Treatment outcome and associated factors among epileptic patients at ambulatory clinic of Mettu Karl Comprehensive Specialized Hospital: A cross-sectional study

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Abstract

Objective: The study was aimed to assess the magnitude and associated factors of 2-year seizure-free status of epileptic patients at Mettu Karl Comprehensive Specialized Hospital (MKCSH).

Methods: A retrospective cross-sectional study was conducted at MKCSH from 12 February 2020 to 11 August 2020. Treatment outcome was measured in terms of seizure control status and seizure frequency. Accordingly, good treatment outcome was declared if the patients had a 2-year seizure-free status and poor if the patient had episodes of seizure in the last 2 years. The pharmaceutical care network Europe guideline was used to assess the presence of medication-related problems. Multivariable logistic regression was used to analyze the variables by using crude odds ratio (COR) and adjusted odds ratio (AOR) with 95% confidence interval (CI). Finally, the predictors of epilepsy treatment outcome were declared if a P-value was ≤0.05.

Results: Over the study period, more than half of the participants (172 (57.7%)) were males. The median age of participants was 29 and majorly distributed to 18–30 classes. More than one-fourth of the patients were suffering from absent seizure 85 (28.5%) and general tonic-clonic seizure 83 (27.9%). The most commonly prescribed medication was Phenobarbitone which accounts 34 (11.41%), whereas Valproic acid 8 (2.68%) was the least prescribed. Overall, less than half 131 (43.96%) of patients developed poor treatment outcomes. The predictors of treatment outcomes were having head the injury (AOR = 5.7; 95% CI: 3.18, 10.31), family history of epilepsy (AOR = 5.6; 95% CI: 3.07, 10.46) and the presence of drug therapy problems (AOR = 5.2; 95% CI: 2.79, 9.69).

Conclusion: The magnitude of poor epilepsy treatment outcome was found to be high. The predictors of epilepsy treatment outcome were the history of head injury, family history of epilepsy and drug therapy problems. Therefore, to improve the treatment outcome of epileptic patients, health care providers should pay close attention to the identified factors. Besides this, the clinical pharmacy service should be implemented to minimize any medication-related problems

Keywords

Associated factors, treatment outcome, epilepsy, MKCSH, Ethiopia

Introduction

Epilepsy is a chronic neurologic disorder characterized by unprovoked frequent seizure attacks which occurred due to excessive discharge of neurons within the central nervous system.[1,2] Globally, about 65 million patients had epilepsy, of whom more than three-fourths of them were in lower resource countries like Ethiopia.[3–5] It is the second leading cause of neurological disability, morbidity and neurological complications.[6]

The mortality rate of epileptic patients was two to three times higher as compared with the general healthy populations. Among a variety of factors associated with poor treatment outcomes of epileptic patients, lack of adequate health care professionals and equipment, non-availability of

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medications, inadequate drug information, low family income and the presence of comorbidity were the most frequently reported.[5,7,8]

Although advancements in the pharmacotherapy of epilepsy, seizure was not fully controlled in about one-third of epileptic patients receiving adequate drug therapy.[1,8] Despite the majority of antiepileptic drugs (AEDs) could treat the different types of seizure types in epileptic patients, the occurrences of medication-related problems could result in poor treatment outcome for epileptic patients.[4]

Nowadays, different adverse drug reactions (ADRs) developed secondary to the use of antiepileptic drugs (AEDs) result in increased hospitalization, change of therapy and unmet goal of therapy. These adverse effects include idiosyncratic reactions, respiratory depression and different neurocognitive effects.[6]

Generally, uncontrolled epilepsy treatment outcome might result in decreasing quality of life, disability, neuropsychological pathology, social stigma, impairment of cognition and mortality.[1,4]

In Ethiopia, the lack of acceptance of patients on modern antiepileptic drugs was highly influenced by their beliefs and cultures as they perceive epilepsy was treated by the traditional healers and spiritual holy water which may push them to not take the medications.[9]

