| Type of seizure          |                   |         | <0.001 |
| GTCS                     | 101(37.4)         | 119(44.1) | 1 | 1 |
| Focal seizure            | 186(6.7)          | 18(6.7) | 0.85(0.42–1.72) |
| Absence seizure          | 2(0.7)            | 3(1)    | 1.27(0.21–7.76) |
| Unclassified seizure     | 5(1.9)            | 4(1.5)  | 0.68(0.18–2.60) |
| Number of AEDs           |                   |         | 0.572 |
| Continued                |                   |         | 1 | 1 |
Disease and treatment related characteristics. The mean (±SD) duration of epilepsy was 5.42 ± 3.08 years and the median (IQR) was 5(3–7) years with a range from 1 to 20 years. More than half (59.6%) of the participants had lived with epilepsy for five or more years and 37.8% had one or more comorbidities. The most commonly identified comorbidity among epileptic patients was psychiatric disorder (20.4%). Generalized tonic-clonic seizure (GTCS), 84.4% was the most commonly diagnosed type of epilepsy. Nearly half (48.5%) of the study participants were on monotherapy of AEDs. Our finding reported that 43% of the patients complained about adverse drug events (ADEs) related to their medication (Table 3).

| Variables | Treatment outcome | Controlled seizure, n (%) | Uncontrolled seizure, n (%) | COR (95% CI) | p-value |
|-----------|-------------------|---------------------------|-----------------------------|--------------|---------|
| One       | 68(25.2)          | 60(22.2)                  | 1.34(0.80–2.23)             | 0.266        |
| Two       | 50(18.5)          | 59(21.9)                  | 3.54(1.47–8.44)             | 0.004        |
| Three     | 8(3)              | 25(9.3)                   |                             |              |
| ADE       | No                | 73(27)                    | 40(14.8)                    | 1            | 1       |
|           | Yes               | 53(19.6)                  | 104(38.5)                   | 3.58(2.16–5.95) | <0.001 |

Table 5. Univariable logistic regression analysis of factors associated with treatment outcome of epileptic patients (n = 270). COD, Crude odds ratio, CI, Confidence interval, AED, antiepileptic drugs, ADE, adverse drug event, GTCS, Generalized tonic-clonic seizure.

| Predictors | Treatment outcome | Controlled seizure, n (%) | Uncontrolled seizure, n (%) | AOR (95% CI) | p-value |
|------------|-------------------|---------------------------|-----------------------------|--------------|---------|
| Gender, female | 42(16)          | 60(21.9)                  | 1.78(0.87–3.71)             | 0.114        |
| Age category  |               |                           |                             |              |
| 18–30       | 70(26)          | 93(34)                    | 1                           | 1            |
| 31–60       | 51(19)          | 48(18)                    | 0.79(0.22–2.92)             | 0.726        |
| >60         | 5(2)            | 3(1)                      | 0.73(0.05–62.2)             | 0.749        |
| Marital status |               |                           |                             |              |
| Married     | 70(26)          | 92(34)                    | 1.55(0.40–6.08)             | 0.526        |
| Single      | 37(13.7)        | 33(12.2)                  | 1.24(0.31–5.01)             | 0.761        |
| Divorce     | 10(3.7)         | 14(5.2)                   | 0.73(0.05–9.74)             | 0.808        |
| Widowed     | 9(3.3)          | 5(2)                      | 1.55(0.40–6.08)             | 0.526        |
| Alcohol use | No               | 123(45.6)                 | 130(48.1)                   | 1            | 1       |
|            | Yes              | 3(1)                      | 14(5.2)                     | 14.87(3.25–68.1) | <0.001 |
| Medication belief |                |                           |                             |              |
| Positive belief | 104(38.5)     | 85(31.5)                  | 1                           | 1            |
| Negative belief | 22(8.2)        | 59(21.9)                  | 3.00(1.30–6.71)             | 0.009        |
| Medication adherence |            |                           |                             |              |
| High adherence | 22(8.2)        | 5(2)                      | 1                           | 1            |
| Medium adherence | 75(27.8)     | 29(10.7)                  | 2.46(0.70–8.77)             | 0.166        |
| Low adherence  | 29(10.7)        | 110(40.7)                 | 11.52(3.25–40.82)           | <0.001       |
| Comorbidity  | No               | 115(42.6)                 | 53(19.6)                    | 1            | 1       |
|            | Yes              | 11(4.1)                   | 91(33.7)                    | 10.35(4.40–24.40) | <0.001 |
| Number of AEDs |                 |                           |                             |              |
| One         | 68(25.2)        | 60(22.2)                  | 1                           | 1            |
| Two         | 50(18.5)        | 59(21.9)                  | 1.09(0.51–2.32)             | 0.819        |
| Three       | 8(3)            | 25(9.3)                   | 1.84(0.57–5.96)             | 0.310        |
| ADE         | No               | 73(27)                    | 40(14.8)                    | 1            | 1       |
|            | Yes              | 53(19.6)                  | 104(38.5)                   | 2.132(0.891–5.102) | 0.089 |

