

International Journal of Bioscience and Medicine
(ISSN:2575-7814)



Prevalence and Associated Factors of Antiepileptic Drugnonadherence Among Epileptic Patients Attending at Out Patient Departement of Dilla University Referral Hospital, Dilla,gedeo,snnpr, Southern Ethiopia

Maregu Shegaw (BSC) 1, Reta kassa (BSC, MPH)2, Yigrem ali (BSC, MSc)3, Negatu Addissu (BSC, MSc)4

1Depratment of Psychiatry, college of health sciences and Medicine , Dilla University,Ethiopia.

2Depratment of public health, college of health and Medical sciences, Dilla University , Ethiopia.

3Department of psychiatry, college of health sciences and Medicine , Dilla University,Ethiopia

4 Department of Pharmacy, college of health sciences and medicine, Dilla University, Ethiopia

ABSTRACT

Background: Antiepileptic drugs are effective in the treatment of epilepsy, but poor adherence to medication is major problem to sustained remission and to functional restoration. Poor adherence to treatment is one of many reasons for pharmacological treatment failure and seizure recurrence. Even though there were studies on the magnitude and associated factors of Antiepileptic drugs non-adherence, there is a shortage of published information regarding the prevalence and associated factors of Antiepileptic drugs none-adherence in Ethiopia.

Objective: To assess prevalence and associated factors of antiepileptic drug none-adherence among epileptic patients attending at Dilla University Referral Hospital. **Methods:** Institutional based cross sectional study design was conducted at Dilla University Referral Hospital from March to May, 2016. A total of 265 individuals was selected by simplerandom sampling method and interviewed by using structured questionnaire. 8 itemMorisky Medication Adherence Scalewas used to assess the prevalence of antiepileptic drug non adherence. Data was coded and exported to SPSS version 20 for analysis. **Results:** The prevalence of Antiepileptic's drug none-adherence in this study was 38.1% and getting medication by payment [AOR=2.009, 95%,CI:1.044, 3.868], Patients who did not got health information about(their illness, duration of treatment and drug side effect) [AOR=0.319,95%,-CI:0.184,0.534], poor social support [AOR=3.06, 95%, CI: 1.47-6.37], skip dose [AOR=2.462,95%,CI:1.375,4.407], patients who were on treatment for 2-5 years [AOR=1.48, 95%, CI: 0.722,3.035] were found to be significantly associated ($p<0.05$). **Conclusion:** The prevalence of antiepileptic drug none-adherence among patients with epilepsy disorder was found 38.1%. Getting medication by payment, did not receive health information about (the illness, duration of treatment, medication side effect), skip dose, on treatment for 2-5 years, and poor social support were found to be the independent predictor of antiepileptic drug none-adherence.

Keywords: Antiepileptic Drugs, prevalence, epileptic patients, Ethiopia

*Correspondence to Author:

Yigrem ali.Department of psychiatry, college of health sciences and Medicine, Dilla University,Ethiopia.
Email: alyigrem @gmail.com

How to cite this article:

Maregu Shegaw et al., Prevalence and Associated Factors of Antiepileptic Drugnonadherence Among Epileptic Patients Attending at Out Patient Departement of Dilla University Referral Hospital, Dilla,gedeo,snnpr, Southern Ethiopia. International Journal of Bioscience and Medicine, 2017; 1:2.

eSciencePublisher®

eSciPub LLC, Houston, TX USA.

Website: <http://escipub.com/>

INTRODUCTION

Epilepsy is a chronic disorder of the brain and is one of the most common serious neurological disorders worldwide with no boundary to age, race, social class, nationality or geographical location(1) . Worldwide around One billion people are affected by neurological disorders, including 50 million who had epilepsy , 24 million with Alzheimer disease & other dementias, and an estimated 6.8 million die each year due to neurological disorders(2). Among patients who had epilepsy; 85% of them found in developing countries and estimated 40 million people do not receive appropriate treatment (1, 3). The overall mortality rate due to epilepsy increased by two to three fold as compared with the general population(4).

Medication none-adherence is defined as a voluntary or involuntary behavior of medication intake which includes: failing initially filling or refilling a prescription, discontinuing a medication before the course of therapy is complete, inability to cross pond with agreed recommendations from health care provider, taking more or less of a medication than prescribed and taking a dose at wrong time(5, 6).

