CLINICAL STUDIES / ETUDES CLINIQUES

FACTORS ASSOCIATED WITH ANTIEPILEPTIC DRUG ADHERENCE IN EPILEPTIC PATIENTS AT A TERTIARY CARE CENTER IN ETHIOPIA: A CROSS SECTIONAL STUDY

FACTEURS ASSOCIES A L'ADHERENCE AUX MEDICAMENTS ANTIEPILEPTIQUES DANS UN HOPITAL DE REFERENCE EN ETHIOPIE : UNE ETUDE TRANSVERSALE

MOLLA Sisay [1]
DEMISSIE Hanna [2]
AYELE Biniyam A. [2]
TSEHAYNEH Fikru [2]
ALI Seid [2]
ZENEBE Guta [2]

1. Neurology unit, Department of Internal Medicine, Haramaya University, Ethiopia.
2. Department of Neurology, Addis Ababa University, Ethiopia.

E-Mail Contact - MOLLA Sisay : sisaymolla80@yahoo.com

ABSTRACT

Background

One of the leading brain disorders in developing countries such as sub-Saharan Africa (SSA) is represented by epilepsy. Non-adherence to epilepsy treatment is a worldwide health problem. Antiepileptic drugs (AEDs) non-adherence rates among patients with epilepsy range from 30% to 50 % and often associated with increased morbidity and mortality.

Objective

The objective of this study was to assess the prevalence of AEDs non-adherence and associated factors in epileptic individuals.

Methods

This is an observational cross-sectional study conducted among epileptic patients at two tertiary care centers in Addis Ababa, Ethiopia. Both descriptive and analytical analyses were used.

Results

A total of 250 epileptic patients were included in the present study. The mean age was 29.4 (±11.5) years. Males accounted for 54%. The prevalence of AEDs non-adherence and comorbid depression was 47.6% and 45.2% respectively. In multivariate logistic analysis, age of the study participants, age at first seizure, and comorbid depression were independent predictors of AEDs non-adherence when adjusted for the covariates. Being single is associated with non-adherence (p=0.008). Nearly two-third of the patients reported having seizure in the past two years despite taking the AEDs. Individuals aged below 30 year were associated with AEDs non-adherence compared to those age above 30 (p=0.01); and co-morbid depression was significantly associated with AEDs non-adherence (p=0.009). Near-significant association was observed between AEDs non-adherence and having seizure in the past two years (p=0.05).

Conclusion

In present study, high prevalence of AEDs non-adherence was observed among epileptic patients. Participants age, age at first seizure, and comorbid depression were found to be independent predictors of AEDs non-adherence.

RESUME

Contexte

L'épilepsie est l'un des principaux troubles neurologiques dans les pays en développement tels que l'Afrique subsaharienne (ASS). La non-adhésion au traitement de l'épilepsie est un problème de santé mondial. Les taux de non-adhésion aux médicaments antiépileptiques (MAE) chez les patients atteints d'épilepsie varient de 30 à 50 % et sont souvent associés à une morbidité et une mortalité accrues.

Objectif

L'objectif de cette étude était d'évaluer la prévalence de la non-adhésion aux MAE et les facteurs associés chez les personnes épileptiques.

Méthodes

Il s'agit d'une étude observationnelle transversale descriptive et analytique, menée parmi des patients épileptiques dans deux centres de soins tertiaires à Addis Abeba, en Ethiopie.

Résultats

Au total, 250 patients épileptiques ont été inclus dans la présente étude. L'âge moyen était de 29,4 (±11,5) ans. Les hommes représentaient 54 % des patients. La prévalence de la non-adhésion aux MAE et de la dépression associée était de 47,6 % et 47,5 % respectivement.

