

Antiepileptic Drug Adherence and Associated Factors Among Adult Epileptic Patients Attending Neurology Referral Clinic in Adama Hospital Medical College, Ethiopia

Tadesse Seda

Department of Neurology, Adama Hospital Medical College, Adama, Ethiopia

Email address:

tadeseda2@yahoo.com

To cite this article:

Tadesse Seda. Antiepileptic Drug Adherence and Associated Factors Among Adult Epileptic Patients Attending Neurology Referral Clinic in Adama Hospital Medical College, Ethiopia. *Clinical Neurology and Neuroscience*. Vol. 3, No. 4, 2019, pp. 93-99.

doi: 10.11648/j.cnn.20190304.15

Received: October 26, 2019; **Accepted:** November 28, 2019; **Published:** December 11, 2019

Abstract: Background- Adherence to anti epileptic medication therapies is a primary determinant of treatment success. Non-adherence to the treatment attenuates most clinical benefits and therefore reduces the overall effectiveness of health systems. However, to our knowledge there is study conducted to what extent epileptic patients adhere to their treatment and factors which affects adherence. Hence, this study aimed to assess antiepileptic drug adherence and factors associated with it among Adult Epileptic Patients Attending Neurology Referral Clinic in Adama Hospital Medical College. Methods- We conducted a cross-sectional hospital based study on epileptic patients who are on antiepileptic medications from April 10 to July 10, 2019. Data were collected from patient above 18 years old. Adherence was measured using the four-item Morisky's medication adherence scale. All consecutive patients coming to Neurology referral clinic during the study period were interviewed until the calculated sample size (322) was obtained. We collected patient demographics, clinical related, questions related to drug intake and adherence. Both Bivariate and multivariate analyses were performed to test for associations. Odds ratio was used to assess strength of association, and level of association determined by p. value <0.05%. Result- out of a total of 340 participants, 322 were willing to participate. Of the 194 participants, 109 (56.2%) were males. The mean age of the participants was 32.10 ± 7.37 years; range 18-56 years. The majority, 61.4% of the participants were taking a single antiepileptic drug. Over all 67.3% (95% CI: 62.9%, 71.9%) of the participants were adherent to their treatment. The most common reported reasons for non-adherence were financial or cost of drugs 39.01 followed by distance 38.5%. Factors which have significant association with adherence to antiepileptic treatment were: being female (AOR=2.04, 95% CI=1.07, 3.87), respondents in primary education (AOR= 2.74, 95% CI= 1.01, 7.46), married (AOR= 3.65, 95% CI= 1.34, 9.89) cost of drug 500 to 999 birr (AOR= 2.59, 95% CI= 1.03, 6.45) and one thousand and more (AOR= 5.14, 95% CI= 2.49, 10.61). Conclusion: Only 67.2% of the respondents were adhered to their treatment which is low when compared with more than 95% standard adherence may be necessary to adequately suppress the epileptic seizures.

Keywords: Epilepsy, Adherence to Anti Epileptic Drugs (AED), Adama Hospital Medical College (AHMC)

1. Introduction

Epilepsy is a neurological condition, which affects the nervous system. Epilepsy is also known as a seizure disorder [1]. It is usually diagnosed after a person has had at least two seizures that were not caused by some known medical condition like alcohol withdrawal, extremely low blood sugar, heart problems or some other medical condition [2]. The global burden of epilepsy is estimated to be 1% [3]

affecting over 65 million people [4]. It has profound physical, psychological and social impacts with a greater impact on a person's quality of life than other chronic diseases [5]. Epileptic patients may also have lower quality of life due to enormous social stigmas [6]. Epilepsy is a major public health problem in low and middle-income countries (LMICs) imposing a large economic burden on the health care system [3]. World Health Organization (WHO) in 2005 reported that 80% epileptic patients lived in developing

countries [3, 7].