Table 6. Multivariable logistic regression analysis of factors associated with treatment outcome among epileptic patients (n = 270). AOD, Adjusted odds ratio, CI, Confidence interval, AED, antiepileptic drugs, ADE, adverse drug event.
Seizure frequency and treatment outcome. Out of the total, 46.6% participants had controlled seizure. Whereas, 38.5%, 8.8%, 5.9% had experienced seizure attacks 1–5 times, 6–10 times, and greater than 10 times, respectively (Table 4).

Factors associated with treatment outcome. Using univariable binary logistic regression analysis, epileptic patients with controlled seizure and uncontrolled were compared using the socio-demographic, disease and medication related characteristics. Accordingly, alcohol consumption [Crude odds ratio (COR): 4.51, 95% confidence interval (CI): 1.26–16.11], negative medication belief [COR: 3.28, 95%CI: 1.86–5.79], low medication adherence [COR: 16.69, 95%CI: 5.82–47.87], presence of comorbidities [COR: 3.54, 95%CI: 1.47–8.44], triple AED therapy [COR: 3.54, 95%CI: 1.47–8.44], and ADE [COR: 3.58, 95%CI: 2.16–5.95] were significantly associated with uncontrolled seizure (Table 5).

On further multivariable binary logistic regression model; Alcohol consumption [adjusted odd ratio (AOR): 14.87, 95% CI: 3.25–68.11], negative medication belief [AOR: 3.0, 95%CI: 1.31–6.71], low medication adherence [AOR: 11.52, 95%CI:3.25–40.82], and presence of comorbidities [AOR: 10.346, 95%CI: 4.387–24.399] were found to be predictors of uncontrolled seizure (Table 6).

Discussion
Currently, therapeutic advances have resulted in meaningful changes in the diagnosis and management of epilepsy30. However, the practice of epilepsy management is inconsistent in different countries depending on the available expertise and resource1. Although evidence has shown that a greater proportion of epileptic patients become seizure free with the optimal use of the available AEDs31–34, less than half of the patients remain seizure free in our study. This could be attributed to the lack of qualified medical personnel, unavailability of medications, poor community knowledge and awareness, and poor health system infrastructure in our setting where resources are limited. Our finding is also quite different from a study done in Gonder, Ethiopia31 in which 82% of the epileptic patients achieve seizure remission over 3 months follow-up period. This variation could be due to the difference in follow-up period (3 months vs. 12 months). In line with our study, the majority of the patients had uncontrolled seizure in other similar studies32–34.

Several studies revealed that alcohol consumption is a risk factor for developing seizure and it increased the risk of seizure in epileptic patients35–38. Similarly, alcohol was found to be a predictor of uncontrolled seizure in our study. This could be explained that alcohol consumption could lead to sleep deprivation, missing meals, missing medications and increase the side effect of AED which were reported as triggering factors of seizure14,35–38. Hence, much should be done on awareness of alcohol use of epileptic patients.