Dans l'analyse logistique multivariée, l'âge des participants à l'étude, l'âge à la première crise et la dépression associée étaient des prédicteurs indépendants de la non-adhésion aux MAE après ajustement pour les covariables. Le fait d'être célibataire était associé à la non-observance (p=0,008). Près de deux tiers des patients ont déclaré avoir eu des crises au cours des deux dernières années malgré la prise des AEDs. Les personnes âgées de moins de 30 ans étaient associées à la non-adhésion aux MAE par rapport aux personnes âgées de plus de 30 ans (p=0,01) ; et la comorbidité dépressive était significativement associée à la non-observance des AED (p=0,009). Une association quasi-significative a été observée entre la non-observance des AED et le fait d'avoir eu une crise au cours des deux dernières années (p=0,05).

Conclusion

Dans cette étude, une prévalence élevée de non-observance des AED a été observée parmi les patients épileptiques. L'âge des participants, l'âge à la première crise et la comorbidité dépressive se sont avérés être des prédicteurs indépendants de la non-observance des AED.

INTRODUCTION

One of the leading brain disorders in developing countries such as sub-Saharan Africa (SSA) is represented by epilepsy. It is estimated that 80% of people living with epilepsy (PWE) around the world, reside in developing world such as Africa (1). In Ethiopia, the prevalence of epilepsy in rural area was estimated to be 5.1 in 1000 and incidence was 64 /100,000 (2). Contrary to the western countries, very few PWE get adequate treatment in low-and middle-income countries (LMIC), whereby the treatment gap reaches around 95 % (1,3). Antiepileptic drugs (AEDs) are effective in treatment of epilepsy whereby about 70% of patients with epilepsy can be seizure free. Good adherence to AEDs will results in remission and functional restoration among individuals suffering from epilepsy (4). In most cases the stigma of the disorder plays a major role in discouraging people from seeking treatment for symptoms and becoming identified with the disorder; in different communities there is a belief that epilepsy is contagious and hesitate to give help a person who has fallen during seizure (5); further worsening the poor adherence of AEDs among PWE.

Epilepsy is widely associated with increased mortality and morbidity. PWE have estimated mortality of two to three times than general population (3). In most developing countries, factors that attribute for treatment gap of epilepsy in includes: limited access to health care facilities, unavailability of AED, lack of awareness of medical treatment, cultural stigmas and poor adherence (6). Non-adherence to medication treatment

regimens is a worldwide health problem. Non-adherence rates among patients with epilepsy range from 30% to 50 % and highly associated with morbidity and mortality of the illness (4–7). Poor adherence to AEDs leads to repeated seizure attack, psychosocial stress; factors contributing to the treatment adherence could be individual factors like demographic and socioeconomic features, perception and beliefs about epilepsy; disease features like seizure frequency and severity; medication use like number of daily doses and side effects, and factors related to patient–provider relationship (4–7). To date, most of the studies conducted to evaluate AEDs adherence among PWE did not account for the influence of variables such as, comorbid depression.

Therefore, the objective of this study was to assess the prevalence of AEDs adherence and associated factors in epileptic individuals in tertiary care centers in Addis Ababa, Ethiopia.

METHODS AND MATERIALS

Study area and design

The study was conducted at the Neurology referral clinic in Tikur Anbesa Specialized Hospital (TASH) and Zewditu Memorial Hospital (ZMH). TASH is the largest specialized referral teaching hospital in the country. Epilepsy is one of the top ten diseases seen at neurology referral clinic. ZMH is one of the tertiary level public hospital affiliated with TASH and located in the vicinity of TASH. Combined, nearly 1,200 PWE /year are seen both at TASH and ZMH. The Study was conducted from April 1st, 2018 to September 30, 2018. This is a facility based observational cross-sectional survey in a sample of an epileptic patients visiting the two neurology referral clinic during study period fulfilling the inclusion criteria; age ≥13 years and on the AEDs treatment for at least six months.

Assessment tools used during the study

Morisky Medication Adherence Scale (MMAS-8) was used for adherence assessment. Sensitivity of this scale was estimated to be 93%, and the specificity was 53%. The medication adherence measure proved to be reliable with good concurrent and predictive validity in primarily low income, minority patients with hypertension. Score of ≤ 2 are to be adherent and >2 are to be non-adherent (8). Depression was assessed using a well validated assessment tool; Patient Health Questionnaire (PHQ)-9 PHQ-9 with a sensitivity of 88% and specificity of 88% for major depression. PHQ-9 score 5, 10, 15, and 20 represents mild, moderate, moderately severe and severe depression (9).