Treatment outcome is affected by several factors including drug-related factors, disease-related factors and patient-related factors. Drug-related factors include pharmacokinetics of the drugs, drug–drug interactions and toxicity, among others. Similarly, irrational prescribing concerning drug selection and inappropriate doses will result in poor treatment outcomes.[4] Besides this, various studies revealed that having different treatment protocols, inaccurate epilepsy diagnosis, inappropriate health care providers, lack of modern diagnostic technology, delay in seeking health care and lack of knowledge were the identified factors in the treatment outcome of epilepsy in developing countries.[10] It is estimated that, about 81% of people with epilepsy suffers from perceived epilepsy stigma, which has a direct influence on treatment options.[11]

Despite epilepsy being a crucial public health problem, there are scanty studies on the treatment outcomes of epilepsy in Ethiopia in general, and no study conducted in our study area. Therefore, this study was designed to determine the magnitude and predictors of treatment outcomes of epilepsy attending at the ambulatory clinic of MKCSH.

Methods

Study area, design and period

A retrospective cross-sectional study was conducted at Mettu Karl Comprehensive Specialized Hospital (MKCSH) from 12 February 2020 to 11 August 2020. MKCSH is found in Mettu town, South West Oromia, Ethiopia which is found 600 km from Finfinne. The hospital has one chronic care follow-up clinic.

Study participants and eligibility criteria

Adult patients (age ⩾ 18 years) with the diagnosis of epilepsy who have been on regular follow-up for at least 2 years 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 2 years, were seriously ill to complete the interview, refused to give consent, and were those with incomplete medical records.

Study variables and outcome endpoints

Epilepsy treatment outcome was a primary outcome. Treatment outcome was measured in terms of seizure control status and seizure frequency. To evaluate epilepsy treatment outcome, the seizure status of the patients in the last 2-year follow-up period was considered. Accordingly, good treatment outcome was declared if the patients had a 2-year seizure-free status and poor if the patient had episodes of seizure in the last 2 years.[3] The Chalfont seizure severity scale was used to assess the seizure status.[12] Hill-Bone Compliance to Therapy Scale was used to measure the adherence level,[13] and ADR was assessed using the Naranjo et al.[14] algorithm of the ADR probability scale. The pharmaceutical care network Europe guideline was used to assess the presence of medication-related problems.

Sample size and sampling technique

The single population proportion formula was used to calculate the required sample size by considering the proportion of epilepsy treatment outcome P = 0.608,[3] which gives the initial sample size of 366. The final sample size becomes 277 after considering the source population of 1040. Up on addition for 10% contingency, it becomes 298. A simple random sampling was used to include study participants.

Data collection process and management

A semi-structured data collection tool was prepared to collect the data and the relevant information about each patient (demographic data and patients' clinical characteristics including seizure-related injury) was collected using an interviewer-administered questionnaire.[1,3–5,8,13,14] To assure the consistency of the data the 5% of the interviewer-administered questionnaire was pretested at the nearby hospital called Bedele General Hospital before actual data collection. The episodes of seizure-related injury were assessed since the diagnosis of epilepsy. Laboratory results, current medications, comorbidities and relevant previous medical and medication histories were collected using a data abstraction format from a medical chart review. Three medical doctors and two clinical pharmacists were recruited for data collection; one clinical pharmacist was assigned to supervise the data collection process.

Statistical analysis

The data were entered into a computer using EPI-data version 3.1. The principal investigators had daily checked and cleaned the data. The data were then exported to statistical software for social sciences (SPSS) 24.0 for analysis. Multivariable logistic regression was used to analyze the variable by using crude odds ratio (COR) and adjusted odds ratio (AOR) with 95% confidence interval (CI). All variables associated with the epilepsy treatment outcome at a P-value ≤0.25 on the bivariate analysis were entered into a multivariable logistic regression analysis to control for confounders. Finally, the predictors of epilepsy treatment outcome were declared if a P-value was ≤0.05.

