

Non adherence to treatment and the associated factors in patients with epilepsy in Southern Ethiopia

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Abstract

Adherence to antiepileptic drug therapy in people with epilepsy is critical for seizure control. Poor adherence to epilepsy treatment, on the other hand, is recognized as a worldwide problem, particularly in developing countries such as Ethiopia. As a result, the current study seeks to ascertain patients' adherence to antiepileptic medications and the factors that influence it at Hawassa University Comprehensive Specialized Hospital in Southern Ethiopia. From February 1 to October 15, 2017, 187 people with epilepsy who were on follow-up at Hawassa University Comprehensive Specialized Hospital underwent a hospital-based retrospective medical review. Adherence was measured using Morisky Medication Scale-8. Data was entered and analyzed using the soft ware Statistical package for social sciences version 20. The results were summarized using cross-tabulations and frequency tables. While binary logistic regression was used to analyze factors associated with adherence to antiepileptic drug therapy, significance was declared at $p < 0.05$. According to the findings of the current study, about nineteen percent of the study participants were non-adherent to their treatment. Compared to patients with monthly income of less than 1000.00 ETB, those who earn > 3000.00 ETB [AOR=0.164, 95% CI (0.038: 0.702)] and those with monthly income between 2000 and 3000 ETB [AOR=0.110, 95%CI (0.026:0.461)] [AOR=0.110, 95% CI (0.026:0.461)] are less likely associated with non-adherent to antiepileptic drugs ($P < 0.05$). Likewise, patients who perceived

epilepsy as psychiatric disorder [AOR=0.250, 95%CI (0.087: 0.716)] compared to those who perceive it as neurologic, and those patients with seizure free period of less than one year [AOR= 0.206, 95%CI(0.076:0.562)] compared to those with seizure free period of more than one year are found to be less non adherent ($p < 0.05$).

Introduction

Epilepsy, one of the most common neurological diseases worldwide, is a chronic brain disorder that affects people of all ages. It affects approximately 50 million people worldwide, with approximately 80% of those affected living in low- and middle-income countries.¹

Adherence to antiepileptic drug therapy is necessary for effective seizure control and for ensuring that changes in patients treatment outcomes can be attributed to the recommended regimen.²

Medication non-adherence continues to be a major source of concern for both health care providers and patients due to the negative effects it has on therapeutic outcomes.³ Poor adherence to Antiepileptic Drug (AED) therapy has been reported to be as low as 20% and as high as 80%,⁴ which is associated with poor epilepsy control, with a reported prevalence of 21-45%.⁵

In patients with uncontrolled seizures due to poor adherence to AEDs, non-adherence to medication regimen accounts for significant worsening of disease, death, increased health-care costs, and impaired productivity (e.g. missing school and work).⁶ Because of the limited health-care system in developing countries, the magnitude and impact of poor adherence are expected to be greater than in industrialized countries.² Even with the best available treatment regimen, more than 30% of People With Epilepsy (PWE) do not achieve complete seizure control. The failure of such a large proportion of PWE to have controlled seizures is attributed to poor adherence to medication(s).⁷

While non-adherence is a problem with many determinants, there is a scarcity of literature on the subject in Ethiopia in general and Hawassa Comprehensive Specialized Hospital (HCSH) in particular. As a result, the purpose of this study is to examine non-adherence to treatment and the factors that contribute to it in patients with epilepsy at HCSH in southern Ethiopia.

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Ethics approval and consent to participate: The study was approved by the Institutional Review Board (IRB) of the College of Medicine and Health Sciences of Hawassa University. Written informed consent was obtained from participants of the study after the objective of the study has been explained to them. Additionally, each of the respondents were assured about the confidentiality of the information they provided as well as their right to withdraw at any time during participation.

Informed consent: Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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Materials and Methods

Study area and period

This study was conducted in Hawassa University Comprehensive Specialized Hospital of Hawassa at Southern Ethiopia,

from February 01, to October 15, 2017 using a cross-sectional study design. Data was explored from a retrospective patient chart review. The sample size was determined using a single population proportion formula with a 95% confidence interval as follows:

$$n = (z\alpha/2)^2 pq / d^2$$

where n = sample size

Z $\alpha/2$ = 1.96 (Z $\alpha/2$ is the 95% confidence interval)

P = estimated prevalence, 30% (taking the non-adherence rate from the study conducted in Amanuel Specialized Mental Hospital.⁸

q = 1-p and d = margin of error (5%)

Substituting all values the calculated sample size was resulted to be 322.