Our finding reported that low medication adherence was significantly associated with uncontrolled seizure. In agreement to our study, many studies have shown that non-adherence to medication was the leading cause poor epilepsy control14,17,18,31,32,38. In addition, our study revealed that patients with a negative medication belief were less likely to have seizure free period compared to those with a positive medication belief. The possible justification for this could be patients with a negative medication belief are less likely to adhere to their medications as revealed by our study and other similar studies14,31,32. Hence, educational programs should be designed to improve the perception of patients about their medication as well as their medication adherence. Our study also reported that epileptic patients with comorbidity were less likely to have controlled seizure than those without comorbidities which is in line other similar studies41–43. Thus, more emphasis should be given to these patients.

Patients with a triple AED therapy and those who experienced ADEs were less likely to have seizure-free period though statistically not significant on the multivariable regression model. Even though evidence-based guidelines recommend the use of monotherapy for the majority of epileptic patients31,44, only 48.5% were maintained on monotherapy in our study. Overall, utilization of monotherapy was found to be low compared to other similar studies14,46,47. This could be due to the absence of specific epilepsy treatment guideline and lack of expertise of healthcare professionals in our setup. Our study reported that 43% of the patients had experienced ADE related to their AED therapy. This finding is higher compared to the studies conducted in Gonder (17.6%) and Jimma (33.4%); Ethiopia31,48. This could be attributed to the higher use of multiple AED therapy in our setting.

Finally, our study is not without limitations. The cross-sectional nature of the study may not provide adequate evidence of causality regarding seizure control status and its predictors. Due to self-report concerns, patients may understate socially undesirable activities like medication non-adherence and negative medication belief.

Conclusion
Our findings revealed that more than half of the epileptic patients have uncontrolled seizure. Epileptic patients with a negative medication belief, comorbidities, low medication adherence and those who consume alcohol were more likely to have uncontrolled seizure. Therefore, particular consideration should be given to these potentially modifiable risk factors. Educational programs about the importance of their medication, adherence, and precipitating factors such as alcohol should be given. Moreover, we recommend researchers to do further longitudinal and interventional studies with more strong study design to provide adequate evidence about the cause-effect relationship between the predictor variables and seizure control.

Data Availability
The dataset of this article is accessible on reasonable request from the corresponding author.