Ethical approval and consent-to-participate

Ethical approval was obtained from the Research Ethics Review Committee (RERC) of Mettu University with reference no CHS/RERC/89/2020. The study protocol was performed following the Declaration of Helsinki. Permission was given by the administrators and medical directors of MKCSH to conduct the study. The pros and cons of the study were explained to the patients who participated in the study, and written informed consent was obtained from patients. The name of patients and prescribers were not written on the tool to ensure confidentiality.

Operational definitions

Treatment outcome: It is to mean whether the seizure is controlled or uncontrolled.

Good controlled: If the patients had a 2-year seizure-free status.[3]

Poorly controlled: If they experienced one or more seizure episodes in the last 2 years.[3]

Result

Socio-demographic characteristics of participants

Over the study period, more than half of the participants 172 (57.7%) were males. About two-thirds of the male patients 100 (33.56%) have good outcome as compared with female (P = 0.26). The median age of participants was 29 years and majorly distributed to the age of 18–30 years class. The majority 235 (78.9%) of participants were single and of which 135 (45.30%) had a good treatment outcome (P = 0.64). Regarding their educational status, about one-fourth 80 (26.85%) of them who attend a high school had a good treatment outcome (P = 0.29) (Table 1).

Table1. Socio-demographic characteristics epileptic patients at ambulatory clinic of MKCSH.

Variables	Category	Treatment outcome		Total	P-value
		Good	Poor		
Sex	Male	100 (33.56%)	72 (24.16%)	172 (57.7%)	0.26
	Female	76 (25.50%)	50 (16.78%)	126 (42.3%)	
Age	18–30 years	70 (23.49%)	97 (32.55%)	167 (56.0%)	0.34
	30–60 years	56 (18.79%)	55 (18.46%)	111 (37.2%)	0.52
	>60 years	12 (4.01%)	8 (2.68%)	20 (6.7%)	0.47
Resident	Urban	59 (19.79%)	66 (22.15%)	125 (41.9%)	0.56
	Rural	100 (33.56%)	73 (24.49%)	173 (58.1%)	
Marital status	Married	15 (5.03%)	16 (5.37%)	31 (10.4%)	0.27
	Single	135 (45.30%)	100 (33.56%)	235 (78.9%)	0.64
	Divorced	7 (2.35%)	3 (1.0%)	20 (6.7%)	0.61
	Widowed	4 (1.34%)	8 (2.68%)	12 (4%)	0.50
Level of education	Uneducated	10 (3.36%)	12 (4.03%)	22 (7.4%)	0.48
	Elementary	45 (15.1%)	53 (17.79%)	98 (32.9%)	
	High school	80 (26.85%)	59 (19.79%)	139 (46.6%)	
	Diploma	10 (3.36%)	9 (3.02%)	19 (6.4%)	
	Degree	5 (1.68%)	15 (5.03%)	20 (6.7%)	
Occupation	Farmer/housewife	43 (14.43%)	44 (14.77%)	77 (25.8%)	0.32
	Trader	19 (6.38%)	22 (7.38%)	41 (13.8%)	0.31
	Government employee	20 (6.71%)	10 (3.36%)	30 (10.1%)	0.54
	Student	45 (15.10%)	55 (18.46%)	100 (33.6%)	0.27
	Labor worker	20 (6.71%)	20 (6.71%)	40 (13.4%)	0.50
	Other	4 (1.34%)	6 (2.01%)	10 (3.4%)	0.69
Monthly income (Ethiopian Birr)	Less than 500	90 (30.20%)	33 (11.07%)	123 (41.3%)	0.37
	500–1000	45 (15.10%)	30 (10.07%)	75 (25.2%)	0.46
	Greater than 1000	46 (15.44%)	54 (18.12%)	100 (33.6%)	0.33

Table 2. Clinical characteristics of epileptic patients at ambulatory clinic of MKCSH.