Antiepileptic drugs (AEDs) are effective in the treatment of epilepsy ,but poor adherence to medication is major problem to sustained remission and functional restoration(7). Poor adherence to treatment is one of many reasons for pharmacological treatment failure and seizure recurrence(8). The mortality rate in none-adherent patients was more than three times higher than that of adherent patients(9) . Even though around 70% of people who had epilepsy may expect to become seizure free with optimum antiepileptic drug (AED) treatment, patients didn't take their antiepileptic drugs appropriately(10).

A twenty review study indicated that one third of epileptic patients report negative experiences which may lead to poor adherence due to drug substitution(11). The consequence of AEDs nonadherence behavior has been associated with: poor seizure control, increased morbidity and mortality along with increased time of

hospitalization, worsened patient outcome, increased health care cost and death(12-14).

The mortality of untreated epilepsy become increase due to status epileptics and falling accident(15). Recurrence seizure will result in poor quality of life, decreased productivity, seizure related joblessness and motor vehicle accident. AEDs non adherent patients had significant negative consequences like dropout from school and work as compared to those who were adherent to AEDs(16).

AEDs nonadherence will also lead to increase burden of inpatient and emergency department services (17, 18). There was a negative relation between medication adherence and frequency of seizures. Patients who had poor seizure control are more likely to be anxious and feel as they are helpless due to their illness (19). Moreover AEDs nonadherence also affects family members socially, economically and psychologically (3, 20). A review study revealed that a number of factors like patient centered, therapy related factors, social and economic factors, and health care system and disease factors were contributed to therapeutic non adherence(21). Problem of non adherence to therapeutic regimen has been a matter of concern not only to the professionals and attendants but also to the country. Approximately 70% of people with epilepsy could lead normal lives if properly treated(22).

Even though there was a study done on the magnitude and associated factors of AEDs none-adherence, there is a shortage of published information regarding the prevalence and associated factors of AEDs none-adherence in Ethiopia. Therefore, assessing and showing the significance of antiepileptic none-adherence might be important to enforce policy makers and different stakeholders and to manage antiepileptic none-adherence.

Methods

Study Area and Period

The study was conducted at Dilla University Referral Hospital (DURH) from March to May ,

2016 which is found in Dilla town, Gedeo zone, SNNPR, Ethiopia. DURH is established in 1977 E.C /1985 G.C as zonal hospital in Gedeo zone with the former name of Dilla Hospital until June 11/2001 E.C that changed in to DURH. It is located 360 km from Addis Ababa, the capital city of Ethiopia, and 90 km from Hawassa, the capital city of SNNPRE. It provides curative and rehabilitative services for about 2 million catchment populations. At the time of its establishment, about 154 staffs were recruited, of them 104 are health professionals and the remaining are supportive staffs. Now the hospital has five wards, namely Medical (39 bed), surgical (26 beds), oby/gyn (9 beds), Pediatrics (18 beds) and psychiatry (12 beds). Currently the hospital serves around 3 million peoples from which 95% belongs to Gedeo ethnic group. There are around 725 epileptic patients who are taking antiepileptic drugs annually.

Sample size determination and technique

It was determined by Level of significance (0.05), Power (0.50) with $z = 95\%$ confidence interval and The value of "p" ($p =$ proportion of prevalence) was taken as 36.8% of antiepileptic drug nonadherence from a study conducted in Jimma University specialized hospital, Southwest Ethiopia to estimate the sample size (17), total sample size for this study is 359. Then the total source of population are 725 that means less than 10,000; therefore it was used correction formula and by considering 10% non response rate, so final sample size 265.

A systematic sampling method was used to select study participants visiting Dilla University Referral Hospital during the study period from a total of 725 epileptic's patients.

Data collection and analyses procedures

Data collection instruments

The instrument has five sections: it includes socio-demographic, clinical and treatment related factors, health care related factors, patient related factors and Morisky 8-item medication adherence questionnaire. A

structured questionnaire was used to collect socio-demographic characteristics and antiepileptic drug nonadherence related factors. Data regarding the regimen of drugs and presence of co morbid illness was collected by asking the patient and reviewing patients' charts. Drug nonadherence was assessed by using 8 item version of self reporting questionnaire of Morisky medication adherence scale (MMAS).