However, the total number of PWE having follow up at HUCSH was small (estimated from registration log-book is 400), finite population correction formula⁹ was used to calculate the exact sample size (nf) as follows:

$$nf = n*N/n+N-1$$

where nf = adjusted estimated sample size

N = population size

Substituting the values, the calculated sample size is 178. With consideration of 10% non-response rate, the final sample size was set to be 195. Systematic random sampling method, set to be every other patient, was used to recruit the samples for the study in each day of the data collection process.

The Validated 8-item, MMAS-8, a self reporting tool was used to assess the patient's adherence level to AED therapy in this study. The MMAS-8 is a generic self-reported, medication-taking behavior scale, validated for hypertension but used for a wide variety of medical conditions, which is the latest version of the scale, with a good internal consistency.¹⁰ It consists of eight items focusing on past medication use patterns. A higher score indicates high level of self-reported adherence. Adherence level is to be categorized as high (Score: 8), medium (Score: 6 and 7) and low (Score: <6). But for ease of analysis in the current study it was categorized in to non adherence (low score) and adherence (medium and higher score).

A data abstraction form was prepared to extract pertinent information from patients' chart. The form contained information on diagnosis, prescribed drugs, years of follow up and treatment, age at first seizure,

seizure free period, adverse effects, and seizure control pattern.

The questionnaire was pretested using 5% of the sample size by the investigators and necessary modifications were done. The collected data were crosschecked by the investigators and supervisors.

Data was collected by trained nurses who trained for two days on how to collect the necessary data from charts. The collected data were checked for completeness, cleaned prior to data entry and then entered using Epi Info™ version 3.1. Data analysis was carried out using Statistical Package for Social Sciences program version 20.

Descriptive statistics like frequency and percentage were used to summarize characteristics and related information of the variables. The Cross-tabular form of descriptive statistics was carried out to relate each variable to non-adherence and seizure control as a univariate. A Chi-square (χ^2) test was

used to see the significance of association of categorical variables to non-adherence.

From the univariate analysis, the variables with a p-value of <0.20 were considered as candidate for further analysis using multi-variable binary logistic regression method so that to assess the predictability of the independent variables of non-adherence. An estimate of Odds Ratios (OR) with the corresponding 95% Confidence Intervals (CI) was used to determine the significant factors. and p-values. The association was declared significant at p<0.05.

Ethical clearance was approved by the Institutional Review Board (IRB) of the College of Medicine and Health Sciences of Hawassa University. A letter of support was asked from chief clinical director of HUCSH. Data was collected after permission was asked from the study subjects following a brief discussion with the people with epilepsy about the purpose and impor-

Table 1. Scio-demographic characteristics of PWE having follow- up at HUCSH, February 01-October 15, 2017.

Variables	Number	%	
Age in years	15-24	63	34
	25-34	71	38
	35-44	31	16
	45-60	17	9
	>60	5	2.5
Sex	Male	98	52
	Female	89	48
Marital Status	Single	96	51
	Married	87	47
	divorced	2	1
	Widowed	2	1
Place of residence	Rural	45	24
	Urban	142	76
Educational Status	No formal education	14	8
	Primary	51	27
	Secondary	62	32
	Tertiary	60	32
Occupation	Student	44	24
	Goernment Employed	43	23
	Merchant	27	14
	Farmer	19	10
	House wife	18	10
	Day laborer	31	20
Ethnicity	Sidama	82	44
	Amhara	25	13
	Oromo	28	15
	wolayta	24	13
	Guraghe	13	7
	Others	15	8
Religion	Protestant	105	56
	Orthodox	60	32
	Muslim	20	11
	Others	2	1
Monthly income in ETB	1000-1999	44	23.5
	2000-2999	41	22
	>3000	42	22.5
	Unknown	15	8

tance of the study and was collected from those who were willing to participate.

Operational definition and definition of terms

Adherence to antiepileptic drugs: The extent to which the patient follows medication instructions. For this study; Adherent: MMAS-8 score of ≥ 6 , Non-adherent: MMAS-8 score of < 6

Controlled seizure: Seizure free for ≥ 1 year.