Variables	Category	Treatment outcome		Total	P-value
		Good	Poor		
Age at onset	<30 years	100 (33.55%)	149 (50.0%)	249 (83.6%)	0.45
	30–40 years	14 (4.7%)	26 (8.72%)	40 (13.4%)	0.52
	≥45 years	2 (0.67%)	7 (2.35%)	9 (3%)	0.28
Frequency of seizure	<3	60 (20.13%)	100 (33.56%)	160 (53.7%)	0.09
	>4	70 (23.49%)	68 (22.82%)	138 (46.3%)	
Duration of epilepsy	<3 years	110 (36.91%)	112 (37.58%)	222 (74.5%)	0.33
	3–5 years	4 (1.34 %)	6 (2.01%)	10 (3.4%)	0.41
	>10 years	25 (8.39 %)	31 (10.40%)	66 (22.1%)	0.48
Length of hospital stay	≤5 years	34 (11.41 %)	48 (16.11%)	82 (27.5%)	0.31
	6–10 years	43 (14.43 %)	43 (14.43%)	86 (28.9%)	0.28
	>10 years	50 (16.78%)	80 (26.85%)	130 (43.6%)	0.64
History of head injury	Yes	70 (23.49 %)	99 (33.22%)	169 (56.7%)	0.003
	No	45 (15.10 %)	84 (28.19%)	129 (43.3%)	
Type of seizure	General tonic-clonic	33 (11.07 %)	50 (16.78%)	83 (27.9%)	0.26
	Focal	43 (14.43 %)	32 (10.74%)	75 (25.17%)	0.47
	Absence seizure	40 (13.42 %)	45 (15.10%)	85 (28.5%)	0.53
	Unclassified	23 (7.72%)	32 (10.74%)	55 (18.46%)	0.42
Family history	Yes	40 (13.42 %)	64 (21.48%)	104 (34.9%)	0.01
	No	96 (32.21%)	98 (32.89%)	194 (65.1%)	
Comorbidity	Yes	43 (14.43%)	49 (16.44%)	92 (30.9%)	0.07
	No	130 (43.62%)	76 (25.50 %)	206 (60.1%)	

Clinical characteristics of the epileptic patients

The treatment outcome was poor in the half of patients 149 (50.0%) who had the onset of seizure of less than 30 years (P=0.45). The most type of seizure was generalized tonic-clonic (GTC) which accounts 83 (27.9%). Among this, a total of 50 (16.78%) were from patients having a poor outcomes as compared with good outcome accounts 33 (11.07%) (P=0.26). The treatment outcome was poor in 99 (33.22%) of the patients who had a history of head injury (P=0.003). About one-fifth 64 (21.48%) of the patients who have a family history of epilepsy had poor treatment outcome (P=0.01) and 49 (16.44%) of the patients who have a comorbidity had a poor treatment outcome (P=0.07) (Table 2).

Medication characteristics of epileptic patients

The most commonly prescribed medication was Phenobarbitone which accounts 34 (11.41%). Among them, 20 (6.71%) were prescribed for patients having a good treatment outcome as compared with poor outcome 14 (4.70%)) (P=0.36). Valproic acid was the least prescribed that accounts 8 (2.68%). Poly-pharmacy was reported among 70 (23.5%) epileptic patients. Drug-related problems were found in 164 (55.0%) participants (Table 3).

Prevalence and types of DRPs

The prevalence of actual or potential DTPs among subjects put on at least a single drug was found to be 164 (55.0%).

A total of 323 DRPs were identified on average, 1.084 DRPs per patient. The three leading categories of drug-related problems found to be a culprit among the sample were needs additional drug therapy 72 (22.29%), dose too low 52 (16.09%) and dose to high 50 (15.48%) (Table 4).

The treatment outcome of patients

Among epileptic patients, the treatment outcome was good in 167 (56.04%) of the patients, and less than half (131 (43.96%)) of patients developed poor treatment outcomes in which their seizure was not controlled despite antiepileptic drugs.