Social support was assessed by using the Oslo 3 item social support scales: the sum score scale ranging from 3-14, which is categorized into poor support 3-8, moderate support 9-11 and strong support 12-14 (36)

Felt stigma was measured by using kilifi stigma scale of epilepsy. It is a simple three point likert scoring system scored as not at all (0), sometimes (1) and always (2). A total of score was calculated by adding of all item scores. The score above 66th percentile of the data indicated presence of perceived stigma(37).

Data collection technique and Data quality control

Data was collected through interview by administering structured questionnaire and by reviewing patients chart. Training was given for data collectors and supervisors about the use of questionnaire, the ethical principle of confidentiality and data management prior to their involvement of data collection for two days was given.

Pre-test was done on 5% of the sample size, at wonago Health centre. Based on the finding of the pre test, the questioner was revised. Data collectors were supervised daily and the filled questionnaires were checked daily by the supervisors and principal investigator for completeness.

Data processing and analysis

The coded Data was checked, cleaned and entered into exported into Statistical Package for the Social Sciences (SPSS window version 20).

The Descriptive summary using frequencies, percentage and median were used to present study results.

A Bivariate analysis was performed to determine the effect each of factors on the outcome

variable. Only factors with p.value <0.2 on Bivariate analyses were kept for multivariate analyses and a p value of < 0.05 on multivariate analyses was considered as statistically significant

Table 1. Socio-demographic characteristics of the study subjects in Dilla University Referral Hospital, 2016 n=265

Socio-demographic characteristic c	Number	Percentage (%)
Age		
18-25	100	37.7s
26-44	122	46.0
>/45	43	16.2
Sex		
Male	140	52.8
Female	125	47.2
Ethnicity		
Gedio	107	40.4
Oromo	75	28.3
Amhara	47	17.7
Gurage	12	4.5
Others	24	9.1
Religion		
Orthodox	119	44.9
Protestant	76	28.7
Muslims	38	14.3
Catholic	20	7.5
Others	12	4.5
Occupation		
Government employee	25	9.4
Farmer	93	35.1
Unemployed	29	10.9
Merchant	25	9.4
Student	52	19.6
Daily labor	37	14
Others	4	1.5
Educational status		
Unable to read and write	88	33.2
Able to read and write	112	42.3
Grade 1-8	21	7.9
Grade 9-12	17	6.4
Collage and above	27	10.2
Marital status		
Unmarried	104	39.2
Married	116	43.8
Divorced	24	9.1
Widowed	21	7.9

Ethical consideration

Ethical clearance was obtained from ethical review board of Dilla University. Formal permission was taken for the hospital. All participants were well informed about the aims and purpose of the study, its contribution to the future development of health system in the country. The right was given to the study participants to refuse or withdraw from participation at any time during data collection without loss of any entitlement.

A total of 265 patients were included in the study and making the response rate of 100% because all of them consented and completed the interview. The study subject was comprised of 140 (52.8%) male and 125 (47.2%) female. The majority [122 (46%)] of the patients were in the age group between years 26-44 of age. The majority of the study subjects 119(44.9%) were orthodox, and 93 (35.1%) were farmers. Majority [116 (43.8%)] of the patients participated in the study were married and only 27 (10.2%) had Collage and above educatio

Result

Table 2: Distribution of patients with epilepsy disorder by clinical and treatment related factors attending at Dilla University Referral Hospital, 2016, n=265.

Variables	Category	Frequency	Percent (%)	
Current AEDs	Phenobarbital	Total prescribed	162	61.1
	Phenytoin	Total prescribed	71	26.8
	Sodium-valproate	Total prescribed	10	3.8
	Carbamazepine	Total prescribed	22	8.3
Medication other than AEDs	No		256	96.6
	Yes		9	3.4
Number of AEDs prescribed	One		210	79.2
	Two		48	18.1
	Three and more		7	2.6
Co morbid illness	No		217	81.9
	Yes		48	18.1
Reported experienced side effects	No		161	60.8
	Yes		104	39.2
Ever skip dose	No		137	51.7
	Yes		128	48.3
Duration on treatment	0.03-1 year		71	26.8
	2-5years		114	43
	6years and above		80	30.2