Despite a high prevalence of epilepsy in LMICs, most people do not receive appropriate treatment. This is due to limited knowledge, poverty, cultural beliefs, stigma, poor health delivery infrastructure, and shortage of trained health care workers [8]. Many Africans believe epilepsy is contagious. As a result of this, they are unwilling to help or touch the person who has fallen during seizure. This kind of belief worsens the stigma [3, 9]. The principle of epilepsy management should be individualized and the selection of treatments should aim to control symptoms as well as to prevent other complications. There are a number of drugs available for treatment of epilepsy in modern therapy [10].

More than 30% of people with epilepsy do not attain full seizure control even with the best available treatment regimen. Failure to have a controlled seizure in such significant proportion of epileptic patients is attributed to poor adherence to medication(s) [11]. Medication non-adherence to antiepileptic medications is detrimental to the perceived outcome of treatment. Non-adherence to medication regimen accounts for substantial worsening of disease, death and increased health care costs [12, 13].

Adherence refers to how patient treatment related behaviors correspond to health professionals' advice. It portrays greater patient involvement in treatment as well as a mutual arrangement of cooperation and agreement between the health provider and the patient [8]. Rates of adherence to antiepileptic drugs are variable in different studies ranging between 20-80%. The adherence rate varies depending on population being studied and method being used, with self report being reported to overestimate adherence [9, 14]. Failure to adhere through forgetfulness, misunderstanding, or uncertainty about clinician's recommendations, or intentionally due to their own expectations of treatment, side-effects, and lifestyle choice are found to be the reasons for non-adherence [15].

Studies investigating factors affecting adherence rate have produced different associated factors. Knowledge of AED and frequency of seizures [16], duration of illness [11, 14], side effects of the drugs [14, 17], uncontrolled seizures and increasing treatment complexity [11, 18] were factors affecting adherence rate of epileptic patients. Although medication adherence and factors associated with it have been extensively studied in the world, very little is known in Ethiopia particularly, in this study area. Therefore, this study will try to assess the rate of medication adherence and associated factors among epileptic patients on follow-up at AHMC.

2. Methods and Materials

2.1. Study Area

The study will be conducted in AHMC. AHMC is located in Central Ethiopia, Oromia regional state, in Adama town, 99 Km from Capital city of Ethiopia, Addis Ababa. Currently the catchment population of AHMC is about 5 million and

serving as referral hospital for the nearby hospitals and the adjacent regions. AHMC provide all types of care (OPD and Admission) to the patients including referral for chronic diseases like hypertension. There are more than 12500 epileptic patients registered and on follow up in AHMC.

2.2. Study Design and Period

2.2.1. Study Period

This research was conducted from April 10 to July 10, 2019.

2.2.2. Study Design

A hospital based cross sectional study design was used among epileptic patients in AHMC.

2.3. Source and Study Population

2.3.1. Source Population

All adult patients registered and on follow up for anti-epileptic treatment in AHMC.

2.3.2. Study Population

All adult patients registered and on follow up for anti-epileptic treatment in AHMC and fulfilling inclusion criteria were included in the study.

Inclusion criteria:-

Patients who met the following criteria were invited to participate in this study: Aged 18 years or older; A diagnosis of epilepsy clinically confirmed by a physician; Patients on antiepileptic medication at least for 3 months before the study period; Patients who can give consent to participate and without acute emergency symptoms during attendance in the clinic.

2.4. Sample Size Determination and Sampling Technique

2.4.1. Sample Size Determination

The sample size calculation was done using single population proportion formula with the following assumption: a 50% prevalence of epileptic patients' adherence, since there is no similar research conducted in the study area, a 5% precision, 95% level of confidence and 10% non-response rate. Samples of 422 patients were required for this study.

2.4.2. Sampling Techniques

Epileptic patients who came for treatment and volunteer to participate were included in the study.

2.5. Study Variables

2.5.1. Dependent Variable

Antiepileptic treatment adherence

2.5.2. Independent Variables

Demographic variables (age, sex, educational qualification, monthly income, marital status, occupation, place of residence, source of medication)

Patient characteristics (type and number of prescribed AEDs, duration of treatment, AEDs, dosage, drug

availability, cost) and Types of seizure.

2.6. Operational Definitions

Medication adherence- is measured by the Morisky Medication Adherence Scale (MMAS-4) and in our study, patients were considered adherent if they scored 0 and patients were considered poor-adherent if they scored 1 or more.