References
1. Falco-Walter, J., Scheffer, I. & Fisher, R. The new definition and classification of seizures and epilepsy. Epilepsy Research 139, 73–79 (2018).
2. Fisher, R. et al. ILAE Official Report: A practical clinical definition of epilepsy. Epilepsia 55, 475–482 (2014).
3. Fisher, R. et al. Epileptic Seizures and Epilepsy: Definitions Proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 46, 470–472 (2005).
4. Nunes, V., Sawyer, L., Neilson, J., Sarri, G. & Cross, J. Diagnosis and management of the epilepsies in adults and children: summary of updated NICE guidance. *BMJ* 344, e281–e281 (2012).
5. Singh, A. & Trevick, S. The Epidemiology of Global Epilepsy. *Neurologic Clinics* 34, 837–847 (2016).
6. De Boer, H., Mala, M. & Sander, J. The global burden and stigma of epilepsy. *Epilepsy & Behavior* 12, 540–546 (2008).
7. Prilipko, L. Atlas epilepsy care in the world 2005. (World Health Organization, 2005).
8. WHO. Epilepsy in The Who African Region: Bridging the Gap. (World Health Organization, 2004).
9. Tzekl- Haimanot, R. et al. Attitudes of rural people in central Ethiopia toward epilepsy. *Social Science & Medicine* 32, 203–209 (1991).
10. Tzekl- Haimanot, R. et al. Community-Based Study of Neuropsychological Disorders in Rural Central Ethiopia. *Neuroepidemiology* 9, 263–277 (1990).
11. Wilson, S. J. et al. Indications and expectations for neuropsychological assessment in routine epilepsy care: Report of the ILAE Neuropsychology Task Force, Diagnostic Methods Commission, 2013–2017. *Epilepsia* 56, 674–81 (2015).
12. Sillanpää, M. & Schmidt, D. Long-term outcome of medically treated epilepsy. *Seizure* 44, 211–6 (2017).
13. Kwan, P., Schachter, S. C. & Brodie, M. J. Drug-Resistant Epilepsy. *N. Engl. J. Med.* 369, 919–26 (2011).
14. Tefera, G. M., Woldehaimanot, T. E. & Angamo, M. T. Poor treatment outcomes and associated factors among epileptic patients at Ambo Hospital, Ethiopia. *Gaziantep Medical Journal* 21, 9–16 (2015).
15. Dua, T., De Boer, H. M., Prilipko, L. L. & Saxena, S. Epilepsy care in the world: Results of an ILAE/IBE/WHO Global Campaign Against Epilepsy survey. *Epilepsy* 47, 1225–31 (2006).
16. Scott, R. A., Lhatoo, S. D. & Sander, J. W. The treatment of epilepsy in developing countries: Where do we go from here? *World Heal. Organ. Bull. World Heal. Organ.* 79, 344–51 (2001).
17. Jones, R. M., Butler, J. A., Thomas, V. A., Peveler, R. C. & Prettew, M. Adherence to treatment in patients with epilepsy: Associations with seizure control and illness beliefs. *Seizure* 15, 504–8 (2006).
18. Mubua, C. K., Ngugi, A. K., Newton, C. R. & Carter, J. A. The treatment gap in developing countries: A systematic review of the magnitude, causes, and intervention strategies. *Epilepsia* 49, 1491–503 (2008).
19. Hovinga, C. A. et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. *Epilepsy Behav* 13, 316–327 (2008).
20. Shen, C. et al. Factors predictive of late remission in a cohort of Chinese patients with newly diagnosed epilepsy. *Seizure* 37, 20–4 (2016).
21. Mohanraj, R. & Brodie, M. J. Early predictors of outcome in newly diagnosed epilepsy. *Seizure* 22, 333–44 (2013).
22. So, E. L. Predictors of outcome in newly diagnosed epilepsy: Clinical, EEG and MRI. *Neurol. Asia* 16, 27–9 (2011).
23. Sperling, M. R. The Consequences of Uncontrolled Epilepsy. *Epilepsia Spec. Issue* 9, 98–109 (2004).
24. Laxer, K. D.
25. Fanta, T., Azale, T., Assefa, D. & Getachew, M. Prevalence and factors associated with perceived stigma among patients with epilepsy in Ethiopia. *Psychiatry journal* 201, 1–7 (2015).
26. Horne, R., Weinman, J. & Hankins, M. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol. Health* 14, 1–24 (1999).
27. Mostafavi, F., Najimi, A., Shariifgard, F. & Golshiri, P. Beliefs About Medicines in Patients with Hypertension: the Instrument Validity and Reliability in Iran. *Mater. Socio. Medica* 28, 298 (2016).
28. Morrisky, D. E., Green, L. W. & Levine, D. M. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med. Care* 24, 67–74 (1986).
29. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub (2013).