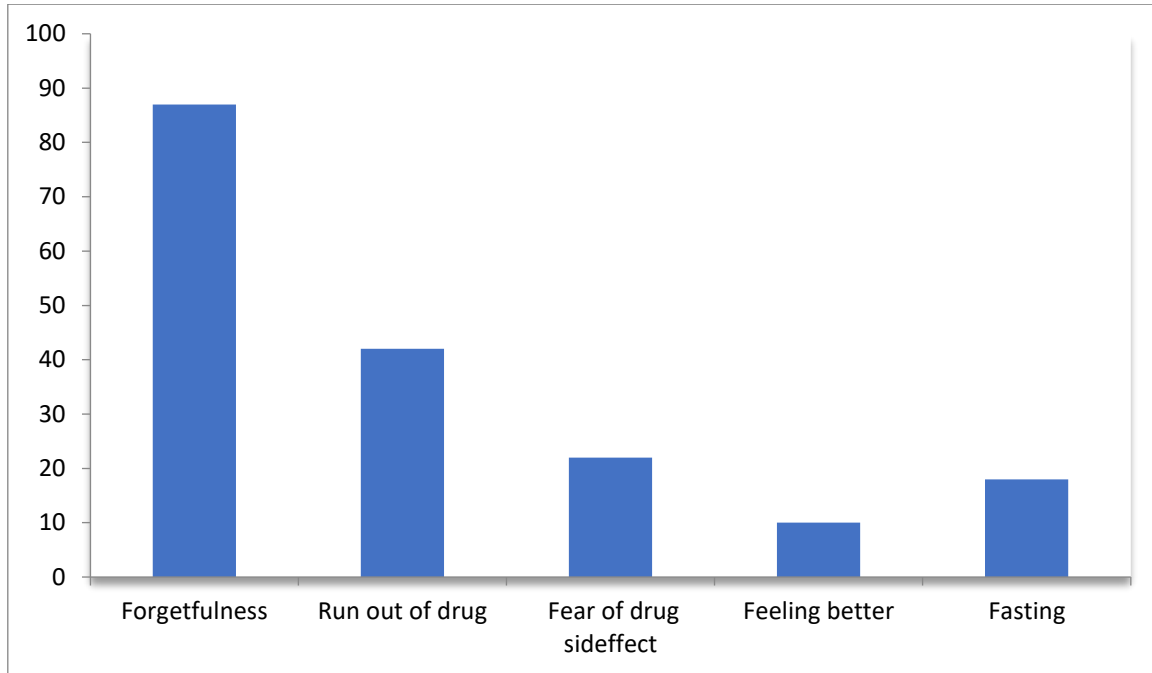


Figure 1 shows the frequency distribution of reasons for Antiepileptic drug dose skip epileptic patients attending at DURH, 2016 n=265

Clinical/Treatment/ Related Factors

More than half of the respondents 210(79.2%) were on monotherapy and Phenobarbital was

the most common prescribed drug. Among the respondents 217(81.9%) had no any co morbid illness and 48(18.1%) had co morbid illness.

Table 3: Distribution of patients with epilepsy disorder by health care and patient related factors attending at Dilla University Referral Hospital,2016, n=265

Variables	Category	Frequency	Percent
How do you get your medication	Freely	78	29.4
	Fee	187	70.6
Health information	No	160	60.4
	Yes	105	39.6
Use substance since starting Medication	No	256	96.6
	Yes	9	3.4
Substance use in 3 month	No	256	96.6
	Yes	9	3.4
Perceived stigma	No	175	66
	Yes	90	34
Social support	strong support	60	22.6
	poor support	76	28.7
	Intermediate support	129	48.7

Depression disorder, HIV, dyspepsia, schizophrenia, and asthma are the type of co morbid illness. Medications which were prescribed concomitantly with AEDs were fluoxetine, haloperidol, cotrimoxazole and amitriptyline. Of 114(43%) were on treatment for 2-5 years and among the participants 104(39.2) reported that they experience side effect and the most reported experienced side effect was sedation. Regarding skip dose 128(48.3) participants were reported missing their dose due to different reasons and the most reason

was forgetting 87(32.8%), run out off drug 42(15.8%) (See table 2).