2.7. Data Collection Tool and Procedure

An interviewer administered questionnaire was used for data collection. A questionnaire was prepared in English and translated into Amharic/Oromifa languages and back translated into English to check its consistency by different persons. The one in Amharic/Oromifa was pre-tested on 20 epileptic patients in AHMC before the start of the actual data collection. Patients involved in pretest were excluded in the actual study. Based on the findings and some minor modification were made. Questionnaire contain: data related to socio-demographic information, clinical related questions, questions related to drug intake and questions related to adherence to antiepileptic medication which measured using an four item Morisky Medication Adherence Scale (MMAS). Data were collected by 3 trained nurses who had data collection experiences.

Adherence to medication

Medication adherence was measured using validated four-item self-reported Morisky Medication Adherence Scale (MMAS-4) [19] with a response choices of “Yes” or “No” for items 1 through 3 and item 4 has a four-point Likert response scale. Each “No” response rated as 1 and each “Yes” response rated as 0. In our study, patients were considered adherent if they scored 0.

2.8. Data Quality Assurance

To ensure the quality of data, one day training was given for data collectors. Before starting to collect data, pre-test and translation of questioner was done. Frequent follow-up were made by the principal investigator to check questionnaire for completeness and accuracy.

2.9. Data Processing and Analysis

Data analysis was made by STATA 12. Descriptive statistics of the collected data was done for most variables in the study using standard statistical parameters: percentages, means and standard deviations. Bivariate and multivariate analyses were performed to test for associations. Variables having p value ≤ 0.25 in the bivariate analyses were entered into a multiple variate analysis. Odds ratio was used to assess strength of association and level of association was determined by p value $< 0.05\%$.

2.10. Ethical Considerations

This study was approved by AHMC Ethical Review Board. Then written letter was submitted to AHMC medical

director and clinic head and permission was obtained. After explaining the objective of the study verbal consent was obtained from each participant

3. Result

3.1. Socio-demographic Characteristics

A total of 342 epileptic patients who fulfill the inclusion criteria were interviewed from Adama Hospital Medical College. Majority of the patients 55.8% were males, 50.0% were aged between 28 to 37 years with the mean (SD) age of 32.10 ± 7.37 years with the age range from 18-56 years. More than three fourth of the patients, 84.8% were rural dwellers, 52.9% were Muslim by religion, 59.4% had no formal education, 59.1% were single, 69.0% Oromo by ethnicity and 59.4% were farmers by occupation (Table 1). NB. * in religion- Wakefata.

Table 1. Socio-demographic characteristics of epileptic patients at Adama Hospital Medical College, 2019.

Variable	Frequency	%
Sex		
Female	151	44.2
Male	191	55.8
Age		
18-27	89	26
28-37	171	50
38-47	72	21.1
48-57	10	2.9
Religion		
Orthodox	80	23.4
Muslim	181	52.9
Protestant	59	17.2
Catholic	11	3.2
Others *	11	3.2
Address		
Urban	52	15.2
Rural	290	84.8
Education		
No formal education	203	59.4
Primary	79	23.1
Secondary	32	9.4
Diploma & above	28	8.2
Marital status		
Single	202	59.1
Married	140	40.9
Ethnicity		
Oromo	236	69.0
Amhara	84	24.6
Gurage	22	6.4
Occupation		
Gov't employed	29	8.5
Farmer	203	59.4
Self employed	68	19.9
Student	31	9.1
House wife	11	3.2

3.2. Concerning Health and Drug Related Variables

The majority 88.9% of the respondents visit the hospital every three months for treatment, 94.7% reported follow the appointment regularly, 64.9% reported having generalized seizure; however, 94.4% of them reported seizure occurred every month and 75.7% had a history of epilepsy for more than a year. Concerning antiepileptic drugs 61.4% of them took only one drug, 40.6% took once per day only 9.1% had history of side effects and the most commonly reported side effect was drowsiness (67.7%). About 70% of the respondents reported un-availability of drugs and 67.8% pay more than 1000.00 birr for treatment every month.