30. Manford, M. Recent advances in epilepsy. *J. Neurol.* 264, 1811–24 (2017).
31. Birru, E. M., Shafi, M. & Getia, M. Drug therapy of epileptic seizures among adult epileptic outpatients of University of Gondar Referral and Teaching Hospital, Gondar, North West Ethiopia. *Neuropsychiatric disease and treatment* 12, 3213 (2016).
32. Pinzona., R., Harsono & Rusdi, I. D. Number of pre–treatment seizure as prognostic factor of convulsive epilepsy in childhood and young adult onset. *Universa Medicina* 25, 105–13 (2006).
33. Ipingbemi, A. E. Management, treatment outcome and cost of epilepsy in a tertiary health care facility in northern Nigeria. *Internet Journal of Medical Update-EJOURNAL* 10, 25–36 (2015).
34. Hassio, T. T. & Desse, T. A. Adherence to treatment and factors affecting adherence of epileptic patients at Yirgalem General Hospital, Southern Ethiopia: A prospective cross-sectional study. *PLoS One* 11, e0163040 (2016).
35. Preci, G. & Viyska, G. Alcohol Abuse and Seizures: Overview of Clinical Notions and Pathogenetic Theories. *International Journal of Clinical and Experimental Neurology* 2, 4–7 (2014).
36. Samokhvalov, A. V., Irving, H., Mohapatra, S. & Rehm, J. Alcohol consumption, unprovoked seizures, and epilepsy: a systematic review and meta-analysis. *Epilepsia* 51, 1177–84 (2010).
37. Zhao, Y. H. & Zhao, W. L. Alcohol and Epilepsy. *Medical Recapitulate* 47, 805 (2011).
38. Rathlev, N. K., Ulrich, A. S., Delanty, N. & D’Onofrio, G. Alcohol–related seizures. *J Emerg Med* 31, 157–63 (2006).
39. Nakhutina, L., Gonzalez, J. S., Margolis, S. A., Spada, A. & Grant, A. Adherence to antiepileptic drugs and beliefs about medication among predominantly ethnic minority patients with epilepsy. *Epilepsy Behav.* 22, 584–6 (2011).
40. Eigenassi, C., Steinberg, W. J. & Rauenheimer, J. E. Beliefs about medication, medication adherence and seizure control among adult epilepsy patients in Kimberley, South Africa. *South Africans Neurol. Pract.* 57, 23–32 (2015).
41. Hitiris, N., Mohanraj, R., Norrie, J., Sills, G. J. & Brodie, M. J. Predictors of pharmacoresistant epilepsy. *Epilepsy Res.* 75, 192–6 (2007).
42. Seidenberg, M., Pulsipher, D. T. & Hermann, B. Association of epilepsy and comorbid conditions. *Future Neurol.* 4, 663–8 (2009).
43. Devinsky, O. Psychiatric comorbidity in patients with epilepsy: implications for diagnosis and treatment. *Epilepsy Behav.* 4, 2–10 (2003).
44. Sethi, N. K. et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology* 85, 1525–6 (2015).
45. Glauser, T. et al. ILAE treatment guidelines: evidence-based analysis of antiepileptic drug efficacy and effectiveness as initial monotherapy for epilepsy seizures and syndromes. *Epilepsia* 47, 1994–200 (2006).
46. Morgan, C. L., Buchan, S. & Kerr, M. P. The outcome of initiation of antiepileptic drug monotherapy in primary care: A UK database survey. *Br J Gen Pract* 54, 781–3 (2004).
47. Hsieh., L. P. & Huang, C. Y. Antiepileptic drug utilization in Taiwan: analysis of prescription using National Health Insurance database. *Epilepsie research* 84, 21–27 (2009).
48. Gurskaya, M., Agala, A. & Chanoe, T. Anti-epileptic drug utilization and treatment outcome among epileptic patients on follow-up in a resource poor setting. *Journal of Young Pharmacists* 6, 47–52 (2014).
Acknowledgements
We would like to acknowledge the data collectors and hospital staffs for their pleasurable cooperation. Our gratitude extended to the epileptic patients for their eager involvement in the study.

Author Contributions
Y.L., A.M. and S.I. conceptualized and designed the study, wrote the original manuscript, performed analysis and interpretation of data, T.D., S.W., T.M., K.G. and G.T. assisted in the study design, data analysis and manuscript evaluation. All authors have made intellectual contribution to the work and have approved the final version of the manuscript for submission.

Additional Information
Competing Interests: The authors declare no competing interests.

Publisher's note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.