Health Care And Patient Related Factors

Among the participants 78(29.4%) had free access to AEDs drugs. Regarding health information about 160(60.4%) participants stated that they did not get health information from their health care provider concerning their illness, drug side effect and duration of treatment. About 90(34%) respondents had perceived stigma and 76(28.7%) had poor social support (see table 3

Prevalence of Antiepileptic Drug Non-Adherence

As measured by the 8 item MMAS, 101(38.1%) of the respondents scored two and more .The

overall prevalence of antiepileptic drug nonadherence among the study participants were found to be 38.1%.

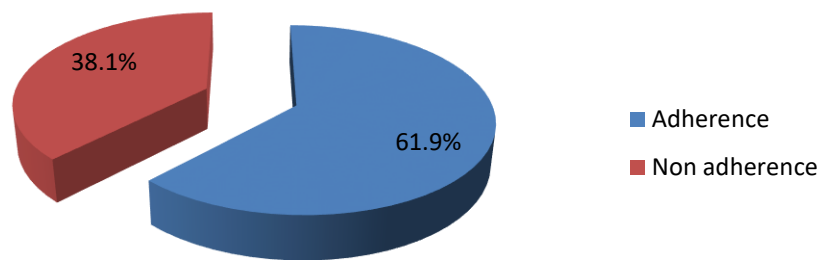


Figure 2: prevalence of antiepileptic drug non adherence among patients with epilepsy disorder attending at Dilla University Referral Hospital, 2016

Factors Associated with Drug Non-adherence

Bivariate Analysis

From the bivariate analysis of antiepileptic drug non adherence in relation to each variable, way of getting medication, received health information from their health care provider, ever skip dose, social support, duration on treatment were variables that fulfilled the minimum requirement (p<0.2) and for further analysis entered to multivariate logistic regression. On the other hand sex, age, occupation, marital status, number of AEDs medication, residence, and current substance use, experienced side effect, substance use since starting medication,

perceived stigma did not fulfill the minimum requirements and were exclude from further analysis.

Multivariate Analysis

During the multivariate analysis of antiepileptic drug non adherence in relation to all independent variables, getting medication by payment [AOR=2.099, 95%,CI:1.044, 3.868], Patients who did not get health information about(their illness, duration of treatment and drug side effect) [AOR=0.319,95%,CI:0.184,0.554], poor social support [AOR=3.06, 95%, CI: 1.47-6.37], skip dose [AOR=2.462,95%,CI:1.375,4.407] and

patients who were on treatment for 2-5 years to be significantly associated ($p < 0.05$). [AOR=1.48, 95%, CI: 0.722,3.035] were found

Table 4: Factors associated with antiepileptic drug non adherence among patients with epilepsy disorder attending at Dilla University Referral Hospital: 2016(n=265).

Independent variables	Drug non No	Adherence Yes	AOR (95% CI)	AOR (95% CI)
Educational Status				
Collage and above	12(44.4%)	15(55.6%)	1	1
Grade 9-12	8(47.1%)	9(52.9%)	0.900(0.266,3.042)	1.111(0.329,3.756)
Grade 1-8	9(42.9%)	12(57.1)	1.067(0.338,3.370)	0.937(0.297,2.962)
Able to read and write	45(40.2%)	67	1.191(0.510,2.781)	0.840(0.360,1.960)
Unable to read and write	27(30.7%)	61(69.3%)	1.807(0.747,4.375)	0.553(0.229,1.339)
Co morbid illness				
No	65(38.9%)	102(61.1%)	1	1
Yes	36(36.7%)	62(63.3%)	1.097(0.656,1.837)	0.911(0.544,1.525)
Reported experienced AED side effect				
No	52(42.6%)	70(57.4%)	1	1
Yes	49(34.3%)	94(65.7%)	1.425(0.866,2.345)	0.702(0.426,1.155)
Getting medication				
Free	18(23.1%)	60(76.9%)	1	1
Payment	83(44.4%)	104(55.6%)	0.376(0.206,0.685)	2.009(1.044,3.868)*
Received health information				
No	77(48.1%)	83(51.9)	3.133(1.805,5.433)	0.319(0.184,0.554)*
Yes	24(22.9)	81(77.1%)	1	1
Substance use since starting medication				
No	99(38.7%)	157(61.3)	1	1
Yes	2(22.2%)	7(77.8%)	2.207(0.449,10.83)	1.78(0.76,4.16)
Ever skip dose				
No	20(24.4%)	62(75.6%)	1	1
Yes	81(44.3%)	102(55.7)	0.406(0.227,0.727)	2.462(1.375, 4.407)*
Duration on treatment				
0.03-1 year	23(25%)	69(75%)	1	1
2-5 year	46(45.1%)	56(54.9%)	0.406(0.220,0.748)	1.48(0.722,3.035)*
6 years and above	32(45.1%)	39(54.9%)	0.406(0.209,0.789)	0.77(0.409,1.478)
Social support				
Strong social support	32(37.1%)	47(62.9%)	1	1
Poor social support	44(56%)	58(44%)	3.23(1.85,5.64)	3.06(1.47,6.37)*
Intermediate support	25(49.5%)	59(50.5%)	1.31(0.78,2.20)	1.39(0.72,2.67)
Perceived stigma				
No	63(57.5%)	54(42.5%)	1	1
Yes	38(66%)	110(34%)	3.01(2.01,4.51)	1.72(0.997,2.97)