Table 2. Health and drug related condition of epileptic patients in Adama Hospital Medical College, 2019.

Variable	Frequency	%
Frequency of visit		
Every month	11	3.2
Every two months	27	7.9
Every three months	304	88.9
Follow regularly		
No	18	5.3
Yes	324	94.7
Type of seizure		
Generalized	222	64.9
Focal	111	32.5
Unclassified	9	2.6
Type of drugs taken		
Phenytoin	155	45.3
Phenobarbitone	142	41.5
Both	45	13.2
Number of drugs		
Only one	210	61.4
Two	95	27.8
Three	37	10.8
Duration of treatment		
<6 months	4	1.2
6 months to < a year	79	23.1
A year or more	259	75.7
Dosage		
Once	139	40.6
BID	129	37.7
TID	74	21.6
Any side effect		
No	311	90.9
Yes	31	9.1
Drug availability		
No	239	69.9
Yes	103	30.1
Estimated Cost of the drugs		
<500 birr	68	19.9
500 to 1000 birr	41	12.0
>1500 birr	233	68.1

3.3. Adherence Related Variables

Concerning adherence variables only 1.5% of respondents reported sometimes forgot taking their medicines, none of them stopped taking or decrease the dose without telling their doctor, 43.0% stated stop taking their medication when they feel their condition is under control, 1.5% of them reported sometimes have difficulty of remembering to take their medications and 32.7% of them reported stop taking their

medication without notifying their Doctors. Most commonly reported reason (39.01%) for stopping their treatment was due to financial issue followed by distance of the hospital 38.5%.

Table 3. Adherence related variables of epileptic patients in Adama Hospital Medical College, 2019.

Variable	Frequency	%
Sometimes forget to take		
Yes	5	1.5
No	337	98.5
Stop taking or decrease dose		
Yes	0	0.0
No	442	100.0
Ever Stop taking feel control		
Yes	147	43.0
No	195	53.0
How often have difficulty		
Almost never	337	98.5
Sometimes	5	1.5
Stop taking without notifying Drs.		
Yes	112	32.7
No	230	67.3
Reason for stop taking drugs		
Financial issue	71	39.01
Unavailability	36	19.8
Distance	70	38.5
Any others	4	0.02

Overall, 67.3% (95% CI: 62.9%, 71.9%) of patients are adherent to anti epileptic Medications (figure 1).

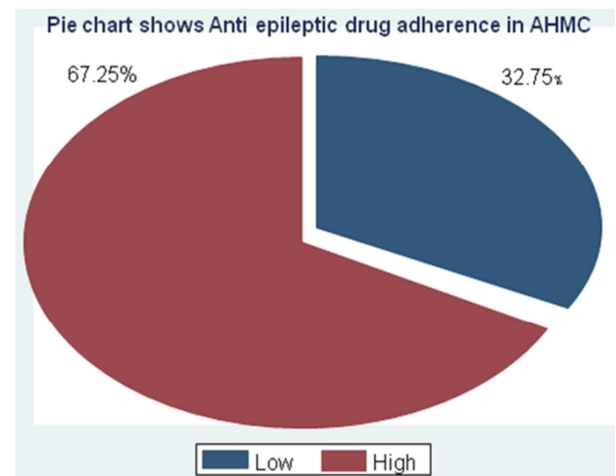


Figure 1. Pie chart shows anti epileptic drugs adherence in Adama Hospital Medical College, 2019.

3.4. Factors Associated with Anti Epileptic Drug Adherence

In bivariate analysis Sex, place of residence, age, Educational status, marital status, occupation, Frequency of visit, type of drugs taken, treatment frequency, and the cost of drugs had a significant association with treatment adherence at a P. value of 0.25.

After controlling possible confounding effects of other covariates four factors remained as significantly independent predictors of AED treatment adherence in multiple logistic regression adjustment: Sex, Educational status, Marital status

and cost of drugs (Table 4).