Statistical analysis

Clinical characteristics were first described by their means, frequency, percentile, and standard deviation. Association were done using chi square or Fisher exact test, logistic regression analysis and results were presented using odds ratio (OR), and p value was set at < 0.05 as statistically significant.

Ethical considerations

Ethical clearance was obtained from Addis Ababa University School of Medicine Neurology Department Ethics Committee. All questionnaires were coded to maintain maximum confidentiality. All patients gave a written or verbal consent before the interview.

RESULTS

Baseline and clinical characteristics of study participants

A total of 250 epileptic patients were included in the present study. The mean age was 29.4 ± 11.5 years. The prevalence of AEDs non-adherence was 47.6% (n=119) and 45.2% fulfilled diagnostic criteria of comorbid depression (Table 1). Those participants age below 30 years shows significant association with antiepileptic drugs non-adherence compared with those above age 30 (Figure 1). Males accounted for 54% (n=135). The majority (92%) came from urban areas. More than half (65.6%) were single. Majority (65.2%) of the participants attended primary education and above; and little more than half of the patients were unemployed. Out of the total participants, nearly two-third of the patients reported having seizure in the past

two weeks despite taking the AEDs. In majority of the epileptic patients (n=215, 86%), the antiepileptic drug was initiated immediately / or after one year. Those individuals who reported stigma shows higher AEDs non-adherence compared to those with no-stigma (Figure 2). Hundred thirty-nine (55.6%) participants were on monotherapy; and more than half (59.6%) of the patients pay for their AEDs by themselves (Table 1).

Risk factors of antiepileptic drugs (AEDs) non-adherence in the study participants

In the present study, individuals aged below 30 year were significantly associated with AEDs non-adherence compared to those above 30 (p=0.01); and no significant difference was observed between gender and AEDs non-adherence (p=0.85). In the present study, single epileptic patients are associated with AEDs non-adherence. No association was observed between non-adherence and employment status; level of education; AEDs polytherapy; and AEDs insurance coverage (Table 2). Co-morbid depression was significantly associated with AEDs non-adherence (p=0.009). In the present survey, near-significant association was observed between AEDs non-adherence and having seizure in the past two years (p=0.05). Higher proportion of AEDs non-adherence was observed among epileptic patients who started AEDs immediately/ or after 1 year, compared to those patients who started AEDs late after epilepsy diagnosis (p=0.08) (Table 2).

Logistic regression analysis of AEDs non-adherence and covariates

In the present study, in multivariate logistic analysis, age of the study participants (AOR 0.94, 95% CI 0.89-0.98, p=0.006); age at first seizure (AOR 1.07, 95% CI 1.03-1.12, p=0.001); and comorbid depression (AOR 1.80, 95% CI 1.01-0.32, p=0.04) were found to be an independent predictors of AEDs non-adherence when adjusted for the covariates. In univariate logistic regression analysis, being single was associated with AEDs non-adherence (COR 2.05, 95% CI 1.20-3.51, p=0.009); however, when adjusted for age, age at first seizure, and comorbid depression, near-significant association was observed (p=0.07) (Table 3).

DISCUSSION AND CONCLUSION

Patients with epilepsy have increased mortality and morbidity compared to general population (10–12). Non-adherence to AEDs considered one of the reasons for such detrimental effect of epilepsy (13,14). The present study found out that 46.7% of patients were non-adherent to their AEDs. Globally the rate of non-adherence range between 30 and 50 % (15–17). The present study is consistent with cross sectional study conducted in Nigeria were the rate of non-adherence was 44.5 % (16), but higher than other studies (10,11,18). The discrepancy in the rate of non-adherence with other study is due to different methods in assessing adherence and sample size. This result highlighted the need to address the poor antiepileptic drug adherence observed among people living with epilepsy in Ethiopia.