Results

Socio-demographic characteristics of the participants

Of the sought total sample size 187 epileptic patients card medical record was reviewed (96% response rate). Of all participants, 98(52%) were male. The majority (38%) of them was in the age group between 25-34 years of age. Fifty one percent of the participants reported to be unmarried; comparable with those who got married (47%). The urban dwellers comprised the large proportion (76%). The educational background of majority of the study participants was found to be secondary and tertiary schools, 32% for both. The majority of them reported to be students; with comparable proportion of those who responded to be employed, 24 and 23% respectively. Financially, majority of them reported a monthly income of < 1000 and $1000-1999$, in ETBs accounting for 24% and 22% respectively (Table 1).

Clinical characteristics of the study subjects

According to the current analysis, in 90 patients (58%) the onset of the first epileptic seizure occurred between the age of 16 to 30. The majority of them (57.5%) had > 5 years of follow up duration at HUCSH. Duration of illness (epilepsy) was > 10 years for 42% of them. The highest proportion of them (56%) had seizure free period of less than one year. In this study, non-adherence level by MMAS-8 was found to 35 (18.5%) as detailed in Table 2.

Patterns of antiepileptic drugs use

On the bases of therapy with AED, monotherapy was found to be the most frequently prescribed treatment modality (84%), with Phenobarbitone being prescribed for the majority of the participants (59%), followed by phenytoin (18%). Among combination therapy, Phenobarbitone with phenytoin was commonly prescribed (11%). Duration of the

use of AED was documented > 5 years for majority of the study participants (63%; Table 3).

Factors associated with non adherence to antiepileptic drugs

In this study, of the potential factors identified by bivariate logistic regression analysis, participants monthly income, knowledge about epilepsy (neurologic, hereditary, psychiatric or evil spirit) and seizure control status were found to be significant factors associated with non-adherence to antiepileptic drugs ($p < 0.05$). Accordingly, patients with monthly income of > 3000.00 ETB were about 16% less likely to be non adherent than those who earn < 1000.00 ETB [AOR=0.164, 95% CI (0.038, 0.702)]. Likewise, patients who's monthly income is between 2000 and 3000 ETB were about 11% [AOR=0.110, 95%CI

(0.026:0.461)] less likely to be non adherent than patients with monthly income of < 1000 ETB. Patients who perceived epilepsy as psychiatric disorder were 25% less likely to be non adherent than those who perceive epilepsy as a neurologic disorder [AOR= 0.250, 95%CI (0.087, 0.716)]. Patients with seizure free period of less than one year are about 21% less likely [AOR= 0.206,95%CI(0.076,0.562)] to be non adherent than those with seizure free period more than one year (Table 4).

Discussion

This study aimed to assess non adherence and the associated factors among PWE at HUCSH in south Ethiopia. The Validated 8-item Morisky Medication Adherence Scale (MMAS-8), a self reporting tool, was

Table 2. Clinical characteristics of People with epilepsy on follow-up at HUCSH, February 01 to October 15, 2017.

Variables	Number	%	
Age at onset of first seizure (n=187)	≤ 5 years	15	10
	6-15 years	57	30
	16-30 years	90	58
	> 30 years	25	13
Duration of follow up at HUCSH (n=187)	1-2 years	21	11
	3-5 years	59	32
	> 5 years	107	57.5
Duration of illness (epilepsy) (n=187)	≤ 5 years	43	23
	6-10 years	66	35
	> 10 years	78	42
Seizure free period (n=187)	< 1 year	105	56
	1-2 years	59	31
	≥ 3 years	23	13
Co-morbidities (n=12)	Hypertension	6	3.2
	HIV	2	1.1
	HIV and Stroke	1	0.5
	Stroke	3	1.6
Adverse effect(s) (n=187)	No	131	70
	Yes	56	30
Adherence (by MMAS-8)	≥ 6	152	81
	< 6	35	18.5
	TOTAL	187	100

Table 3. Patterns of Antiepileptic drugs use by peoples with epilepsy at HUCSH, February 01-October 15, 2017.