Female respondents were two times more likely to be adherent than their male counterparts (AOR=2.04, 95% CI=1.07, 3.87). With regard to educational status, respondents in primary education were 2.7 times more likely to adhere to their treatment compared with who had no formal education (AOR= 2.74, 95% CI= 1.01, 7.46). Married

respondents were 3.6 times more likely to be adherent than those who were single (AOR= 3.65, 95% CI= 1.34, 9.89). Respondents who pay 500 to 999 birr (AOR= 2.59, 95% CI= 1.03, 6.45) and one thousand and more (AOR= 5.14, 95% CI= 2.49, 10.61) per month to buy drugs were found to be adherent compared with who reported less than 500 birr to buy drugs (table 4).

Table 4. Factors affecting anti epileptic medications adherence in Adama Hospital Medical College, 2019.

Variable	Adherence		COR (95%CI)	AOR (95%CI)	P. Value
	High	Low			
Sex					
Female	120	31	2.85 (1.75, 6.44)	2.04 (1.07, 3.87)	0.029
Male	110	81	0	0	
Address					
Urban	25	26	0	0	0.594
Rural	87	204	2.25 (0.23, 4.12)	1.45 (0.37, 5.77)	
Educational status					
No formal education	79	124	0	0	0.047
Primary	9	70	4.95 (2.34, 10.48)	2.74 (1.01, 7.46)	
Secondary	10	22	1.40 (0.63, 3.12)	1.25 (0.24, 6.43)	0.793
Diploma & above	14	14	0.63 (0.29, 1.41)	0.92 (0.13, 6.41)	0.940
Age					
18-27	19	70	0	0	0.771
28-37	48	123	0.69 (0.38, 1.28)	1.15 (0.43, 3.08)	
38-47	37	35	0.26 (0.13, 0.51)	0.54 (0.18, 1.66)	0.285
48-57	8	2	0.07 (0.01, 0.35)	0.22 (0.03, 1.49)	0.122
Marital status					
Single	94	108	0	0	0.011
Married	18	122	5.89 (3.35, 10.39)	3.65 (1.34, 9.89)	
Occupation					
Gov't employed	9	20	0	0	0.735
Farmer	72	131	0.82 (0.35, 1.89)	0.76 (0.15, 3.79)	
Self employed	13	55	1.90 (0.71, 2.07)	0.76 (0.19, 3.07)	0.705
Student	12	19	0.71 (0.24, 2.07)	0.20 (0.03, 1.28)	0.092
House wife	6	5	0.38 (0.09, 1.56)	1.13 (0.13, 9.94)	0.909
Frequency of visit					
Every month	8	9	0	0	0.114
Every two months	12	35	3.33 (0.72, 15.37)	4.50 (0.69, 29.04)	
Every three months	92	212	6.14 (1.59, 23.68)	2.76 (0.51, 14.88)	0.236
Type of drugs taken					
Phenytoin	48	107	0	0	0.072
Phenobarbitone Both	37	105	1.27 (0.77, 2.11)	1.81 (0.94, 3.45)	
Dosage / frequency					
Once	27	18	0.29 (0.15, 0.59)	0.59 (0.25, 1.41)	0.246
BID	36	103	0	0	0.265
TID	53	76	0.50 (0.29, 0.84)	0.67 (0.33, 1.36)	
Cost of drugs					
<500 birr	23	51	0.78 (0.42, 1.44)	0.92 (0.41, 2.04)	0.836
500 to 999 birr	45	23	0	0	0.041
1000 to 1500 birr	21	20	1.86 (0.84, 4.11)	2.59 (1.03, 6.45)	
	46	187	7.95 (4.37, 14.45)	5.14 (2.49, 10.61)	0.0001

4. Discussion

A series of conceptual reconsiderations and therapeutic advances in recent years has resulted in meaningful changes in the classification, diagnosis, and treatment of epilepsy. However, the practice of managing epilepsy appears to differ in different countries depending on the available expertise, resources and selecting types of AED. Drug Adherence is a primary determinant factor for treatment success. Non-adherence to medications is widely recognized as a major public health concern, and contributes to patient morbidity,

mortality and healthcare costs [20]. In this regard this study tried to identify the magnitude and most important factors which affects epileptic patients to adherence to their AED Medications in AHMC.