In the present study, higher proportion of non-adherence was observed in younger, single, and those study participants who reported stigma. Many of the studies including local regarding factors associated with poor treatment adherence found longer treatment duration, forgetfulness, complex therapy, cost of the drug and comorbid illness (14–17,19). In this study comorbid depression found to be predictor of poor adherence which is consistent with one study in china (12). In the present study, factors such as; being single and feeling of stigma because of their diagnosis was associated with higher proportion of AEDs non-adherence. These is consistent with previously reported studies; which identified the following factors influencing adherence including: specific beliefs about medications, being depressed or anxious, poor medication self-administration management, being married, uncontrolled recent seizures, frequent medication dosage times, being female, and financial or cost of drugs (5,6,20,21). Therefore, it's important to tackle these factors in epileptic patients to improve their AEDs adherence.

In the present observation, younger study participants, having seizure in a younger age, and experiencing seizure in the past two years were associated with antiepileptic drugs non-adherence. These results are consistent with previously reported studies (4,6,20–23). This highlighted on the need to focus on the younger epileptic patients to improve their adherence and frequently assessing their antiepileptic medications schedules; this way we may able to detect those having poor adherence and able to intervene earlier.

Through logistic regression, age at first seizure, being single and comorbid depression showed association with poor adherence. Previous studies also showed consistent findings with the present study (22–25).This finding necessitate screening of patient regularly for comorbid depression and giving emphasis regarding

treatment adherence among younger age groups. In the present study, comorbid depression was observed in nearly half of the study participants. This is consistent with previously reported studies which shown that the prevalence of depression is higher in those with epilepsy as compared to matched healthy controls (26–28). Depression is the most common comorbid psychiatric disorder in patients with epilepsy, yet it remains under- recognized and under-treated and reported by nearly 43% (26–28). This result further supports the need to include routine screening of depression among epileptic patients in Ethiopia; in order to identify, diagnose, and treat early. The limitations of this study include: small sample size and lack of healthy control groups. In summary, the present study showed high prevalence of antiepileptic medication non-adherence among epileptic patients in Addis Ababa, Ethiopia. Furthermore, participants age, age at first seizure, and comorbid depression were found to be independent predictors of AEDs non-adherence. We recommend conducting a future prospective control study in order to consolidate the present results.

Declarations:

Consent to publish: Participants consent for publication is not applicable.

Availability of data and materials: All data sets on which the conclusions of the manuscript rely are available as spread excel sheets documents and available from the corresponding author on reasonable request from the journal.

Competing interests: The authors declare they have no competing financial interests.

Table 1: Baseline characteristics of study participants (n=250)

Characteristics	Values
Age in years (mean, 1SD)	29.4 (11.5)
Age of first seizure in years (median, IQR) n=206	16 (11 – 25)
Living in the urban area (n, %)	230 (92)
Male (n, %)	135 (54)
Marital status (n, %)	
Single	164 (65.6)
Married	86 (34.4)
Educational status (n, %)	
No education/ or read and write only	87 (34.8)
Primary education and above	163 (65.2)
Employment status (n, %)	
Unemployed	137 (54.8)
Employed	90 (36)
Others	23 (9.2)
Seizure in the past two years (n, %)	168 (67.2)
AEDs initiation after diagnosis (n, %)	
Immediately/ or after 1 year	215 (86)
After 2 years and above	35 (14)
Antiepileptic drugs (n, %)	
Monotherapy	139 (55.6)
Poly therapy	11 (44.4)
AEDs insurance coverage (n, %)	
Insurance based	101 (40.4)
Non-insurance	149 (59.6)
AEDs adherence (n, %)	
Non-adherent	119 (47.6)
Adherent	131 (52.4)
No-depression (n, %)	137 (54.8)
Depression (n, %)	113 (45.2)

Table 2: Risk factors of AEDs non-adherence in the study participants (n=250)