Variables	Number	%	
Type of AED used	Phenobarbitone	110	59
	Phenytoin	34	18
	Carbamazepine	13	7
	Phenobarbitone and Phenytoin	20	11
	Phenobarbitone and Carbamazepine	4	2
	Phenytoin and Carbamazepine	6	3
The no. of AED used	One drug	157	84
	Two drugs	30	16
Duration of AED use/treatment	1-2 years	27	14
	3-5 years	43	23
	> 5 years	117	63

Table 4. Factors associated with non adherence to treatment in patients with epilepsy HUCSH, February 01-October 15, 2017.

		Adherence status to AED		COR (95% CI)			AOR(95%CI)		
		No (%)	Yes (%)						
Monthly income	<1000ETB	3 (6.4)	44 (93.6)		1			1	
	1000-1999ETB	5 (10.2)	44 (89.8)	0.600	0.135	2.665	0.761	.159	3.635
	2000-3000ETB	6 (34.8)	30 (65.2)	0.128	0.034	0.477**	0.110	0.026	0.461**
	>3000ETB	11 (24.43)	34 (75.6)	0.211	0.054	0.815*	0.164	0.038	0.702*
Knowledge about epilepsy	Neurologic	7 (12.7)	48 (87.3)		1			1	
	Hereditary (1)	3 (9.11)	30 (90.9)	1.458	0.350	6.078	1.404	0.304	6.490
	Psychiatric (2)	24 (25.5)	70 (74.5)	0.425	0.170	1.066	0.250	0.087	0.716*
	Evil spirit (3)	1 (20.0)	4 (80.0)	0.583	0.057	5.998	0.605	0.048	7.704
Whether Epilepsy is controlled by modern drug	Yes	25(23.1)	83 (76.9)	0.481	0.216	1.071	0.630	0.251	1.580
	No	10 (12.7)	69(87.3)		1			1	
Seizure control status	Controlled (seizure free period \geq 1yr)	7 (8.5)	75 (91.5)		1			1	
	Uncontrolled (seizure free period of <1yr)	28 (26.7)	77 (73.3)	0.257	0.106	0.623**	0.206	0.076	0.562**
Number of AEDs used	Monotherapy	27 (17.2)	130 (82.8)		1			1	
	Dual therapy	8 (26.7)	22(73.3)	0.571	0.230	1.418	0.747	0.252	2.213

Note: * is statistically significant at $p < 0.05$, ** is statistically significant at $p < 0.01$.

used in this study which revealed a non-adherence rate of 18.5%. In contrast to this, higher percentage of non-adherence rate was documented in previous studies; like in Yirgalem Hospital, Ethiopia 68%,⁵ Northern Nigeria 67.4%,¹¹ Ambo Hospital, Ethiopia 53.8%¹² and Dessie referral hospital (34.1%).¹³ The probable reason for the discrepancies could be due to the difference in sampling methods, and operational definitions for non-adherence to AEDs in which the current study considered only low score (<6 MMAS-8) excluding medium scores. Besides, as one would expect, in self report non adherence measures, patients could overvalue their adherence and report low non adherence to AEDs.

Patients with higher monthly incomes (>3000ETB) were less likely to be non-adherent. This was consistent with the study in India.¹⁴ Patients with better income might have better opportunity for education in turn awareness towards the adherence, In the current study patients who perceive epilepsy as a psychiatric disorder were less likely to be non-adherent. While such perception is reported in previous studies,^{15,16} the possible reason for being more adherent to the medication could be their better awareness on psychiatric disorders in which adherence is important to control the disease.¹⁷ Patients with uncontrolled seizure (seizure free period of less than one year) are less likely to be non-adherent. This is not unexpected as most patients with epilepsy prefer adherence to AEDs to reduce or even combat their seizure frequency effectively.¹⁸

Like any other study, the current study is not without limitation. One obvious limitation is the use of self-reported MMAS-8 method for adherence assessment that

might have caused over estimation of adherence status. The cross-sectional nature of the study didn't allow for follow up observation, an approach with better design to assess risk factors associated with non-adherence status, consequently, in the current study design, there is generally no evidence of a temporal relationship between non adherence and factors associated with it while such evidence is more stronger. However these limitations do not invalidate the findings.

Conclusions

The non-adherence rate was discovered to be 18.5%. Monthly income, knowledge of epilepsy, and seizure control status were found to have a statistically significant relationship with AED adherence. As a result, the hospital should devise strategies to improve current adherence levels.

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