Key: * statistically significance

Discussion

Non adherence to treatment is one of many reasons for pharmacological treatment failure and seizure recurrence. In this study the prevalence of antiepileptic drug non adherence among patients with epilepsy disorder was 38.1% with [95%, CI: 32.3, 44.9].

It was greater than in studies done in USA 26% (18). The probable explanation for this difference may be due to: the study design used, the of treatment was 21.5year. In this study the participants who were on two medications was 18.1% and the mean of treatment duration was 1.9 years and the difference in Nigeria might be due to socio-demographic characteristics and poly-therapy which was 85%of the participant took three and above AEDs. The difference in Palestine might to be due to sample size, chronic illness and prescribed medication: the sample size in Palestine was small, 13.7% had other chronic diseases and more than half of the patients 63.2% were on poly-therapy but in this study 37% the respondent had co morbid illness and 18.1% were on two medications.

From the study participants who were buying AEDs medications, the odds of being non adherence was about 2 times more likely to be non adherence as compared with patients who were getting their AEDs medication free of charge [AOR=2.009, 95%,CI:1.044, 3.868]. From all patients who were buying their medication 104(55.6%) were known to be non adherent. This study was in line with a study done in Kenya (34).

From all patients who did not get health information 160(60.3%) were known to be non adherent. This finding was not in line with Egypt's study in which all patients include in the study (100%) did not get any health education about epilepsy from nurses but 6% received health education from physician (33).The possible reasons might be health care providers may not have adequate time, poor doctor-patient relationship, negligence and might feel fatigue to explain related conditions with the disease and the treatment for their patients.

Concerning social support ,participants who had poor social support were three times more likely to be nonadherence as compared with patients who had strong social support [AOR=3.06, 95%,

medication prescribed, methods used to measure the non adherence and as well as difference in socio-demographic characteristics of the study participant or due to study area. But the nonadherence was smaller than those studies in Brazil, Nigeria and Palestine which were 66.2%, 67.4% and 64% respectively (28, 31, 40) The difference from Brazil study might be due to duration of treatment and prescribed AEDs which were 71.1% of the respondents were on two to five AEDs and the mean duration

CI:1.47-6.37].. The study was in line with a study done in Egypt(33). Among participants 210(46.7%) were skipped their medication dose at least once during their treatment. They have different reasons for skipping. Forgetting 87(32.8%) was the most reported reason for skipping dose.

Regarding the duration of treatment for those patients who were on treatment 2-5 years, the odds of being non adherence were about 1.488 times more likely to be non adherence compared with patients who were on treatment 3 month to 1 year [AOR=1.488, 95%, CI: 0.722,3.035]. As the study illustrated while treatment duration increases, the respondents more likely to be non adherent. The study was not similar with studies done in Kenya and Egypt (33,34). This could be due to decreased the willingness to follow their treatment as well as forgetfulness to follow the treatment for long period of time by patients and also the treatment duration increases the patient might feel better and more likely to be non-adherent to their treatment given.