Characteristics	AEDs non-adherent (n=119, 47.6%)	AEDs adherent (n=131, 52.4%)	X^2 p value
Male (n, %)	65 (26)	70 (28)	0.85
Female (n, %)	54 (21.6)	61 (24.4)	
Marital status (n, %)			
Single	88 (35.2)	76 (30.4)	0.008
Married	31 (12.6)	55 (22)	
No education/ or read and write only	36 (14.4)	51 (20.4)	0.15
Primary education and above	83 (33.2)	80 (32)	
Employment status (n, %)			
Unemployed	67 (26.8)	70 (54.8)	
Employed	40 (16)	50 (20)	0.72
Others	12 (4/8)	11 (4.4)	
Seizure in the past two years			
Yes	87 (34.8)	81 (37.4)	0.05
No	32 (39)	50 (20)	
AEDs initiation after diagnosis			
Immediately/ or after 1 year	107 (42.8)	108 (43.2)	0.08
After 2 years and above	12 (4.8)	23 (9.2)	
Antiepileptic drugs (n, %)			
Monotherapy	67 (26.8)	72 (28.8)	0.83
Poly therapy	52 (20.8)	59 (23.6)	
AEDs insurance coverage (n, %)			
Insurance based	52 (20.8)	49 (19.6)	0.31
Non-insurance	67 (26.8)	82 (32.8)	
No-depression	55 (22.0)	82 (32.8)	0.009
Depression	64 (25.6)	49 (19.6)	

Table 3: Logistics regression analysis of AEDs non-adherence and covariates

Covariates	COR	95% CI	p value	AOR	95% CI	p value
Age in years	0.98	0.96-1.00	0.05	0.94	0.89-0.98	0.006
Age at first seizure in years	1.01	0.98-1.02	0.86	1.07	1.03-1.12	0.001
Comorbid depression						
No-depression	Ref.					
Depression	1.95	1.17-3.22	0.01	1.80	1.01-3.23	0.04
Marital status						
Married	Ref.					
Single	2.05	1.20-3.51	0.009	1.98	0.94-4.19	0.07

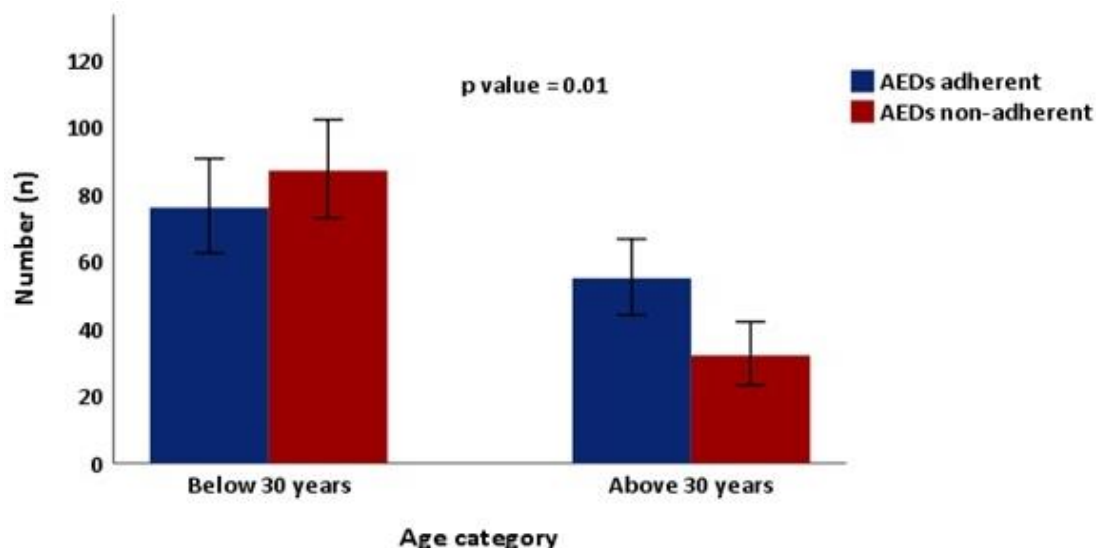COR: Crude odds ratio; AOR: Adjusted odds ratio; CI: Confidence interval; Ref.: Reference