The rate of adherence to AEDs in this study comparable with a community-based study done in rural background of India (71.1%) [21], However, it is lower than the study done in Brazil 66.2% [18], and USA (71%) [22]. The study reported in a recent hospital-based study from Riyadh, SA, by Gabr and Shams [23], Palestine (85.3%) [11] and India (98.6%) [24] and Bangalore, India (72.3%) [25]. But, higher than that of Jimma, Ethiopia (58.5%) [13], Yirgalem (32%)

[26], China (51.9%) [14] and Saudi Arabia (62.7%) [23].

The probable reason for these discrepancies could be due to the differences in the methodology and sample size used for assessing adherence rate. It could also be due to cultural behaviors of participants and good or poor control of seizure, availability and cost of the drugs. People living in different countries have difference in their cultures and social values and hence can have variation in their behavior towards epilepsy and treatment. In the most of countries, medication adherence is a growing concern to clinicians, healthcare providers' health sectors and other stakeholders. Such concern is due to the mounting evidence that non-adherence is prevalent and it is associated with adverse outcomes and higher costs of the care [27]. These findings emphasize that the importance of raising awareness and promoting knowledge about the importance of AED adherence and behavior changes towards epilepsy.

The findings of this research revealed married patients had a higher level of adherence as compared to unmarried patients. This finding similar with a study conducted in Yirgalem hospital [26]. This may be, married patients are supported and remaindered by their partners in taking the prescribed medication(s).

The effect of gender is one an important contributing factor affecting medication adherence. Similar to other studies women were more likely to adherent to AEDs as compared to men [18, 28, 29]. This may be explained, since females are always serious to matters related to health and more curious than men and adhere to their treatment. Another explanation could be, male patients are more conscious about the stigmatization and concerned with outside activities and mayn't want to take their medications in front of others.

It is believed that as educational level increases, patients are more awareness about the disease and the importance of adherence to their medications. Some studies showed that lower education level in general and illiteracy has negative impacts to medication adherence [25]. A study conducted by Elise AG. D. et al. [30] showed that higher level of educations were associated with positively illness representation. Our study supports that the respondents who completed primary school had more to adherence to AEDs medications. A potential reason may be, educated patients are more skeptical towards the use of their medication. Therefore, Ministry of health, Health Bureaus at different level, in the public sectors should ensure the availability of the AED for long durations in the public sector. Health care providers have to work jointly to increase awareness on treatment adherence. Health education to improve literacy and community promotion on behavior changes towards epilepsy are import.

The monthly cost of medication in private sectors (p-value: 0.00036) were found to be significantly associated with non-adherence [26]. This is consistent with a Chinese study which found that inability and cost of the drugs have significantly influenced adherence [14]. However, in our study patients spend more than 500 birr per month to buy drugs were more adherent to their medication as compared to those who spent less than 500 birr. Generally people in Ethiopia believe that

drugs with high cost have more quality. So, patients who pay more believe that the drug is more effective and can control their epilepsy. It could also be due to unmeasured effects of other variables. Therefore, the health care providers should work on increasing patient's awareness to avoid this perception and behaviors.

5. Conclusion and Recommendation

5.1. Conclusion

The finding of this study on AED adherence is low when compared with more than 95% standard adherence to adequately suppress seizure recurrence. This means, missing one or more doses of AED regimen per week is enough to cause treatment failure and trigger seizures [31]. The finding of this research showed, being female gender, educational status, marital status and low cost of the AED had a significant association with good treatment adherence.

5.2. Recommendation

Therefore, we recommend Federal Ministry Health Regional health Bureau and hospitals should work jointly to make available and affordable antiepileptic drugs. Training is required for Health professionals in prescribing and selecting AED, and devising strategies to improve medication adherence. There should be adherence counselling and health educational interventions at health care providing areas to improve drug adherence among patients taking AED.

Acknowledgements

My great thanks go Daniel G/Tsadik for his continuous support and constructive comments throughout the study. Grateful thanks to the Staffs working in Neurology Referral Clinic for data collection and study participants for their cooperation in the success of this work. Finally great thanks to my wife, Sr. Shasho Negassa for generating new ideas, continuous support and encouragement.

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