Factors associated with treatment outcome of epileptic patients

The results of the bivariate analysis revealed that frequency of seizure, history of head injury, comorbidity, drug therapy problem and family history of epilepsy were shown associated with treatment outcome. In the multivariate analysis, variables including the history of head injury, drug therapy problem and family history of epilepsy kept their association after controlling confounders. Patients who had head injury were 5.7 times more likely to have poor treatment outcomes when compared with patients who had no history of head injury (AOR=5.7; 95% CI: 3.18, 10.31). The probability of poor treatment outcome was 5.6 times higher among patients who have a family history of epilepsy than their counterparts

Table 3. Commonly prescribed medications among epileptic patients at ambulatory clinic of MKCSH.

Drugs given	Treatment outcome		Total	P-value
	Good	Poor		
Phenytoin + Insulin	4 (1.34%)	5 (1.68%)	9 (3%)	0.26
Phenobarbitone + Chlorpromazine	5 (1.68%)	5 (1.68%)	10 (3.4%)	0.29
Carbamazepine + Phenytoin	4 (1.34%)	12 (4.03%)	12 (4.0%)	0.51
Phenobarbitone + Amitriptyline	8 (2.68%)	12 (4.03%)	20 (6.7%)	0.58
Phenobarbitone	20 (6.71%)	14 (4.70%)	34 (11.41%)	0.36
Phenytoin	15 (5.03%)	16 (5.37%)	31 (10.4%)	0.62
Phenobarbitone + Valproic acid	10 (3.36%)	12 (4.03%)	22 (7.4%)	0.50
Phenytoin + Phenobarbitone	11 (3.69%)	11 (3.69%)	21 (7.05%)	0.49
Phenobarbitone + Nifedipine	13 (4.36%)	19 (6.38%)	32 (10.74%)	0.52
Valproic acid	3 (1.0%)	5 (1.68%)	8 (2.68%)	0.58
Aspirin + Phenobarbitone	4 (1.34%)	6 (2.01%)	10 (3.4%)	0.28
Loratadine + Valproic acid + Chlorpromazine	10 (3.36%)	12 (4.03%)	22 (7.4%)	0.32
Phenobarbitone + Carbamazepine	8 (2.68%)	4 (1.34%)	12 (4.02%)	0.31
Phenytoin + Valproic acid	10 (3.36%)	14 (5.0%)	24 (8.36%)	0.55
Phenobarbitone + Amitriptyline	14 (5.0%)	17 (5.70%)	31 (10.7%)	0.41

Table 4. Types of drug therapy problems of the patients admitted to medical ward of MKCSH.

Types of drug therapy problems	Frequency (n)	Percentage (%)
Ineffective drug therapy	42	13.00%
Non-adherence	48	14.86%
Dose too high	50	15.48%
Needs additional drug therapy	72	22.29%
Dose too low	52	16.09%
Unnecessary drug therapy	49	15.17%
ADR	10	3.09%

ADR: adverse drug reaction.

(AOR = 5.6; 95% CI: 3.07, 10.46). Moreover, patients who had drug therapy problems were 5.2 times more likely to develop poor treatment outcome compared with patients who had no therapy problems (AOR = 5.2; 95% CI: 2.79, 9.69) (Table 5).

Discussion

This institution-based retrospective study assessed epilepsy treatment outcomes and its associated factors among ambulatory patients. Accordingly, 44% of patients developed poor treatment outcomes (37.9%–49.7% CI). This finding is lower than a findings from the United Kingdom, Aydel Hospital and Mizan-Tepi University Teaching Hospital where 57%, 53.4% and 60.8% of patients had poor treatment outcomes, respectively.[1,3,15] This dissimilarity may be related to the gap in the study period and the difference in study design. The recent finding is congruent with the previous studies conducted in Qatar, the Amhara region, Ambo Hospital and Jimma University Specialized Hospital (JUSH) where 46%, 44 %, 44.7% and 43.3% of patients had poor treatment outcomes, respectively.[5,8,16,17] The recent finding is higher than the cross-sectional studies conducted in the United States and Scotland where 8% and 36.3% of patients had poorly controlled seizures.[18,19] Similarly, it is higher than a study conducted in Tikur Anbessa Specialized Hospital (TASH) in which 34.4% of patients developed uncontrolled seizures.[4] The possible reason for this discrepancy could be due to differences in study design and socio-demographic variation in the two populations.