Figure 1: Bar graph showing association between those below age 30 years and antiepileptic drugs (AEDs) non-adherence.
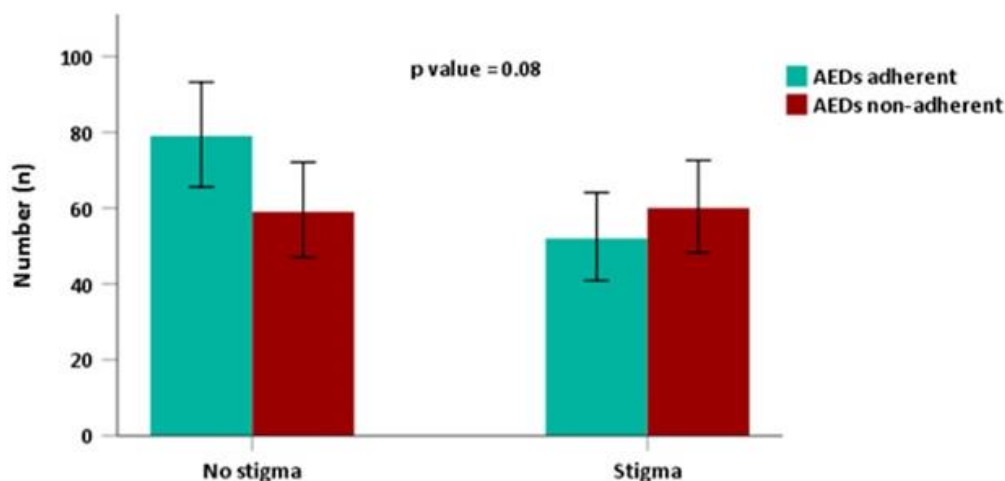

Figure 2: Bar graph showing a near-significant association between stigma and antiepileptic drugs (AEDs) non-adherent study participants

REFERENCES

1. AHMED I, ABERA TESEMA A, DEMEKE T. Medication Adherence and Associated Factors Among Patients with Epilepsy at Follow Up Clinics of Jimma Town Public Hospitals, Jimma, South West, Ethiopia, 2019. J Pharmacol Clin Res. 2020;8(1):34-44.
2. BUCK D, JACOBY A, BAKER GA, CHADWICK DW. Factors influencing compliance with antiepileptic drug regimes. Seizure. 1997;6(2):87–93.
3. CHOWDHURY S, PHANI AK, DAS P, AHAMMED Z, KAYASTHAGIR PK, MD HASSANUZZAMAN. Adherence to Antiepileptic Drugs and Seizure Control Among Patients with Epilepsy. Chattagram Maa-O-Shishu Hosp Med Coll J. 2020;19(1):68–73.
4. CHAKA A, AWOKE T, YOHANNIS Z, AYANO G, TAREKE M, ABATE A, NEGA M. Determinants of depression among people with epilepsy in Central Ethiopia. Ann Gen Psychiatry. 2018 Jun 13;17:27. doi: 10.1186/s12991-018-0197-z.
5. DE OLIVEIRA-FILHO AD, MORISKY DE, NEVES SJF, COSTA FA, DE LYRA DP. The 8-item Morisky

Medication Adherence Scale: Validation of a Brazilian-Portuguese version in hypertensive adults. Res Soc Adm Pharm. 2014;10(3):554–61.

6. DEVI DT, SHANTHI S, RAMYA EJ. Adherence to antiepileptic drugs for epileptic patients attending neurology outpatient department in tertiary care center-A prospective observational study. Natl JPhysiol Pharm Pharmacol. 2021;11(4):360-6.

7. DESSIE G, MULUGETA H, LESHARGIE CT, WAGNEW F, BURROWES S. Depression among epileptic patients and its association with drug therapy in sub-Saharan Africa: A systematic review and meta-analysis. PLoS One. 2019;14(3):1–16.

8. DIOP AG, DE BOER HM, MANDLHATE C, PRILIPKO L, MEINARDI H. The global campaign against epilepsy in Africa. Acta Trop. 2003;87(1):149–59.

9. DIOP AG, HESDORFFER DC, LOGROSCINO G, HAUSER WA, Epilepsy and mortality in Africa: A review of the literature. Epilepsia. 2005;46:33–5.