Conclusion

The prevalence of antiepileptic drug nonadherence among patients with epilepsy disorder was found to be 38.1 %

Getting medication by payment, did not receive health information about (the illness, duration of treatment, medication side effect), skip dose, on treatment for 6 years and above, and poor social support were found to be the independent predictor of AEDs non adherence.

Recommendations

Based on the findings and the conclusions, the following recommendations were forwarded for respective bodies.

To ministry of health

In order to improve adherence, it is better to design and implement programs that address getting medication free of charge

To Dilla University Referral Hospital

The hospital should develop standard protocol for the management of epileptic patients and manuals which describe strategies of drug selection, dosing, frequency of drug and duration of treatment.

To health care providers

The health care providers should give time to provide the appropriate health information about disease condition, drug side effect, duration of treatment and the consequence of dose missing.

To researchers

The researchers better to further study with other study design to provide strong evidence regarding the prevalence and associated factors

References

1. Organization WH. Neurological Disorders: Public Health Challenges: World Health Organization; 2006 2006. 233 p.
2. Stump E. WHO Report: Millions Have Neurological Disorders Worldwide. *Neurology Today*. 2007;7(7).
3. Organization WHO, others. Atlas: epilepsy care in the world. 2005.
4. O'Donoghue MF, Sander J. The mortality associated with epilepsy, with particular reference to sudden unexpected death: a review. *Epilepsia*. 1997;38(s11):S15-S9.
5. Osterberg L, Blaschke T. Adherence to medication. *New England Journal of Medicine*. 2005;353(5):487-97.
6. Hugtenburg JG, Timmers L, Elders PJM, Vervloet M, van Dijk L. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. *Patient Prefer Adherence*. 2013;7.
7. Dekker PA, Organization WHO, others. *Epilepsy: a manual for medical and clinical officers in Africa*. 2002.

of epileptic drug non adherence among patients with epilepsy disorder

Competing interest

All authors declare that they have no conflict of interest associated with the publication of this manuscript.

Authors' contribution

Maregu Shegaw conceived and designed the study and collected data in the field, performed analysis, interpretation of data, and draft the manuscript. Reta kassa, Yigrem Ali and Negatu Addisu also involved in the design, analysis, and interpretation of data and the critical review of the manuscript. All authors approved and read the final manuscript.

Acknowledgement

This study was not funded by any organization, and not covered by any financials .

8. Sabaté E. Adherence to Long-term Therapies: Evidence for Action: World Health Organization; 2003 2003. 228 p.
9. Kwan P, Schachter SC, Brodie MJ. Drug-resistant epilepsy. *New England Journal of Medicine*. 2011;365(10):919-26.
10. Sander JW. The Use of Antiepileptic Drugs—Principles and Practice. *Epilepsia*. 2004;45:28-34.
11. Hla akonsen H, Toverud E-L. A review of patient perspectives on generics substitution: what are the challenges for optimal drug use. *GaBi J*. 2012;1(1):28-32.
12. Neligan A, Bell GS, Johnson AL, Goodridge DM, Shorvon SD, Sander JW. The long-term risk of premature mortality in people with epilepsy. *Brain*. 2011;134(2):388-95.
13. Kaddumukasa M, Kaddumukasa M, Matovu S, Katabira E. The frequency and precipitating factors for breakthrough seizures among patients with epilepsy in Uganda. *BMC neurology*. 2013;13(1).
14. Cramer JA, Wang ZJ, Chang E, Powers A, Copher R, Cherepanov D, et al. Healthcare utilization and costs in adults with stable and uncontrolled epilepsy. *Epilepsy & Behavior*. 2014;31:356-62.