Evidence has shown an association between head injury and treatment outcome[11,19]; likewise, in our study patients who had a history of head injury were 5.7 times more likely to develop poor treatment outcomes when compared with their counterparts. Also, this association is consistent with a study conducted at Mizan-Tepi University Teaching Hospital.[3]

In this study, the odds of poor treatment outcome was 5.6 times higher among patients who had a family history of epilepsy compared with their counterparts. This finding is consistent with a findings from Scotland and Qatar.[17,19]

Table 5. Multivariable logistic regression analysis results of factors associated with epilepsy treatment outcome among epileptic patients at chronic care follow-up of MKCSH.

Variables	Categories	Treatment outcome		COR (95 % CI)	AOR (95 % CI)	P-value
		Good	Poor			
Frequency of seizure	<3	100 (33.56%)	60 (20.13%)	1	1	0.086
	>4	67 (22.48%)	71 (23.83%)	1.77 (0.91, 2.2.81)	1.40 (0.89, 4.01)	
History of head injury	Yes	67 (22.48%)	102 (34.23%)	5.3 (3.14, 8.79)	5.7 (3.18, 10.31)	0.012
Comorbidity	Yes	33 (11.07%)	59 (19.80%)	3.3 (1.99, 5.56)	2.66 (0.78, 6.09)	0.157
Drug therapy problem	Yes	75 (25.17%)	89 (29.87%)	2.6 (1.61, 4.19)	5.2 (2.79, 9.69)	<0.001
Family history	Yes	35 (11.74%)	69 (23.15%)	4.2 (2.53, 6.96)	5.6 (3.07, 10.46)	0.04

AOR: adjusted odds ratio; CI: confidence interval; COR: crudes odds ratio.

Epileptic patients who have drug therapy problems was 5.2 times more likely to develop poor treatment outcomes as compared with those who had no drug therapy problems. This finding was not supported by the literature. The possible reason for this association may be the fact any problem in therapy come up with poor treatment outcome and non-adherence.

In our study, the most type of seizure was generalized tonic-clonic (GTC) which accounts 83 (27.9%). Among this, a total of 50 (16.78%) were from patients having poor outcomes as compared with good outcome accounts 33 (11.07 %). This was consistent with the study of Saudi Arabia[20] and Mizan-Tepi University Teaching Hospital, Southwest Ethiopia.[3] The reason for this might be patients having a generalized tonic-clonic (GTC) seizure may present with violent body movements and often prominent autonomic changes. As a result, the health care seeking in those populations is higher than other types of seizures.

Phenobarbitone was the most commonly administered AED 34 (11.41%). Among them, 20 (6.71%) were prescribed for patients having a good treatment outcome as compared with poor outcome 14 (4.70%). This is consistent with the study of the University of Gondar Teaching Hospital.[21] On the contrary, Valproic acid was commonly prescribed in Saudi Arabia.[19] This might be due to the physicians' preferences and availability of the drugs. As limitation, the study was a single center and a retrospective study and the causal effect relationship were not determined.

Conclusion

The magnitude of poor epilepsy treatment outcome was found to be high. Factors like the history of head injury, family history of epilepsy, and drug therapy problems were shown significant association with treatment outcome. Therefore, to improve the treatment outcome of epileptic patients, health care providers, as well as local, regional and national governments, should pay close attention to the identified factors. Besides this, the clinical pharmacy service should be implemented to minimize any medication-related problems.

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Supplemental material

Supplemental material for this article is available online.

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