10. EJELIOGU EU & COURAGE A. Prevalence and factors associated with non-adherence to antiepileptic drugs among children with epilepsy in Jos, Nigeria. Niger J Paediatr. 2020 Aug 6;47(3):240-5.

11. ETTINGER AB, GOOD MB, MANJUNATH R, EDWARD FAUGHT R, BANCROFT T. The relationship of depression to antiepileptic drug adherence and quality of life in epilepsy. Epilepsy Behav. 2014;36:138–43.

12. FADARE JO, SUNMONU TA, BANKOLE IA, ADEKEYE KA, ABUBAKAR SA. Medication adherence and adverse effect profile of antiepileptic drugs in Nigerian patients with epilepsy. Neurodegener Dis Manag. 2018;8(1):25–36.

13. 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.

14. FULLER-THOMSON E, BRENNENSTUHL S. The association between depression and epilepsy in a nationally representative sample. Epilepsia. 2009;50(5):1051–8.

15. GOVIL N, CHAHAL S, GUPTA N, KALOTI AS, NADDA A, SINGH P. Factors Associated with Poor Antiepileptic Drugs Adherence in below Poverty Line Persons with Epilepsy: A Cross-Sectional Study. J Neurosci Rural Pract. 2021;12(1):95–101.

16. GUO Y, DING XY, LU RY, SHEN CH, DING Y, WANG S, TANG YL, DING MP. Depression and anxiety are associated with reduced antiepileptic drug adherence in Chinese patients. Epilepsy Behav. 2015;50:91-5. doi: 10.1016/j.yebeh.2015.06.042.

17. GARNETT WR. Antiepileptic drug treatment: Outcomes and adherence. Pharmacotherapy. 2000;20.

18. HASISO TY, DESSE TA. Adherence to treatment and factors affecting adherence of epileptic patients at Yirgalem General Hospital, Southern Ethiopia: A prospective cross-sectional study. PLoS One. 2016;11(9):1–12.

19. IBINDA F, ODERMATT P, KARIUKI SM, KAKOOZA-MWESIGE A, WAGNER RG, OWUSU-AGYEI S, ET AL. Magnitude and factors associated with nonadherence to antiepileptic drug treatment in Africa: A cross-sectional multisite study. Epilepsia Open. 2017;2(2):226–35.

20. KANNER AM. Depression and Epilepsy : A New Disorders. Epilepsy Curr. 2006;6(7):141–6.

21. 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. Lancet Neurol. 2012;11(8):688–96.

22. O' ROURKE G, O' BRIEN JJ. Identifying the barriers to antiepileptic drug adherence among adults with epilepsy. Seizure. 2017;45:160–8.

23. SEBERA F, VISSOCI JRN, UMWIRINGIRWA J, TEUWEN DE, BOON PE, DEDEKEN P. Validity, reliability and cut-offs of the patient health questionnaire-9 as a screening tool for depression among patients living with epilepsy in Rwanda. PLoS One. 2020;15(6):1–16.

24. SHEGAW M. 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. Int J Biosci Med. 2017;1:2. DOI: 10.28933/ijbm-2017-07-1401

25. SURENDRAN AK, PUNNOOSE MP. A Cross-sectional study on comorbid depression among epileptic adults: experience from a tertiary hospital in Southern India. IP Indian J Neurosci. 2020;6(4):257–62.

26. SEDA T. Antiepileptic Drug Adherence and Associated Factors Among Adult Epileptic Patients Attending Neurology Referral Clinic in Adama Hospital Medical College, Ethiopia. 2019;3(4):93–9.

27. TEKLE-HAIMANOT R, FORSGREN L, EKSTEDT J. Incidence of epilepsy in rural central Ethiopia. Epilepsia. 1997;38(5):541–6.

28. WEATHERBURN CJ, HEATH CA, MERCER SW, GUTHRIE B. Physical and mental health comorbidities of epilepsy: Population-based cross-sectional analysis of 1.5 million people in Scotland. Seizure. 2017;45:125–31.