15. Newton CR, Garcia HH. Epilepsy in poor regions of the world. *The Lancet*. 2012;380(9848):1193-201.
16. Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. *Epilepsy & Behavior*. 2008;13(2):316-22.
17. Getachew H, Dekema NH, Awol SS, Abdi AA, Mohammed MA. Medication adherence in epilepsy and potential risk factors associated with non adherence in tertiary care teaching hospital in southwest Ethiopia. *Gaziantep Medical Journal*. 2014;20(1):59-65.
18. Faught RE, Weiner JR, Guérin A, Cunnington MC, Duh MS. Impact of nonadherence to antiepileptic drugs on health care utilization and costs: findings from the RANSOM study. *Epilepsia*. 2009;50(3):501-9.
19. Jones RM, Butler JA, Thomas VA, Peveler RC, Prevett M. Adherence to treatment in patients with epilepsy: Associations with seizure control and illness beliefs. *Seizure*. 2006;15(7):504-8.
20. Martins HH, Alonso NB, Guilhoto LMFF, Guarânia MSB, Yacubian EMT. Clinical, Psychosocial and Scientific Note. *J Epilepsy*. 2009;15(4):192-6.
21. Jin J, Sklar GE, Oh VMS, Li SC. Factors affecting therapeutic compliance: A review from the patient's perspective. *Therapeutics and clinical risk management*. 2008;4(1).
22. Organization WHO others. Epilepsy in the WHO Eastern Mediterranean region: bridging the gap 2010 2010.
23. Davis KL, Candrilli SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. *Epilepsia*. 2008;49(3):446-54.
24. Brown I, Sheeran P, Reuber M. Enhancing antiepileptic drug adherence: a randomized controlled trial. *Epilepsy & Behavior*. 2009;16(4):634-9.
25. Chapman SCE, Horne R, Chater A, Hukins D, Smithson WH. Patients' perspectives on antiepileptic medication: relationships between beliefs about medicines and adherence among patients with epilepsy in UK primary care. *Epilepsy Behav*. 2014;31:312-20.
26. Carpentier N, Jonas J, Frismand S, Vignal J-P, Rikir E, Baumann C, et al. Direct evidence of nonadherence to antiepileptic medication in refractory focal epilepsy. *Epilepsia*. 2013;54(1):e20-e3.
27. Kyngäs H. Compliance with health regimens of adolescents with epilepsy. *Seizure*. 2000;9(8):598-604.
28. Ferrari CMM, de Sousa RMC, Castro LHM. Factors associated with treatment non-adherence in patients with epilepsy in Brazil. *Seizure*. 2013;22(5):384-9.
29. Liu J, Liu Z, Ding H, Yang X. Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. *Epileptic disorders*. 2013;15(3):289-94.
30. Virág L, Murgaš M, Kuželová M. Pharmacotherapeutic adherence and quality of life in paediatric outpatients with epilepsy. *Acta Facultatis Pharmaceuticae Universitatis Comenianae*. 2012;59(Supplement VI):76-83.
31. Sweileh WM, Ihbesheh MS, Jarar IS, Taha ASA, Sawalha AF, Zyoud SeH, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. *Epilepsy & Behavior*. 2011;21(3):301-5.
32. Ogboi Sonny J, Babajide F, Ademola O A, Olabunmi O, Agu P U. Evaluation of Factors Influencing Medication Adherence in Patients with Epilepsy in Rural Communities of Kaduna State, Nigeria. *Neuroscience & Medicine*. 2011;2011.
33. El-Shamaa ET. Factors Contributing To Therapeutic Compliance Of Epileptic Patients And The Suggestive Solutions. *Journal of Biology, Agriculture and Healthcare*. 2013;3(3):22-35.
34. Mbuba CK, Ngugi AK, Fegan G, Ibinda F, Muchohi SN, Nyundo C, et al. Risk factors associated with the epilepsy treatment gap in Kilifi, Kenya: a cross-sectional study. *The Lancet Neurology*. 2012;11(8):688-96.
35. Srivastava K, Arora A, Kataria A, Cappelleri JC, Sadosky A, Peterson AM. Impact of reducing dosing frequency on adherence to oral therapies: a literature

- review and meta-analysis. *Patient Preference Adherence*. 2013;7:419-34.
36. Bøen H. Characteristics of senior centre users—and the impact of a group programme on social support and late-life depression. *Norsk epidemiologi*. 2012;22(2).
37. Kathomi Mbuba C. *Epilepsy treatment gap, associated risk factors and intervention strategies in Kilifi, Kenya*: University of Basel; 2011.
38. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. *The Journal of Clinical Hypertension*. 2008;10(5):348-54.
39. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical care*. 1986;24(1):67-74.
40. Nakhutina L, Gonzalez JS, Margolis SA, Spada A, Grant A. Adherence to antiepileptic drugs and beliefs about medication among predominantly ethnic minority patients with epilepsy. *Epilepsy & Behavior*. 2011;22(3):584-6

